Introduction

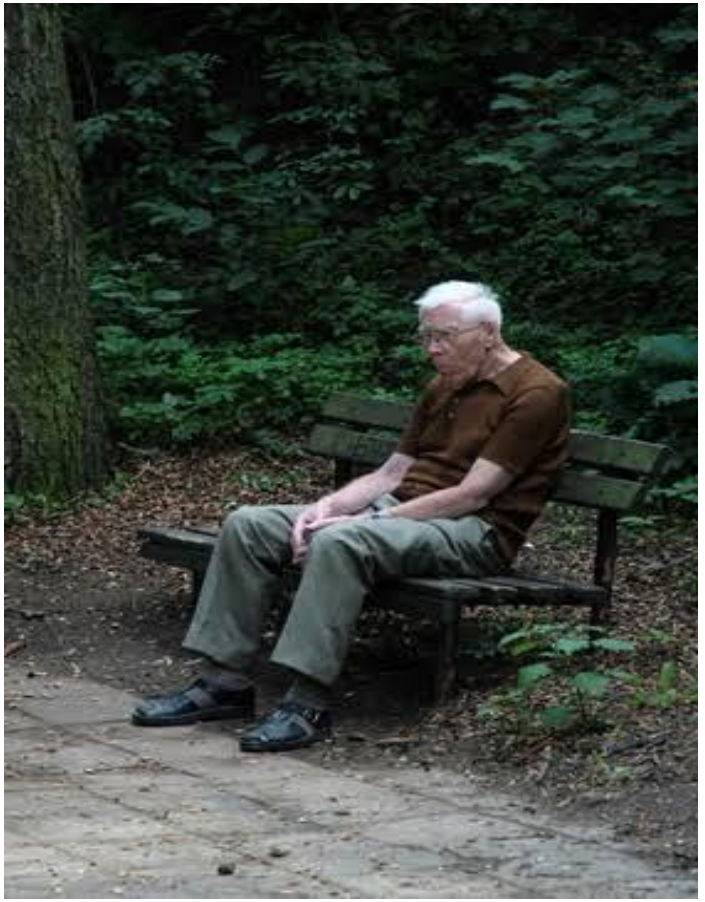
- The most common neuropsychiatric outcomes of stroke are depression, anxiety, fatigue, and apathy, which each occur in at least 30% of patients
- Emotional lability, personality changes, psychosis, and mania are less common but equally distressing symptoms
- The cause of these syndromes is not known, and there is no clear relation to location of brain lesion

Post-stroke Neuropsychiatric problems

- Depression
  - Major
  - Minor
- Mania and Bipolar
- Disorder
- Anxiety Disorders
- Pathological Laughing and Crying (PLC)
- Witzelsucht
- Apathy
- Aggression
- Psychosis

ML Hacket et al. Lancet Neurol 2014; 13: 525–34


"I'm fine."
Feeling
I'm
Nothing
to Everyone



Incidence of PSD

- Approximately 1/3 of people will experience clinically significant depression at some point following a stroke
- 19.3% and 18.5% of stroke survivors had major depression or minor depression, respectively, in acute care rehabilitation settings
- No significant difference in incidence between hemorrhagic and infarct strokes

ML Hacket et al. Stroke 2005; 36: 1330-1340
G Ostir et al. J Am Geriatr Soc. 2011 February ; 59(2): 314–320.

PSD associated with

- Poor functional recovery – may delay recovery by 2 years.
- Poor social outcomes
- Reduced quality of life
- Reduced rehabilitation treatment efficiency
- Increased cognitive impairment
- Increased mortality

ML Hacket et al. Lancet Neurol 2014; 13: 525–34

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A biopsychosocial model of PSD

- Psychosocial factors
  - Pre-stroke history of depression
  - Personality and coping style
  - Inadequate social support
  - Level of disability
- Biological factors
  - Location of stroke – left cortical and subcortical lesions risk is controversial
  - Exact neuroanatomical mechanism is unknown
  - Presumed disruption in amine pathways

Early Predictors of PSD Carota, et al. (2005)

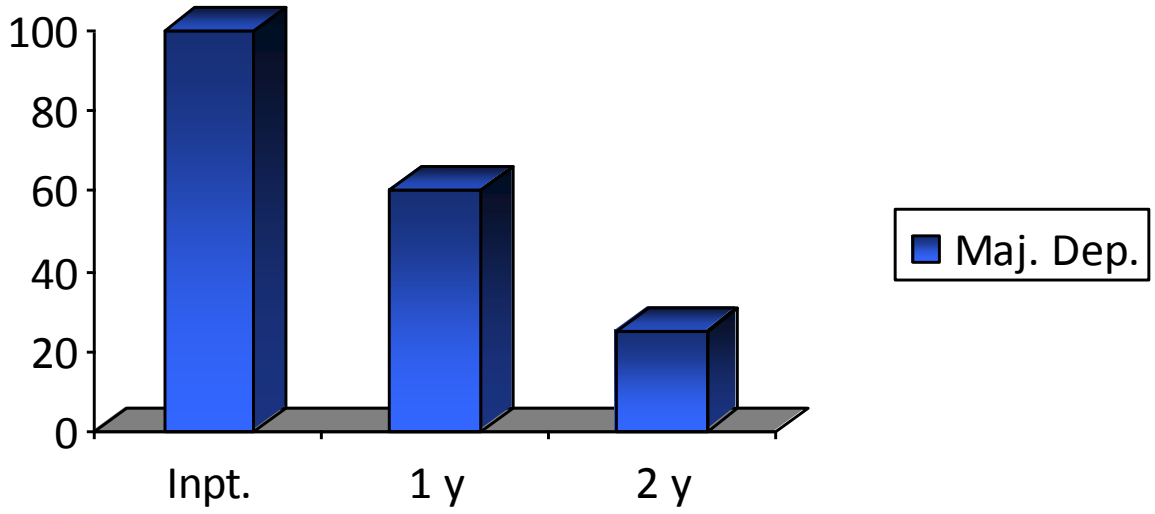
- Low Barthel Index score

  http://www.strokecenter.org/trials/scales/barthel.pdf
- Age <68 years
- Crying in first few days
  - Pathological crying (not associated with PSD)
  - Emotionalism (41% developed PSD)
  - Catastrophic reaction (63% developed PSD)

Major PSD

- Recovery significantly better in major PSD than minor PSD with nearly 75% resolution in symptoms after two years.

