Transient Global Amnesia

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Amnestic Disorders

- Differs from delirium and dementia because major problem is short-term memory only.
- Impairment may be due to hemorrhage in mamillary bodies, or degenerative changes in the dorsal medial nucleus of the thalamus
- Most common cause is alcoholism

General Amnesic Syndrome

- Definition

A permanent, stable and global disorder of memory due to organic brain dysfunction which occurs in the absence of any other extensive perceptual or cognitive disturbance.

NB. Permanency
Stability
Pervasiveness
Specificity

Clinical Features of the Amnesic Syndrome

1. Profound difficulty or total inability to acquire new material (anterograde amnesia)
2. Preservation of immediate memory as measured by tasks such as digit span
3. Preservation of semantic memory
4. Preservation of procedural learning
5. Some retrograde amnesia (variable across patients)

Neuopathology

Brain structures implicated:

1. Bilateral damage to the mesial temporal lobes of both the right and left hemispheres

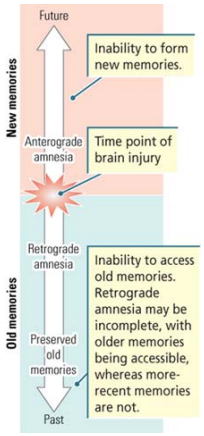
   Within these areas the hippocampus has been seen to represent the crucial structure

2. Structures within the diencephalon and specifically:
   Nuclei within the thalamus
   Mamillary bodies
   Mamillo-thalamic tract
   Fornix

All above structures represent part of the limbic system

Varieties of Amnesia

- Anterograde Amnesia
  - Inability to acquire new memories
  - *Global Anterograde Amnesia*
    - Impairment in the ability to form new memories across a variety of areas
- Retrograde Amnesia
  - Inability to remember old memories



Varieties of Amnesia

- Time-Dependent Retrograde Amnesia
  - Severity of injury determines how far back in time the amnesia extends

Transient global amnesia

- Transient inability to learn new info
- Variable retrograde amnesia that "shrinks" following recovery
- Level of conscousness and personal identity intact
- Due to transient vascular insufficiency of the mesial temporal lobe, or medicines, tumors, arrhythmias, cerebral embolism
- Also have risk problems for stroke

***Panel 1:* Diagnostic criteria for transient global amnesia by Caplan[37] and Hodges[18]**

- Presence of an anterograde amnesia, which is witnessed by an observer
- No clouding of consciousness or loss of personal identity
- Cognitive impairment limited to amnesia
- No focal neurological or epileptic signs
- No recent history of head trauma or seizures
- Resolution of symptoms within 24 h
- Mild vegetative symptoms (headache, nausea, dizziness) might be present during the acute phase

- Lancet Neurology 2010;9:205-14

Epidemiology

- Prevalence: Estimates vary, 2.9 -10 cases per 100,000 population
- Mortality/Morbidity: The mean annual recurrence rate is thought to be low (4-5%). No long-term morbidity or death.
- Race: No consistent racial predilection is known.
- Gender: No sex predilection has been observed. Men: transient global amnesia occurs more often after a physical precipitating event. Women: may be more associated with emotional precipitating events, a history of anxiety, or pathological personality.
- Age: Typically older than 50

Precipitating Events

- Emotional stress
- Physical exertion
- Medical procedures
- Valsalva maneuvers
- Sexual intercourse
- Immersion in cold water
- Chronic headaches/migraines

Panel 2: Considerations in the differential diagnosis of acute amnestic syndromes

- Ischaemia in the posterior cerebral circulation
- Intoxication, adverse drug side-effects
- Complex focal seizures, transient epileptic amnesia, post-ictal conditions
- Psychogenic fugue, dissociative disorders
- Post-traumatic amnesia
- Hypoglycaemia

Panel 4: Practical guide for the bedside diagnostic evaluation of acute transient global amnesia

Signs supportive of diagnosis

- Are there strenuous physical activities or strong emotional events preceding the onset of symptoms?
- Are symptoms limited to loss of memory (eg, three-word test/word list, recall of recent events)?
- Does the patient repetitively ask the same questions?
- Is the patient cooperative, able to follow your requests, and able to correctly name things?

Signs not supportive of diagnosis

- Are there indications of a hypoglycaemia, trauma, seizure, or recent changes in medication?
- Is there evidence of further neurological signs?
- Is the patient agitated, sleepy, or drowsy?
- Can the patient recall details and the temporal course of the acute episode?
- Is there a sole retrograde amnesia?
- Are there repetitive amnestic episodes (>3 per year)?

