WHAT IS LIFE?

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NEURAL PLASTICITY
For good and for bad
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THE BRAIN IS PLASTIC

• The blueprint for the central nervous system is laid down by genetics (and epigenetics), but its organization and function is constantly revised ("MICROUS COURSE CORRECTIONS")
ACTIVATION OF NEURAL PLASTICITY

• Can be beneficial
• Can be harmful, cause diseases (PLASTICITY DISORDERS)
• Is necessary for normal development of the central nervous system
WHAT IS NEURAL PLASTICITY?

• Neural plasticity is a property of the nervous system that is only apparent when activated.
• Plastic changes comprises:
  – synaptic efficacy,
  – formation or elimination of synapses, axons and dendrites
  – programmed cell death
• When activated it can:
  – change the function of the brain and spinal cord
  – re-direct the flow of information
WHAT CONTROLS ACTIVATION OF NEURAL PLASTICITY?

- Lack of stimulation of sensory systems
- Stimulation “neurons that fire together wire together” (Hebb, 1949).
- Other environmental factors
- Unknown factors
BENEFICIAL EFFECT OF ACTIVATION OF NEURAL PLASTICITY
ACTIVATION OF NEURAL PLASTICITY AFFECTS THE QUALITY OF LIFE

• Benefit:
  – Recovery from trauma (stroke)
  – Adapt to changing demands

• Harm (Plasticity disorders):
  – Cause pain (central neuropathic pain)
  – Tinnitus (ringing in the ears)
  – Hyperactivity of motor functions (spasticity)
ACTIVATION OF NEURAL PLASTICITY CAN HELP RECOVERY FROM TRAUMA
Make use of redundancy

• Re-route information that has been processed in the damaged parts of the brain to intact parts
• Not all brain functions have redundancy
  – Speech is exclusively left side of the brain
ACTIVATION OF NEURAL PLASTICITY CAN HELP ADAPTING TO CHANGING DEMANDS

- Use of prostheses
  - Cochlear and brainstem implants to treat deafness requires reprogramming of hearing
  - The use of artificial limbs requires reprogramming of motor control
COCHLEAR IMPLANTS

- Bypasses the frequency selectivity in the cochlea
- Bypasses neural transduction in the hair cells and activate auditory nerve fibers directly
- Bypasses two-tone inhibition
- Bypasses the frequency dependent basilar membrane traveling time
GENERAL PRINCIPLE FOR COCHLEAR IMPLANTS

FROM MØLLER, 2006
THE BASIS FOR MODERN COCHLEAR IMPLANTS
THE CHANNEL VOCODER
Developed for analysis-synthesis telephony in 1950’s

- Provides only spectral information
- Extracts the energy in a few (8-14) frequency bands
- Discards fine temporal information
"CHANNEL VOCODER"
COCHLEAR IMPLANT PROCESSOR
ADDING MORE CHANNELS WAS A MAJOR IMPROVEMENT IN SPEECH DISCRIMINATION

How many channels are needed for good speech discrimination?
From Møller, 2006 after Dorman 2000
The principles of the channel vocoder is similar to that of trichromatic color vision. Only three filters channels provide information about all nuances of color.
Place coding alone is sufficient for speech discrimination

Temporal coding alone is sufficient for speech discrimination

The normal auditory system has considerable redundancy
NEURAL PLASTICITY IS NECESSARY FOR THE USE OF COCHLEAR IMPLANTS

The young brain is more malleable than the adult brain.
The P1 component of auditory evoked potentials is an objective measure of adaptation to cochlear implants, thus a sign of the plastic changes.

TIME OF IMPLANTATION IS IMPORTANT

From Sharma and Dorman 2006
ACTIVATION OF NEURAL PLASTICITY CAN CAUSE HARM

“PLASTICITY DISORDERS”

- Pain (central neural neuropathic pain)
- Severe chronic tinnitus
- Spasm
- Spasticity
- Synkinesis
ACTIVATION OF NEURAL PLASTICITY INVOLVES A CASCADE OF STRUCTURES

THIS IS SIMILAR TO OTHER DISORDERS SUCH AS DIABETES TYPE 2
Normal Neuropathic PAIN

Nociceptive

Pathophysiologic

Inflammation

Normal

Neuropathic
ACUTE PAIN

SPINOThALAMIC TRACT

CENTRAL PAIN PATHWAYS PROJECT TO PRIMARY CORTICES WITH SPATIAL INFORMATION ("WHERE")

OBJECTIVE INFORMATION ("WHAT") PROJECTS TO MANY DIFFERENT PARTS OF THE CNS (FOR EXAMPLE THE LIMBIC SYSTEM)

From: Møller: Sensory Systems, 2003
THERE ARE DIFFERENT TYPES OF PAIN

**Pain**

- **Stimulation of nociceptors**
  - **Somatic pain**
    - Fast pain
    - Slow pain
  - **Visceral pain**
  - **Referred pain**
  - **Muscle pain**

- **Non-nociceptor pain**
  - **Inflammatory**
  - Lesions to nerves or CNS
  - **Neuropathic pain**
  - Central neuropathic pain