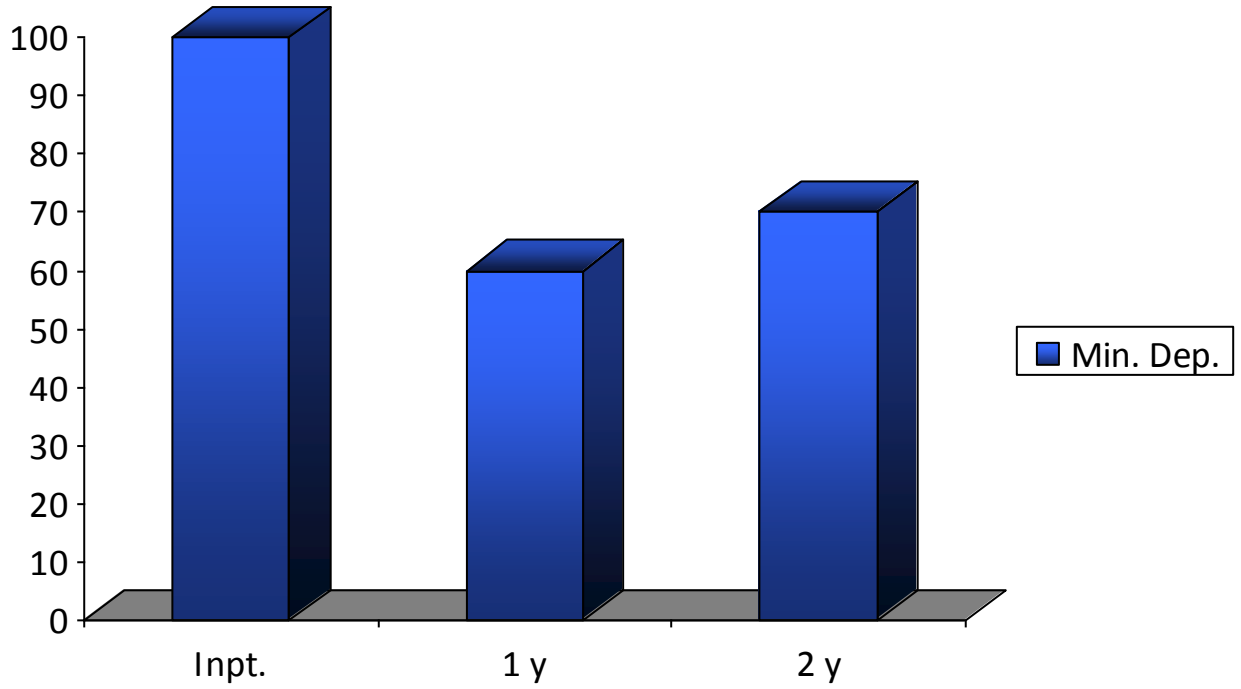
Chemerinski & Robinson, 2000.



Minor PSD

- Prognosis worse in patients with minor depression.

Chemerinski & Robinson, 2000



PSD and mortality

- Patients with either Major or Minor PSD are 3.4 times more likely to die during a 10 year period post-stroke than non-depressed patients.
- Patients with PSD and few social contacts have an even increased mortality rate: 90% died in Morris et al cohort.

American Journal of Psychiatry. 150(1), 124-129.

Diagnosis of PSD

- Difficult to reliably diagnose
- Post-stroke depression under-diagnosed by non-psychiatric physicians in 50-80% of cases.

  Shuebert, et al. 1992
- Widespread belief that depression is simply an understandable psychological reaction or grief response.

Overlapping Neurological impairment presents diagnostic challenges Gaete, et al., 2008

- Cognitive deficits
- Fatigue
- Apathy – motivational disorder found in 23-57% of patients with stroke.
  - Not correlated with depression
  - Depression correlated with memory and executive functioning deficits
- Anosognosia – lack of awareness, denial or underestimate of sensory, cognitive of affective impairment (60% in R-CVA, 24% L-CVA)

DSM-IV Diagnostic criteria for major depression

Five or more of the following present **during two week period** and representing a change in function, **one symptom must be either depressed mood or loss of interest**

- **Depressed mood most of the day for most days.**
- **Marked reduction in interest or pleasure in most activities**
- Significant weight loss or gain, significant increase or decrease in appetite
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness; inappropriate guilt
- Reduced ability to think or concentrate
- Recurrent thoughts of death or suicide

Treatment for Post-stroke Depression

- Tricyclic antidepressants
- SSRI and SNRI Antidepressants
- Psychostimulants
- Counseling and Psychotherapy

Effectiveness of antidepressant treatment of PSD

- Meta-analysis of studies of antidepressant therapy conclude that this treatment modality may be beneficial to patients with PSD

  Chen, Y, et al, 20006

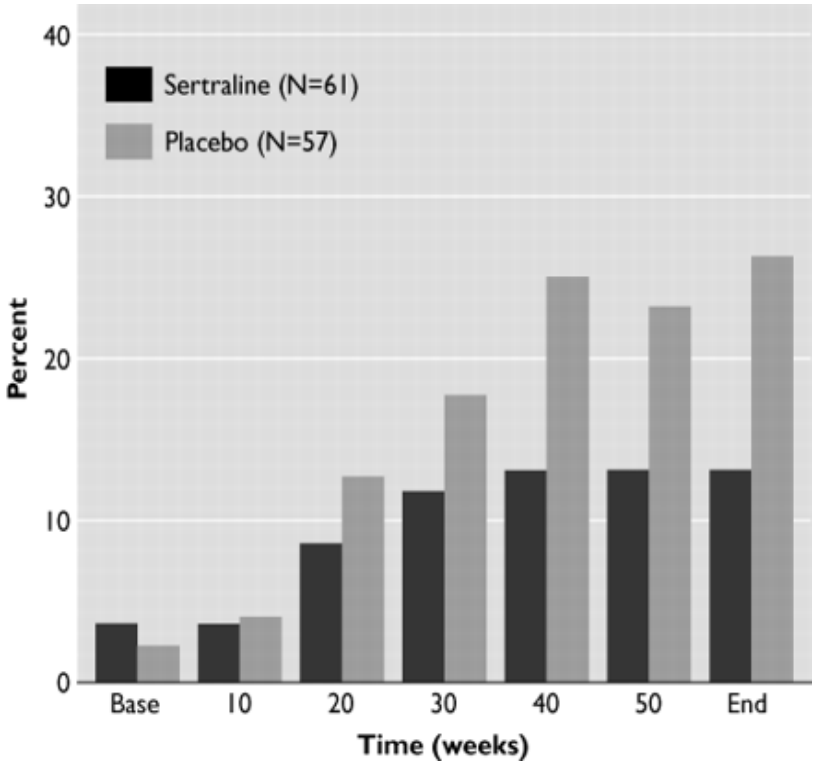
- Tricyclic antidepressants are as effective as newer generation elective serotonin reuptake inhibitors (SSRI) but with greater side effects reported..