Anatomy of the Hippocampus

- Granule Cells
  - Stellate cells of the *dentate gyrus*
  - "Sensory" cells
- Pyramidal Cells
  - Cells of *Ammon's horn*
  - "Motor" cells

Early Hippocampal Damage

- Early damage leads to the inability to remember:
  - Familiar surroundings or where objects are located
  - Appointments or events
  - Daily activities
- However, can remember:
  - Factual knowledge
  - How to read, write, and speak

Neural Connections to the Hippocampus

- Damage to the fimbria-fornix pathway
  - Retrograde and anterograde amnesia
- Damage to the temporal stem
  - Contributes to amnesia
- Severing of connections between the posterior neocortex and the temporal lobe
  - May produce amnesia

Damage to the Hippocampus

- Studies of hippocampal patients demonstrate four conclusions:
  - Anterograde deficits are more severe
  - Episodic memories are more affected than semantic memories
  - Autobiographic memory is especially affected
  - Patients cannot time travel to the past or future

Differential Diagnosis

- Brain tumor
- Stroke
- Intracerebral/subarachnoid bleed
- Complex partial seizure
- Migraine
- Toxins/drugs
- Acute coronary syndrome
- Hepatic encephalopathy

Characteristic Features

- **TGA**: sudden onset often precipitated by exercise, immersion in water, emotional stress, etc; dense anterograde amnesia with repetitive questioning, lasts 4 – 10 hours, rarely recurs, etiology unknown
- **TEA:** recurrent, brief (usually < 1 hour) amnesic episodes, often occur upon waking, may be associated with olfactory hallucinations or automatisms, responds to anticonvulsant medication, persistent memory deficits
- **Psychogenic amnesia**: history of 'organic amnesia', psychiatric illness and/or substance abuse, may be triggered by mild head injury or highly emotional event, extensive retrograde amnesia often with loss of personal identity, preserved new learning, duration usually several days at least

Panel 3: Diagnostic criteria of transient epileptic amnesia[41,42]

- History of recurrent witnessed episodes of transient amnesia
- Cognitive functions other than memory judged to be intact during typical episodes by a reliable witness
- Evidence for a diagnosis of epilepsy based on one or more of the following:
  - Epileptiform abnormalities on electroencephalography
  - The concurrent onset of other clinical features of epilepsy (eg, lip-smacking, olfactory hallucinations)
  - Clear response to anticonvulsant therapy

Postconcussion syndrome

- Follows a history of head trauma resulting in cerebral concussion
- LOC, posttraumatic amnesia, less commonly, post-traumatic seizures
- Impairment in attention, concentration, performing simultaneous cognitive tasks, and in learning new information, or recalling information shortly after the injury
- Not a form of dementia

Pathophysiology

- **On PET and DWI**, blood flow to specific brain areas that involve memory appears to be disrupted transiently during TGA. This includes the thalamus and/or mesial temporal structures (in particular the amygdala and hippocampus).
  - Hakan et al demonstrated tiny increases in signal in the left parahippocampal gyrus and splenium of the corpus callosum on DWI in one patient. This method of imaging allows detection of hyperacute ischemic change. Eustache et al reported a PET study consistent with a spreading depression in the left lateral frontal cortex. This case also featured oligemia in the left occipital cortex. Strupp et al found mainly medial temporal changes on DWI in 7 of 10 patients with TGA. They suggested that cellular edema or spreading depression could be responsible, not just ischemia.
- Winbeck et al found a significant incidence (10/28) of acute DWI changes in patients with TGA, which is comparable to the TIA group (21/74). Although the patients who presented with a TIA had a higher prevalence of vascular risk factors, those in the TGA group (who had DWI changes) were found to have significantly more carotid atherosclerosis.
- Nakada et al demonstrated via **high-resolution T2-reversed MRI** a high incidence of hippocampal cavities compared with their normal or disease controls. The authors conclude that their findings may indicate that TGA can be associated with neuronal loss in the CA1 region of the hippocampus.

Pathophysiology

- Generally, the territory of the ***vertebrobasilar system*** is most often rendered ischemic and dysfunctional. Since ischemia typically does not progress to infarction, symptoms are expected to resolve completely.
- Yamane et al reported rather diffuse cerebral hypoperfusion on **SPECT** that improved months later upon repeating the test in a patient with TGA. Yang et al also reported hypoperfusion in the ***cerebellar vermis*** that recovered by the time of follow-up examination.
- Bartsch et al found that in 7 patients with TGA, 4 had a diffusion abnormality corresponding with a **T2 lesion** in the ***CA-1 sector of the hippocampus***. **MRS** revealed a lactate peak. This represents an acute stress reaction of this particular area and indicates the pathological substrate of TGA.

Investigations of a Patient With TGA

Laboratory Studies

- CBC count with differential
- Electrolyte panel
- Screening clotting tests, including prothrombin time (PT), activated partial thromboplastin time (aPTT), INR

When stroke must be ruled out.

Brain MRI and/or CT scan: To rule out a stroke possibility, especially if significant risk factors are present.

MRI with **DWI :** higher resolution DWI imaging increased detection of hippocampal lesions

ECG, EEG

If symptoms have occurred more than once, then at least a routine EEG should be done to help investigate a seizure possibility by demonstrating any interictal activity.

TREATMENT AND MANAGEMENT

Medical Care

- Once transient global amnesia (TGA) is diagnosed, provide reassurance to the patient and schedule at least one follow-up visit with a neurologist

DIET

- No dietary restrictions are necessary.

ACTIVITY

- Avoid activities that could produce an unusual increase in intrathoracic pressure.

- THANK YOU FOR YOUR ATTENTION