DEMENTIA CASES

Problem #1

Phineas Gage is a hard-working, diligent, reliable, responsible, Intelligent. good-humored, deeply religious, family-oriented man until he is involved in an accident at which time an explosion occurs and a crowbar is driven into his brain. It transacts the orbit and pierces the frontal lobes. Amazingly, he has only a brief loss of consciousness and although he is rendered blind due to optic nerve damage, he has no other motor, sensory, language, or memory impairment.

Over the course of time, several subtle and unfortunate changes in personality and behavior are noted. These include:

- 1. He becomes unreliable and fails to come to work and when present he is "lazy."
- 2. He has no interest in going to church, constantly drinks alcohol, gambles, and "whores about."
- 3. He is accused of sexually molesting young children.
- 4. He ignores his wife and children and falfls to meet his financial and family obligations.
- 5. He becomes "lazy" and fails to complete any task at work or at home. He has lost his sense of humor.
- 6. He curses constantly and does so in inappropriate circumstances.

Questions

- 1. What portion of the brain ig most likely affected?
- 2. What is the function of this region?
- 3. Why are there no other cortical disturbances detected?

Answers

This case represents a classic example of frontal lobe injury. Located on the medial and undersurfaceof the frontal lobes is the limbic system. Dysfunction to the frontal lobe may result in profound behavioral abnormalities. In patients with "functional" psychiatric disorders (depression, anxiety, schizophrenia), metabolic abnormalities have been detected in the frontal lobes-"lobectomy" was performed in patients with severe mental illness. (A relic of one of the early neurosurgical instruments is on display in the pharmacy museum in the French Quarter. Modern neurosurgery is more advanced. Somewhat.)

2. In addition to the personality and behavioral features, the frontal lobes play a role in these mental tasks:

- sustaining attention
- shifting attention
- initiating mental and motor activity
- inhibiting socially unaccepatable behavior (words or actions)

3. Because the injury spared the language, memory, motor, sensory, and visual cortex regions, there are no other neurological impairments. It is truly amazing the Phineas Gage survived his injury and that there were no other neurological impairments except that "Phineas Gage was no longer Phineas Gage."

Problem #2.

HM was a young man who developed epilepsy during his adolescence. He had multiple and recurrent seizures which persisted despite treatment with appropriate anti-epileptic medications. Because medical therapy "failed," a neurosurgeon proposed surgery consisting of bilateral temporal lobe resection to include the hippocampus. This was done because EEG showed abnormal electrical discharges arising from the temporal cortex. The operation was deemed a success but immediately the family knew that something,as not right with HM. He became alert, attentive, and cooperative. He could converse with people but if they left the room and returned several minutes later, HM had no recollection of the prior conversation. His ablilty to form new memories had disappeared. HM's memory from a few minutes from the present was a blank. Despite the fact that HM could consolidate no new memories and became totally dependent upon others, he remained calm and without depression or anger.

- What happened to HM?
- What structures are damaged?

Answers

- The temporal lobes are essential to memory. The ablation of both temporal lobes including the hippocampus explains the memory impairment (amnesia). HM can perceive, encode, decode, and recognize objects and their meaning but he cannot hold any thoughts or memories for storage and then retrieve it. His cognitive (inteciectual) functions which are not dependent upon memory remain intact.

- Patients who have injury to one temporal lobe and have an intact contralateral temporal lobe do not suffer this type of memory impairment. Unilateral temporal resection is an accepted treatment for medically refractory seizures, but only after neuropsychological assessment indicates that the non-resected temporal lobe can store and retrive memories. The hippocampus is the critical element in the memory system. Remember the the "left" brain has function for language and logicial thinking, whereas the "right" brain functions for spatial, visual, and artistic thinking. Despite ths split in fuction, both temporal lobe systems are necessary for an intact memory system. If the temporal lobes are damaged by trauma, tumor, infection, or alcoholism, the memory sytem may be devastated. We have different memory systems including olfactory, gustatory, visual and verbal types. The type of memory impairment may be dependent upon where the most pronounced temporal lobe injury has occured. Because the frontal lobes and their connections were not injured, behavior and personality were not altered. Because of the case of HM, we now know to avoid bilateral resection.

Clinical Problem #3

52 year-old man is noted to have memory difficulties. He forgets to pay several bills and forgets several business appointments. His wife reports that he appears depressed and is not his usually jovial self. He acts strangely and inappropriately, having an affair with a 15 year-old high school sophomore. Neurological examination shows the following abnormalities.

- Disorientation for year, month and day.
- Inability to remember 3 unrelated objects at 5 minutes.
- Inability to accurately draw geometric shapes.
- Concrete thought processes and inability to think abstractly.

CT, MRI show no evidence of brain atrophy; SPECT shows reduced perfusion in frontal, temporal and parietal regions bilaterally.

Questions

- What is the clinical diagnosis?
- Why are CT/MRI normal?
- What is the significance of abnormal SPECT?
- Would increasing cerebral blood flow improve cognitive function?
- Is there any medication that might enhance memory capability?

Responses

- Dementia, most likely of the pre-senile Alzheimer type. In the early stages of this disorder, there may be clinical evidence of cognitive or intellectual deterioration; however, CT and MRI may not yet show evidence of brain atrophy (shrinkage) . In the later stages, there should be anatomical evidence of brain atrophy and pathological studies would show loss of neurons. There are other pathological changes e.g. neurofibrillary tangles, amyloid deposits, in Alzheimer disease.