Effectiveness of antidepressant treatment of PSD

- SSRIs have been the most widely studied class of antidepressants
- Citalopram (Celexa) is the single most widely studied agent in PSD
- Selective serotonin/norepinephrine reuptake inhibitors such as venlafaxine and duloxetine are also increasingly utilized.

Prophylactic treatment to prevent PSD

- Mirtazapine has shown promise in as acute treatment for prevention of PSD Niedermaier et al., 2005
- Sertraline has shown promise in the prevention of PSD as well as in treatment of PSD symptoms. Poulsen, et al, 2003



Psychostimulant as treatment for PSD

- Limited research regarding use of psychostimulants in PSD
- Increasing clinical use reported, especially in patients with marked vegetative symptoms, apathy, and lethargy
- Masand, et al psychostimulant study results
  - Primary stimulants used were methylphenidate (Ritalin) and Dextroamphetamine
  - 82% of patients improved with 77% showing marked improvement
  - 51% responded in one day, an additional 34% by the second day
  - Only 2% relapse during treatment
  - 15% incidence of side effects
  - No cases of anorexia, appetite improved with mood.

Non-pharmacological Interventions

- **Counseling and psychotherapy** have show little efficacy early in the coarse of PSD
- Psychotherapy more effective as adjustment issues emerge later in post-stroke recovery
- **Early intervention with structured group problem-solving interventions** effective in improving quality of life and functioning in both patients and significant others (SO)
- Psychotherapy with SO shown to significantly improve functional outcomes for patients and may reduce PSD.

Anxiety

- For patients to meet diagnostic criteria for a generalised anxiety disorder, **anxiety symptoms must be present for 6 months**, **plus at least three** of the following:
  - Feeling wound-up,
  - Tense, or restless;
  - Fatigue
  - Difficulty concentrating;
  - Irritability;
  - Substantial muscle tension
  - Difficulty sleeping.

- Results of a systematic review (39 cohorts including 4706 people) indicated that **24% of stroke patients had anxiety symptoms** as assessed by a the Hamilton Depression Rating Scale and **18% had an anxiety disorder in the first 5 years after stroke.**
- Three cohort studies (856 people) reported anxiety ranged from 38% to 76%.
- **Antidepressant drugs alone or with psychotherapy** might reduce anxiety symptoms,

Poststroke Emotional Lability

DSM-5 describes emotional lability in patients as **unstable emotional experiences and frequent mood changes,** with emotions that are easily aroused, intense, or out of proportion to events and circumstances

- Pathological laughing or crying
- Emotional incontinence,
- Involuntary emotional expression disorder, and
- Pseudobulbar affect

- Emotional lability can **coexist with depression**
- Symptoms are **generally mild and transient**, **but if severe, can cause great distress, embarrassment and avoidance of social contact**

Poststroke Emotional Lability Robinson, 1997

- Pathological Laughing and Crying Scale (PLCS) is a valid screen for this phenomenon.
- **Citalopram** found to be effective in reducing symptoms.
- **Usually found in basal ganglia lesions** and may be independent of PSD
- Hackett and colleagues reported that **antidepressant treatment** reduced the frequency and severity of emotional lability.

Hackett ML, Yang M, Anderson CS, Horrocks JA, House A. Pharmaceutical interventions for emotionalism after stroke.2010;

Fatigue after stroke

- **Physiological (or normal) fatigue** is a state of general tiredness that develops acutely after overexertion and improves after rest
- **Pathological fatigue** refers to constant weariness unrelated to previous exertion levels and not usually ameliorated by rest
- Associated with depression, pain, poor sleep and reduced physical activity

Fatigue after stroke treatment

- **Treadmill aerobic training and (CBT)** cognitive–behavioural therapy together is better

- Seek and **treat potentially reversible causes** (eg, anaemia or depression)

www.thelancet.com/neurology **Vol 13 May 2014**

Post stroke Apathy syndrome Robinson, 1997

- Apathy is the **lack of feeling, emotion or interest** in one's surroundings or activities
- ***Disorder of motivation with diminished goal directed behaviour and cognition***
  - Seen in 11% of stroke patients.
  - Often misdiagnosed as PSD.
  - Typically a result of deep posterior subcortical lesion.
  - Responds well to psychostimulants.

- **In 2009, some diagnostic criteria for apathy** were proposed
  - That require **diminished motivation (core feature) for 4 weeks** or more
  - Two other symptoms (**reduced goal-directed behaviour and functional impairments**.
- These criteria largely build on studies of apathy done in people with dementia; whether they are appropriate for stroke is not known.
- Apathy is associated with **worse functional outcome and a higher risk of subsequent depression.**

Mania


AT MY NEXT APPOINTMENT, I TOLD KAREN A BRILLIANT NEW IDEA I HAD FOR GETTING MY WORK DONE DESPITE MY UNMEDICATED MOOD SWINGS.
I'll plan various comics projects to do when I'm depressed!
The manic-me-now will take care of the depressed-me-then!!
I'll write them down & start them now, to finish later!
I have plenty of ideas!
silk pajama top

Mania

- Mania is defined as a prominent and **persistently elevated,expansive, or irritable mood**, accompanied by changes in energy or activity
- Accompanying symptoms are hyperactivity, pressured speech (highly talkative and difficult to interrupt), flight of ideas, grandiosity, decreased sleep, distractibility, or poor judgment
- Prevalence of the disorder is low (≤2%)

Personality disorders

- Mainly disinhibition and irritability
- Most distressing symptoms for carers and family members
- **Irritability** is characterised by impatience, flashes of anger, rapid mood changes, or quarrelling
- **Disinhibition** is characterised by impulsivity, tactlessness or vulgarity.
- Vary from 12% to 53% of patients after stroke
- Post-hoc analysis, antidepressant treatment significantly reduced irritability symptoms

Psychosis and psychotic symptoms

Means severe distortion in thought content

- The most prominent symptoms of psychosis include **delusions and hallucinations**
- Visual hallucinations are more common in patients with occipital strokes (12%) and Auditory hallucinations were present in 0.8% patients who had a cortical stroke, although they might be more common after subcortical strokes
- Delirium might have caused the psychotic symptoms of some of these patients

Considerable overlap exists between the neuropsychiatric syndromes

- Depression frequently coexists with anxiety and emotional lability
- Fatigue is a symptom of depression and anxiety
- Apathy is associated with depression and cognitive impairment
- Personality changes are associated with emotional lability, depression and cognitive impairment.

