Fundamental Nature of Brain Sciences

Our Humanity is Determined by our Brains

• How we think and feel
• How we sense and respond to the world around us
• How we communicate with others
• How we control our movements
• How we learn and remember
The knee-jerk reflex.
Fundamental Nature of Brain Sciences

Health Care Issues - Size of the Problem

• Over 600 brain-related diseases

• Total annual costs, $579 billion in 1998
Cost and Impact of Neurological and Psychiatric Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Patients (in millions)</th>
<th>Cost (in billions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinson’s Disease</td>
<td>0.5</td>
<td>6</td>
</tr>
<tr>
<td>Head Injury</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Alzheimer’s Disease</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>Blindness/Vision loss</td>
<td></td>
<td>38.4</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td>17.5</td>
</tr>
<tr>
<td>Addiction</td>
<td></td>
<td>30.4</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td>30</td>
</tr>
</tbody>
</table>

Total Patients: 160
Total Cost: 100
Parkinson’s Disease
Loss of Dopamine Neurons of the Substantia Nigra
Parkinson’s Disease

- Slowness of Movements
- Rigidity
- Rest Tremor
- Postural Imbalance
Parkinson’s Disease

Excitatory
Inhibitory
Exc/Inhib
GABA
Glu
GABA
GABA
DA
VA/ VL
GABA
GABA
GABA
GABA
GABA
GABA
GABA
Stimulation
Parkinson's Disease
Motor cortex
Premotor cortex
Frontal eye fields
Glu
Glu
D1-
D2?
D2 - D1?
DA
GABA/ ENK
Excitatory
Inhibitory
Exc/Inhib
Brainstem and spinal cord
Neuromodulation Therapies

• Movement Disorders
  – Parkinson’s disease
  – Dystonia
  – Spasticity

• Epilepsy

• Pain Management

• Bowel and Bladder Dysfunction

• Psychiatric Disorders
  – Obsessive-Compulsive Disorder
  – Eating disorders
  – Affective disorders
  – Schizophrenia
Brain-Machine Interface

Play depression deep brain stimulation video here
Play video on stimulation for depression

deep brain stimulation for depression

http://www.youtube.com/watch?v=JOI83Wku_rg&NR=1
Play monkey video here: on Youtube: brain machine interface monkey arm videos

Play human video here:
Hockberg8.mov
Hockberg5.mov


Another set of videos from Nature:
set of explanatory videos human brain machine interface from Nature
http://www.nature.com/nature/focus/brain/video/
α-secretase

APP

APPα

α-secretase

β-secretase

γ-secretase

Aβ peptides

β-sheets

Intermediates

Fibrils

Aggregates

Amyloid Plaque

Cellular Dysfunction

Neurotoxicity

Beneficial Effects

Inflammation?
Alzheimer’s Treatments in Discovery and Development

• Secretase inhibitors
  – Prevent production of amyloid

• Aggregation inhibitors
  – Prevent accumulation/plaques

• Immunotherapy
  – Prevent inflammation
BOX 56.1

CASE HISTORY OF H.M.

This 27-year-old motor winder, a high school graduate, had had minor seizures since the age of 10 and major seizures since the age of 16. Despite heavy and varied anticonvulsant medication, the major attacks had increased in frequency and severity through the years until the patient was quite unable to work. The etiology of this patient's attacks is not clear. He was knocked down by a bicycle at the age of 9 and was unconscious for 5 min afterward, sustaining a laceration of the left supraorbital region. Later radiological studies, however, including two pneumoencephalograms, have been completely normal, and the physical examination has always been negative. Electroencephalographic studies have consistently failed to show any localized epileptogenic area.

On September 1, 1953, bilateral medial temporal-lobe resection was carried out, extending posteriorly for a distance of 8 cm from the midpoints of the tips of the temporal lobes, with the temporal horns constituting the lateral edges of resection.