- SPECT shows physiological evidence of reduced perfusion and resumed reduced metabolism. This is more sensitive test than CT/MRI.

- Although there is reduced brain perfusion, techniques to increase cerebral blood flow will not enhance brain function. The reduced brain perfusion is a manifestation of primary neural depression; therefore as there is reduced brain mass, there is need for reduced blood flow.

- In Alzheimer dementia, there is a central cholinomimetic disorder. Drugs that enhance acetylcholine function are effective in enhancing memory.

CLINICAL PROBLEM #4

Joh is a highly successful merger-acquisition attorney. He is married and has two teenage girls who want to attend Brown University (although Tulane University is a close second). Immediately after his 50th birthday, John announces he plans to give up his partnership in his law firm and investigate the Lincoln assassination, which he believes is a communist conspiracy. He spends all family savings and goes bankrupt. When he is found in the streets of Old Metairie naked one evening, he is brought to a psychatry hospital. He is psychotic, delusional, very fidgety, and cannot sit still.

Questions.

- What are potential explanatioins?
- What neurotransmitter may be involved?
- What is potential risk for his daughters?
- Can John be treated?

Responses

- John could have schizophrenia, drug indueces psychoses, or Parkinson's disease. There are many other possible biochemical disorders which are less likely but I will focus on these

conditions. Schizophrenia rarely develops in midlife and has much earlier onset. Perform drug screen, as cocaine could casue the clinical features described.

- Assume drug screen is negative and that John's family has a "dark secret." John's grandfather died in a psychatric hospital of an unspecified "mental illness." Consider Huntington's disease, which causes psychoses and involuntary chorea (fidgety motor activity). Examine patient for evidence of chorea, which is present. CT or MRI may show caudate atrophy and even if normal, PET shows reduced caudate metabolism. There is is reduced stiatal GABA levels awith decrease in glutamate decarboxylase in striatum.

- Due to family history and the fact that their father has Huntington's disease, the girls are "at risk." This disorder is an autosomal dominant. By chromosomal analysis, we can determine if there is expanded trinuceotide (CAG) on chromosome 4. Both Brown and their HMO want these tests done before their applications are considered. The psychoses and chorea can be treated with dopamine blocking agents, such as phenothiazines; however, this does not affect the pathogenetic mechanism of this disorder. The thoeyry of enhanced excitatory neurotoxins and reduced inhibitory neurotransmitter (GABA) may only be partly correct. The disorder progresses and patients become demented and wasted presumably to continuous muscle jerks (chorea)

Clinical Problem #5

50 year-old CEO develops abdominal pain and is found to have tender abdomen-on examination. Liver function studies are markedly abnormal and serum amylase is markedly elevated. Abdominal CT shows a mass. At surgery, he is found to have pancreatic pseudocyst. In the surgical recovery room, he awakens and is delirious and tremulous. He is treated with CNS tranquilizers and this calms him. Two days later, he awakens but his recent memory is quite poor but remote memory is intact. He can not remember any of three unrelated objects at 5 minutes.

Questions

- What caused the memory impairment?
- What area of the brain would most likely show pathological change?
- What treatment should be initiated?

Responses

- Based upon the clinical features, this patient most likely has alcohol-induced damage even though no statement is made to suggest "chronic alcoholism". Initially, he is "delirious" and "tremulous" and this suggest major alcoholic withdrawal syndrome which occurs after abrupt cessation of alcohol. As the patient awakens and shows poor recent memory, this is consistent with Wernicke-Korsakoff syndrome.

- Pathological changes include necrotic and hemorrhagic microscopic lesions involving mammillary bodies, periaqueductal midbrain, paraventricular thalamus and hypothalamus.

- This disorder results from specific deficiency of vitamin B-one (thiamine). This in an essential cofactor for decarboxylation of pyruvate and alpha-ketoglutarate. Replacement therapy with thiamine should cause improvement in memory function. Perhaps we could prevent this disorder by supplementing alcoholic beverages with thiamine; however, that would save millions of dollars but markedly adversely impact the taste of alcoholic beverages. (There is

considerable debate about whether alcholic beverages should taste great, or merely be less filling.)

Case #6

50 year-old chronic alcoholic CEO of large managed Care Company develops midepigastric pain especially following alcohol ingestion. (No, the Housestaff Association did not poison his drink.) Two days after he stops drinking he experiences generalized single seizure. After he regains consciousness he is agitated and confused. He is hospitalized and he receives intravenous fluids (dextrose and saline) and phenytoin. Two hours later he becomes increasingly agitated diaphoretic and tachycardia. He reports bugs are crawling on him and there are fish swimming in the IV solution. For the agitation he is treated with Librium. 24 hours later he is calm and more alert; however, he can not remember the date or where he is presently located. When he gets out of bed, he is incoordinated. Exam shows recent memory impairment, gait ataxia, horizontal and vertical nystagmus, absent ankle jerks, reduced vibration and proprioception in the feet.

Questions

- What are the potential causes of the seizure?
- What are the potential causes of the hallucinations and agitated mental state?
- What are the potential causes of gait impairment and memory disturbance?