DELIRIUM

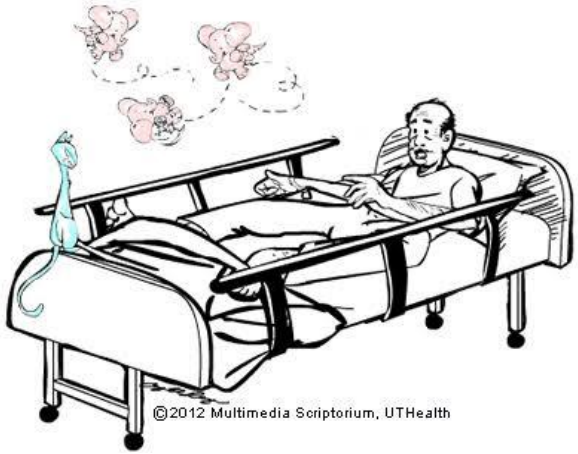
- Most common mental disorder
- Up to 87% of elderly patients
- As many as 75% are not recognized by the physician caring for the patient
- Characterized by: acute mental status change and inattention and disorganized thought or altered level of consciousness

Hallmark: acute onset and fluctuating clinical course

- Most often drug related (40%) - but all other organic causes must be ruled out

Risk Factors for Delirium

- Age
- Decreased cognitive Reserve
- Infection (sepsis, pneumonia)
- Drugs
  - Benzodiazepine dose
  - Fractures of long bones
- Pre-existing dementia
- Sleep deprivation
- Addiction (Tobacco, Smoking, Alcohol)



Steps to Prevent Delirium

Risk Factor	Amelioration
Benzodiazepine high dose	Use benzodiazepine push (e.g. lorazepam 1-2 mg every hour as needed) Alternative agent (propofol, dexmedetomidine)
Sleep deprivation	Quiet ICU at night (pagers on vibrate, lights dim) ICU rooms with natural light
Disorientation	Family visitation or open ICU hours Frequent re-orientation

Treatment of Delirium

BEST IS PREVENTION: Avoid sleep deprivation, increase cognitive stimulation, talk to the patient, play music, early mobilization, avoid dehydration, electrolyte disturbances, and hypoxia

- High index of suspicion, frequent screening
- Treatment should be more prompt (prevent sequelae)
- Stop offending drugs (benzos and narcotics misused to treat “confusion”)

Treat with antipsychotics – drug of choice remains haloperidol

- Monitor for prolonged QT
- Interacts with multiple othe drugs common in ICU
- Neuroleptics not well studied in the ICU may be helpful in non-agitated delirium like risperidone, olanzapine, ziprasidone)

Pseudoseizures

Pseudoseizures

- A gradual onset over several minutes, with a prolonged duration of seizures (> 5 minutes) without hypoxia or other vital sign abnormalities
- Variable features or pattern; most true seizures have a stereotyped pattern
- A lack of self-injury (e.g., no tongue biting, incontinence, or self-harm)
- Out-of-phase jerking and nonrhythmic clonic activity

- Bilateral motor activity with preserved consciousness
- Avoidance of noxious stimuli during the event
- No postictal confusion
- Bilateral motor activity and loss of consciousness—with a normal EEG at the time of the “seizure”
- Ability to recall events that occurred during the episode

POST STROKE PSYCHIATRIC MANIFESTATIONS

DR N. R. ICHAPORIA
MD DM NEUROLOGY
JEHANGIR HOSPITAL PUNE

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Post stroke neuropsychiatric manifestations

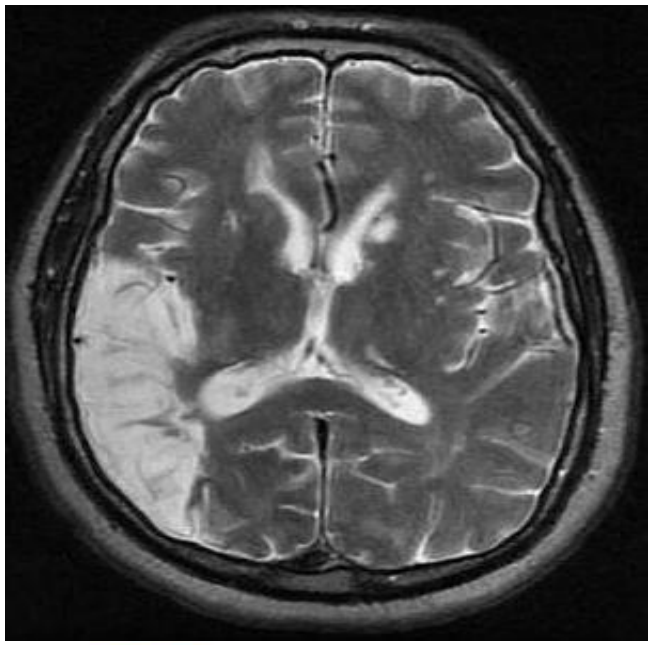
- Introduction
- Depression
- Anxiety
- Emotional lability
- Fatigue after stroke
- Apathy
- Mania
- Personality disorder.
- Psychosis and psychotic symptoms
- Symptoms related to location of lesion

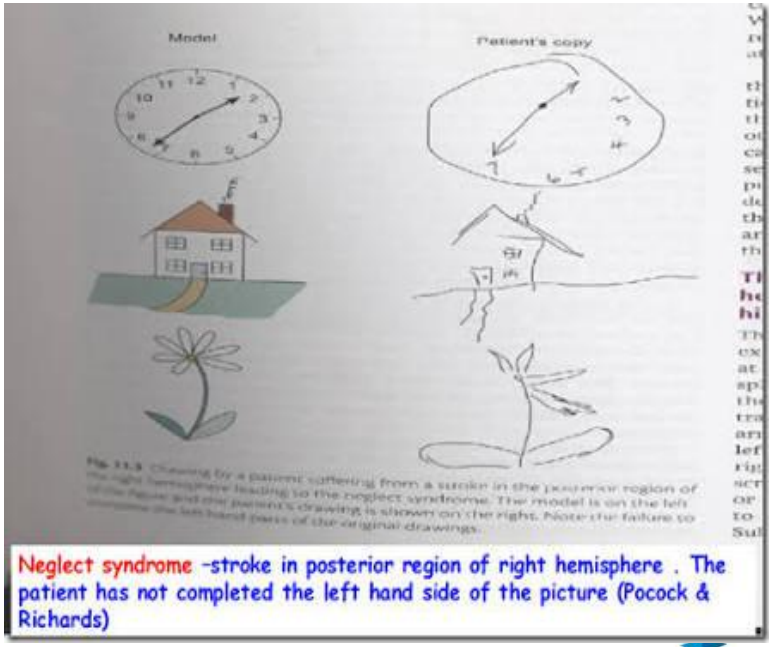
Neuropsychiatric symptoms of different lobe lesions