After operation, the patient was drowsy for a few days, but his subsequent recovery was uneventful apart from the grave memory loss already described. There has been no neurological deficit. An electroencephalogram taken 1 year after operation showed increased spike-and-wave activity, which was maximal over the frontal areas and bilaterally synchronous. He continues to have seizures, but these are less incapacitating than before.

A psychological examination was performed on April 26, 1955. The memory defect was immediately apparent. The patient gave the date as March 1953, and his age as 27. Just before coming into the examining room, he had been talking to Dr. Karl Pribram, yet he had no recollection of this at all and denied that anyone had spoken to him. In conversation, he reverted constantly to boyhood events and seemed scarcely to realize that he had had an operation.

On formal testing, the contrast between his good general intelligence and his defective memory was most striking. On the Wechsler-Bellevue Intelligence Scale, he achieved a full-scale IQ rating of 112, which compares favorably with the preoperative rating of 104, the improvement in arithmetic being particularly striking. An extensive test battery failed to reveal any deficits in perception, abstract thinking, or reasoning ability, and his motivation remained excellent throughout.

On the Wechsler Memory Scale his immediate recall of stories and drawings fell far below the average level and on the “associate learning” subtest of this scale he obtained zero scores for the hard word associations, low scores for the easy associations, and failed to improve with repeated practice. These findings are reflected in the low memory quotient of 67. Moreover, on all tests we found that once he had turned to a new task the nature of the preceding one could no longer be recalled; nor the test recognized if repeated.

In summary, this patient appears to have a complete loss of memory for events subsequent to bilateral medial temporal lobe resection 19 months before, together with a partial retrograde amnesia for the 3 years leading up to his operation, but early memories are seemingly normal and there is no impairment of personality or general intelligence.

Edited from Scoville and Milner.11
Touring 'U' program shows kids the organ of the mind

After the kids had listened to descriptions of the motor cortex, the cerebellum and the temporal lobe, graduate student Peter Maken stepped forward and told the kids they could see what was inside the two hemispheres of the brain "when we slice the brain right down the middle."

"Oooohhhhh!" was the sound that spontaneously came from the 90 fourth-graders sitting at long tables in the room. A few groans followed.

Then, while some of the students started doing eye tests to find the blind spot we all have in our visual field, others started using tennis balls to measure their peripheral vision. Meanwhile, Flanders, Maken, scientist Marco Santello and graduate student Kevin Engel went to the small cardboard boxes at one end of the room and began pulling out the brains. Human brains in their entirety and sliced in half were taken in clear plastic bags to small groups of students and explained in detail. There was a little giggling, then most of the students were transfixed. "Why are there wrinkles?" one student asked. "That's the cortex, that's what makes us different than animals," Maken replied.

"Is this real?" a girl asked as she touched a brain through the plastic bag. "When people die, some donate their brains to science, and that's what these are," said Flanders. "It feels hard because it has been fixed in formaldehyde. A real brain in life would feel like Jell-O, sort of squishy."

Flanders turned the brain. "Here is where information from your nose comes in, and information from the eyes comes in here, at the optic nerves."

Within minutes the kids who had already seen the brains found their blind spot, tested their peripheral vision and moved on to other activities typical of 10-year-olds — being rowdy and having fun.

Tennis balls bounced off the walls, kids used patches intended to cover one eye to cover both eyes, then played monster. Yardsticks were wielded as swords and stickball bats.

"I got the information about the program from the principal, and it sounded good," Pearson said as a tennis ball bounced by. "And they (the university) offered it to us and it was free. Do you know how hard it is to get free programs in here?"

Within a few minutes the brains were back in their boxes and the teachers had the children back under control.

Pearson was asked if she thought that there are any future scientists in the room. "This could spark something in one of them," she said. "You never know."
Side Effects:
Feeling dizzy. Rise slowly several minutes from sitting or lying positions. Be careful driving or operating machinery.
Scientists’ Little Helpers

Methylphenidate (Ritalin and Adderall)

Modafinil (Provigil)

Beta Blockers (propanolol)
Drawing of human brain
Structures found in the fresco are indicated with a heavy line

- Sulcus
- Pituitary
- Pons
- Spinal cord