*From: Møller: Neural Plasticity and Disorders of the Nervous System, 2006*
SOMATIC PAIN
From stimulation of pain receptors
CENTRAL NEUROPATHIC PAIN

Pain that is caused by abnormal neural activity in the brain caused by activation of neural plasticity
THE DORSAL HORN OF THE SPINAL CORD IN A PATHOLOGIC MODE

Redirect somatosensory information to pain circuits causing **alldynia** (light touch cause painful sensation)
TINNITUS

Sensation of sound in the absence of any physical sound
TINNITUS IS ASSOCIATED WITH RE-ROUTING OF INFORMATION

- Involves non-classical sensory pathways
From: Møller: Sensory Systems, 2003

RE-ROUTING OF INFORMATION

Classical auditory pathways

Non-classical pathways

From: Møller: Sensory Systems, 2003
Connections between the classical and the non-classical auditory systems and the amygdala involve both the “high route” and the “low route”
EXPOSURE TO LOUD NOISE AND HEARING LOSS CAN CAUSE TINNITUS

Tinnitus is associated with changes in non-auditory parts of the brain
Hippocampus: Normal stable place cells

After Goble et al. 2007
Place-cells are affected after noise exposure

After Goble et al 2007
DEPRIVATION OF INPUT CAN GIVE SYMPTOMS OF PLASTICITY DISORDERS

- Hyperactivity (tinnitus)
- Pain
BALANCE DISORDERS
An example of re-routing of information

- Awareness of head movement
- Vertigo
  - benign paroxysmal positional nystagmus
  - disabling positional vertigo
SPASM

Involuntary muscle contractions, often associated with synkinesis (simultaneous contractions of different muscles)
IRRITATION OF THE FACIAL NERVE ROOT AND HEMIFACIAL SPASM

IRRITATION OF CNVII ROOT & UNKNOWN FACTOR ➔ FAULTY PROGRAM ➔ CHANGE IN FUNCTION OF FACIAL MOTONUCLEUS ➔ SPASM AND SYNKINESIS
CONCLUSION

• Activation of neural plasticity can make information reach other parts of the CNS than normally receive such information
• This may occur by unmasking of dormant synapses or creation of new structures
• This explains why plasticity disorders can be associated with many different kinds of symptoms and sign
NORMAL DEVELOPMENT OF AN INDIVIDUAL ORGANISM DEPENDS ON:

• Genetics (and epigenetics)
• Environmental factors
• Unknown factors
ACTIVATION OF NEURAL PLASTICITY IS NECESSARY FOR NORMAL CHILDHOOD DEVELOPMENT

- Postnatal plastic changes involve a cascade of events in a series of structures
- The events are controlled by a program that most likely is created prenatal
NORMAL CHILDHOOD DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM INVOLVES ACTIVATION OF PLASTICITY

- Apoptosis (programmed cell death)
- Adjustment of synaptic efficacy
- Pruning of axons and dendrites
POSTNATAL DEVELOPMENT

Plastic changes provide “midcourse correction” of the genetically controlled (Darwinian) development of the nervous system
DEVELOPMENTAL DISORDERS

Postnatal development going awry:
For example: *Autism spectrum disorders*
AUTISM

• Problems with social interactions
• Abnormal perception of sensory input
• Symptoms may be associated with abnormal involvement of the amygdala
AUTISM

• SPECULATION:
• Insufficient postnatal pruning and programmed cell death are involved in autism
  – The amygdala and other brain structures in autistic children have a higher packing density of cells than normal
The programs that control childhood development may be faulty but symptoms may come from structures that are normal but receive faulty input.
FACTORS TO CONSIDER WHEN TREATING PLASTICITY DISORDERS

• Abnormal neural activity can be caused by pathology or by receiving abnormal activity
• Neural plasticity is controlled by *programs* that are of genetic and epigenetic in origin and modified by environmental factors
• Neural plasticity may create *bistable* neural circuits
PLASTICITY DISORDERS ARE CHARACTERIZED BY ABNORMAL NEURAL ACTIVITY IN SEVERAL STRUCTURES
WHICH OF THE STRUCTURES THAT HAVE ABNORMAL ACTIVITY SHOULD BE TARGET FOR TREATMENT?

- Pathologic structures: May cure the disorder
- Structures that receive pathologic input: May ameliorate symptoms during treatment
- Bistable structures must be reversed
IN SUMMARY
THE BRAIN IS PLASTIC, BENEFICIAL OR HARMFUL

• Expression of neural plasticity provides “mid-course corrections” of genetic programs
• Adapt to changing demands; re-route information to functioning parts of the CNS
• Cause tinnitus and central neuropathic pain
• Cause systems can operate in different modes, being “bistable”
WHAT IS LIFE?

IT DEPENDS ON THE OBSERVER
(SIX BLIND MEN AND AN ELEPHANT)

LIFE IS DYNAMIC;
FOR GOOD AND FOR BAD

LIFE PROVIDES OPPORTUNITIES
"I DOUBT, THEREFORE I THINK; THEREFORE I AM"

Descartes 1596-1650