Parietal lobe damage

1. Effects of unilateral parietal lobe damage

- Corticosensoary syndrome and sensory extinction
- Hemineglect



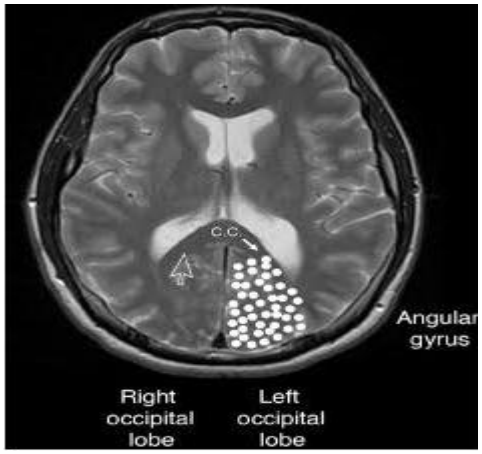


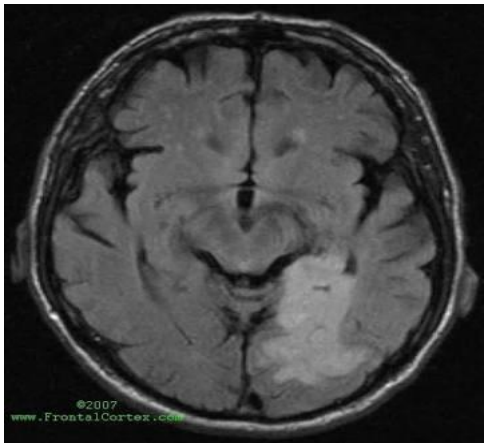
Neglect syndrome -stroke in posterior region of right hemisphere . The patient has not completed the left hand side of the picture (Pocock & Richards)

2. Effects of dominant parietal lobe damage

a) **Alexia:** inability to recognise words

Alexia without agraphia: retain capacity to write fluently but cannot read





Alexia with agraphia: inability to read or write.

It is a dominant angular gyrus lesion

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Gerstmann Syndrome

- Left (dominant) inferior parietal lesion)
- Characteristic tetrad:
  - Finger agnosia (inability to distinguish fingers on the hand)
  - Right--- left disorientation
  - Acalculia (difficulty in learning or comprehending mathematics)
  - Dysgraphia(inability to write)

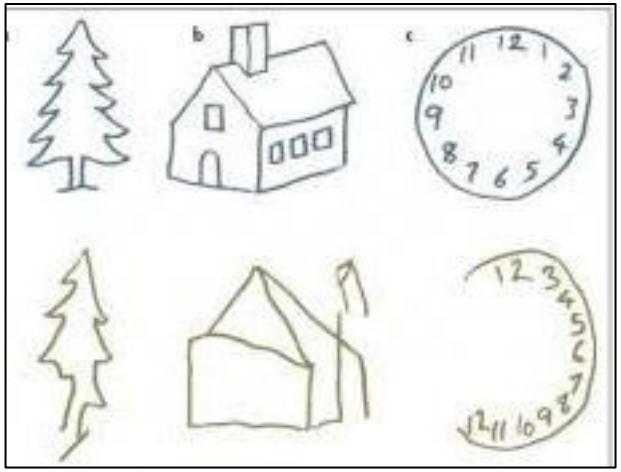
One or more of this manifestaton may be associated with word blindness (alexia) and homonymous hemianopia

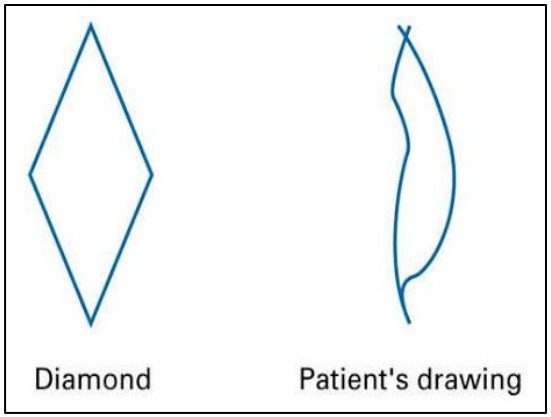
Apraxia

- Inability to do learnt activities
- Due to parietal lobe damage
- Constructional apraxia
- Ideomotor / Ideational apraxia

Constructional Apraxia

- Inability of patients to copy accurately drawings or three dimensional constructions
- Common disorder after right parietal stroke





Ideational apraxia

- The failure to conceive or formulate an action to command
- Sensory areas 5 and 7 in dominant parietal lobe, supplementary and premotor cortices of both cerebral hemispheres and integral connections involvement
- Difficulty in “WHAT TO DO”

Ideomotor apraxia

- Patient may know and remember the planned action but because of interrupted areas or connections, he cannot actually execute it
- It is a block in “HOW TO DO”
- They can no longer use common implements like brushing teeth, combing hair

3. Effects of non dominant parietal lobe damage

- Visuospatial disorders
- Topographic memory loss
- Anosognosia
- Dressing and constructional apraxia
- Confusion
- Prosopognosia & Autoprosopognosia.

Effects of frontal lobe damage

- **Speech and language disorders** related to dominant lobe-iconic speech, telegramatic speech
- **Cognition and intellectual changes**- impairment of capacity for goal directed mental activity, thought problem
- **Abulia**-diminition of number of movements, spoken words and thoughts
- **Akinetic mutism-** non paralysed, alert, capable of movement and speech,lies or sits motionless and silent for days/weeks
- **Bradyphrenia**-slowness of thinking
- Urine incontinence

Behavioural disinhibition

- Hyperactivity syndrome or organic drivenness
- Due to dorsolateral frontal lesions
- Brief and intense involvement with meaningless activity
- Abnormal social behaviour

Effects of temporal lobe damage

- Auditory illusions and hallucinations
- Auditory agnosia
- Word deafness- auditory, verbal agnosia(WERNICKE'S aphasia)
- Dreamy states with seizures(focal temporal lobe seizure)
- Korsakoff syndrome
- Kluver-Bucy syndrome: compulsion to attend all visual stimuli, hyperorality, hypersexuality, blunted emotional reactivity

Effects of occipital lobe damage

- Homonymous hemianopia
- Alexia without agraphia
- Alexia with agraphia
- Loss of topographic memory and visual orientation
- Cortical blindness
- Achromatopsia- loss of perception of colour
- Prosopagnosia- impaired face recognition

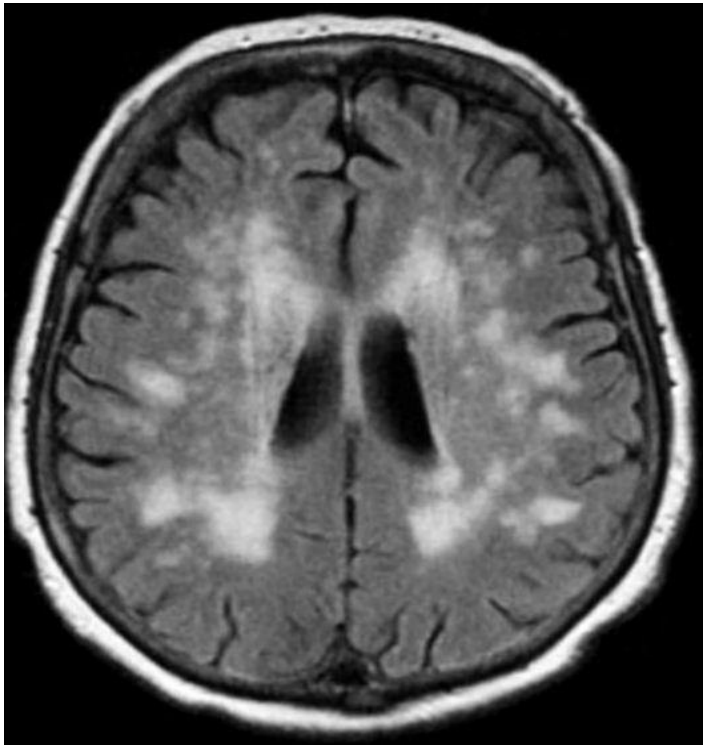
Cognitive impairment

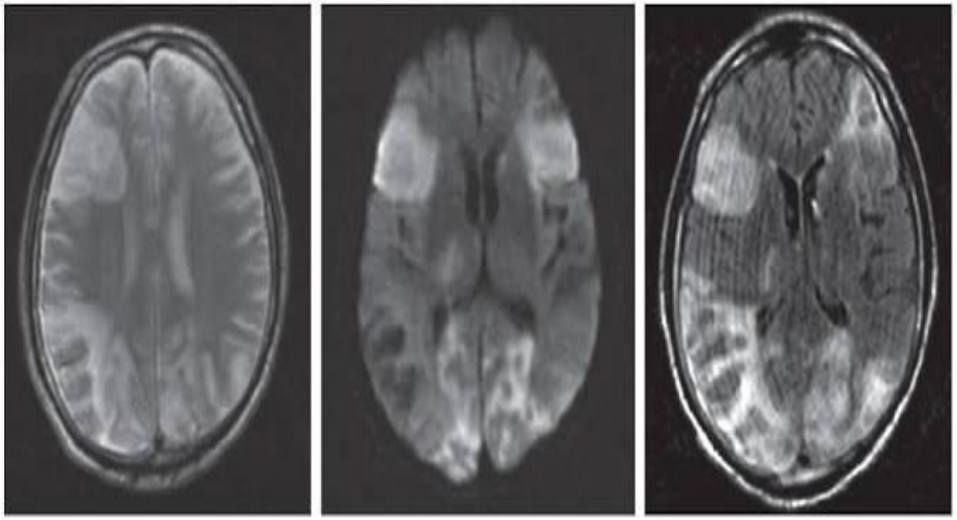
- Alzheimer's dementia
- Frontotemporal lobe dementia (Pick's dementia)
- Lewy body dementia
- Parkinson's disease with dementia

- **<u>Vascular dementia:</u>**
  - Multi-infarct dementia
  - CADASIL
  - Binswanger dementia

Vascular Dementia: Multi infarct dementia

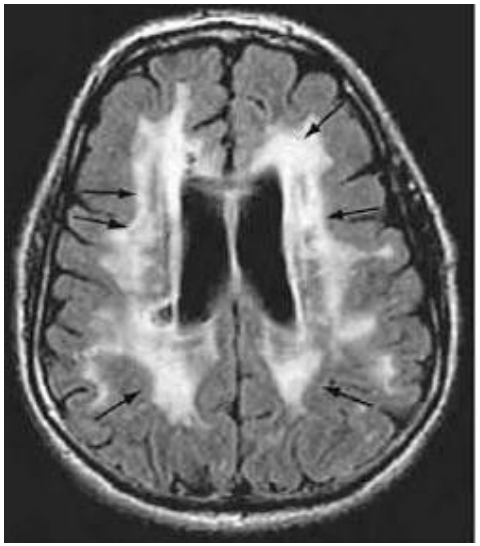
- Sudden or stepwise onset
- A/W vascular risk factors
- Focal neurological deficits followed by cognitive impairment
- Imaging shows Generalized volume loss with multiple cortical, subcortical and basal ganglia infarcts, patchy or confluent periventricular white matter lesions

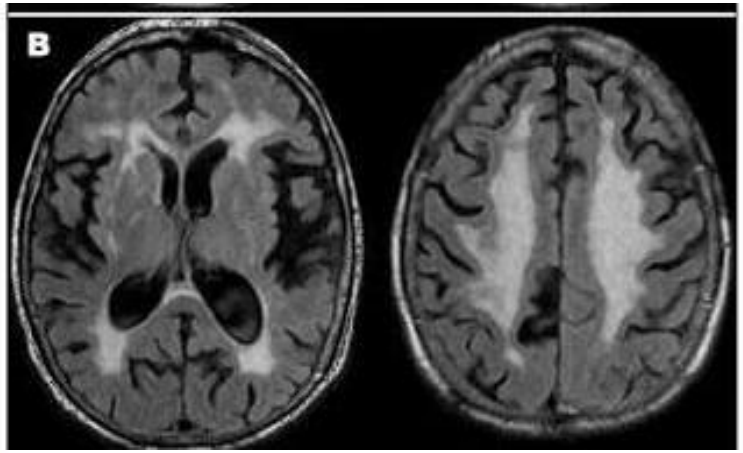




Vascular Dementia: Binswanger

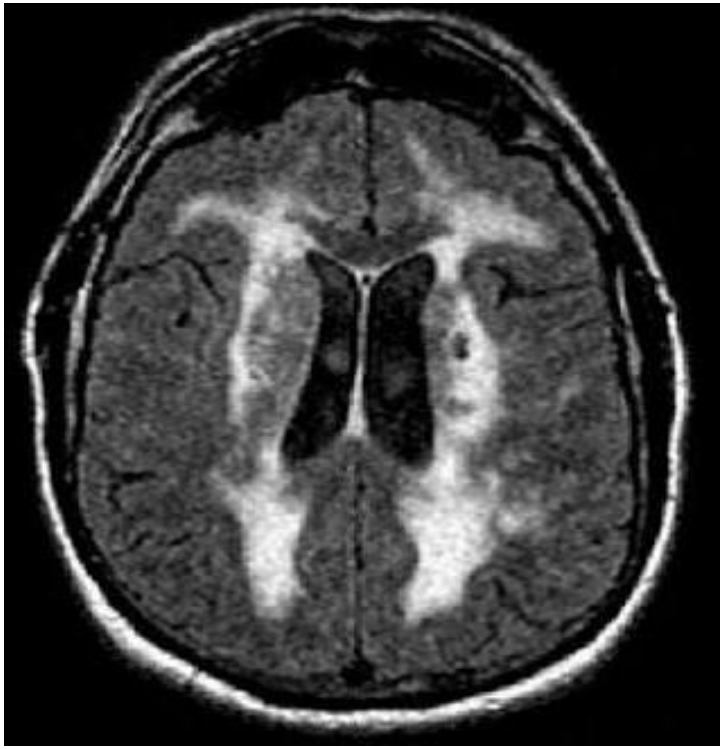
- Subcortical arteriosclerotic encephalopathy
- a/w hypertension
- Generally >55 years
- Slowly progressive
- Involves white matter

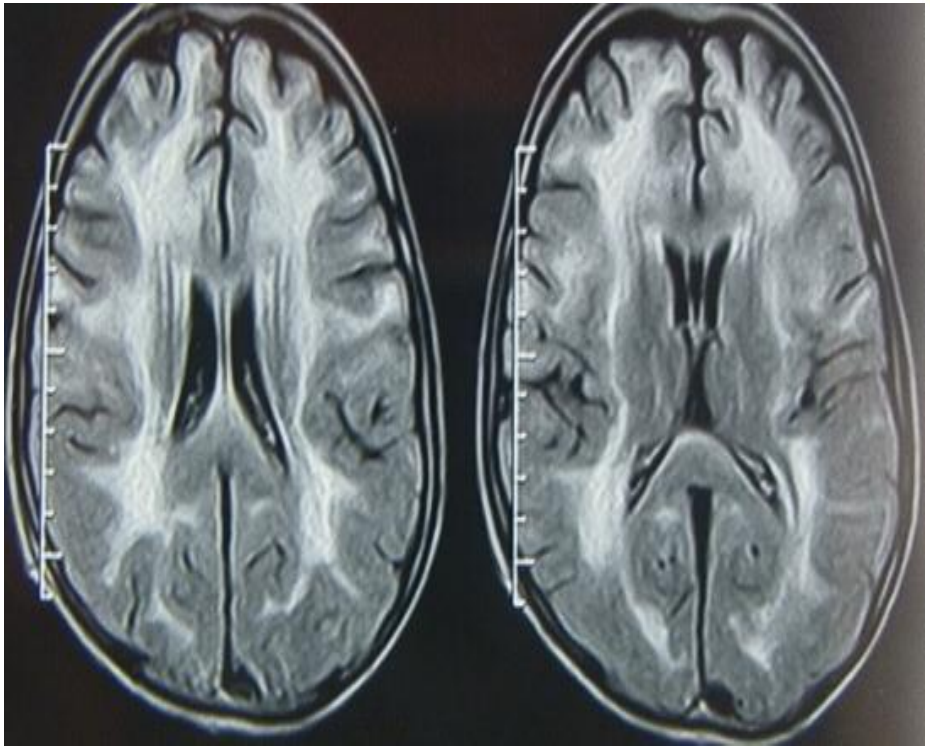




Vascular dementia: CADASIL

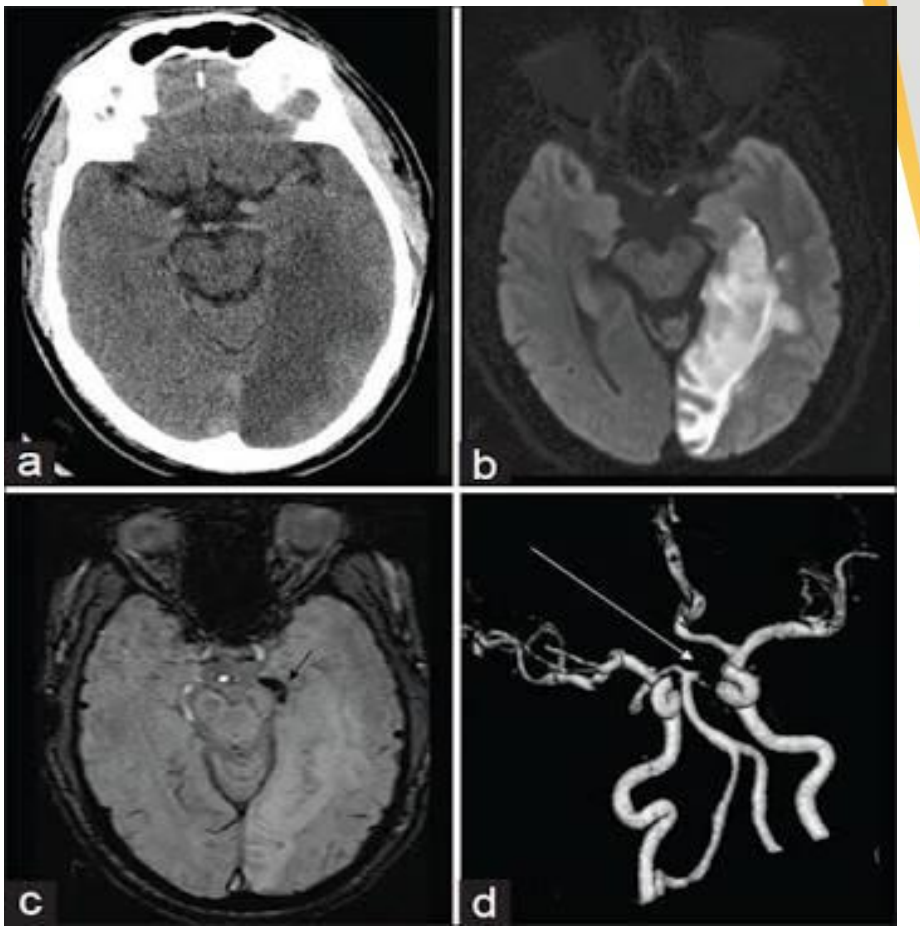
- CADASIL: Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy
- Inherited arterial disease- Notch 3 gene on chromosome 19
- Begins in young adults with TIA's and strokes
- Typical involvement of temporal white matter, internal capsule and subinsular regions





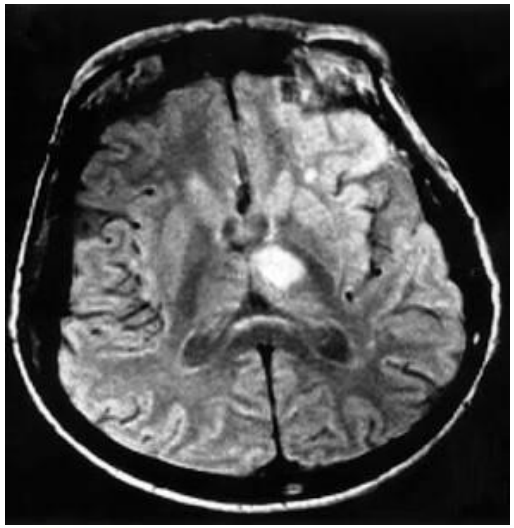
Left PCA stroke: Single vessel dementia

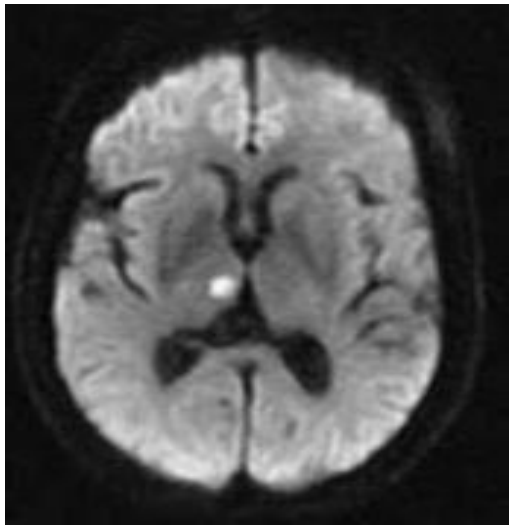
Infarction of medial temporal lobe, fornices and medial thalamic nuclei may result in permanent anterograde amnesia



Anterior Thalamic infarct

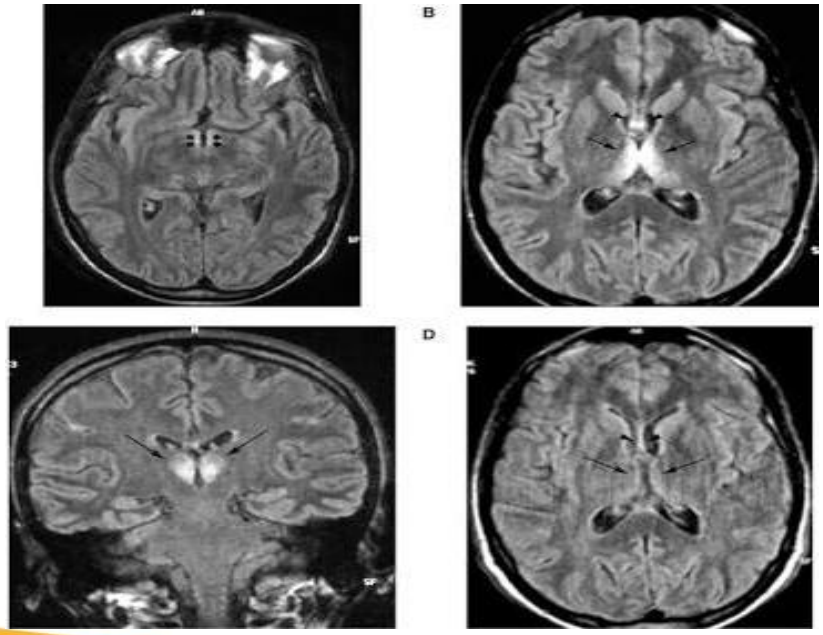
- Acute severe perservative behavior which is apparent in thinking, speech, memory and executive tasks, increased sensitivity to interference
- Memory disturbance and apathy can be persistent





Wernicke-Korsakoff syndrome

- Anterograde amnesia
- A/W diencephalic lesions mainly in anterior thalamic nuclei



Distinguishing types of crying

- **Pathological crying** linked to infarct in basis of pontis and corticobulbar pathways and occurs in response to mood incongruent cues
- **Emotionalism** is crying that is congruent with mood (sadness) but patient is unable to control crying as they would have before stroke
- **Catastrophic reaction** is crying or withdrawal reaction triggered by a task made difficult or impossible by a neurologic deficit (e.g. moving a hemiplegic arm)

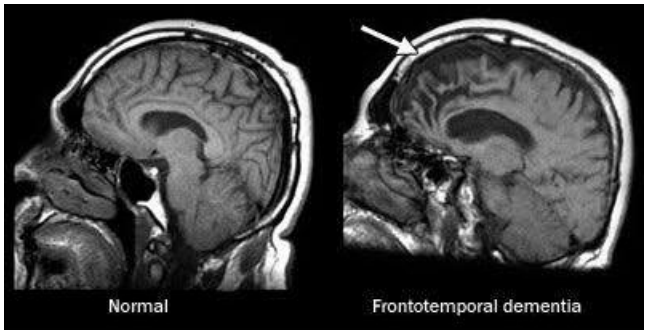
Emotionalism and catastrophic reaction

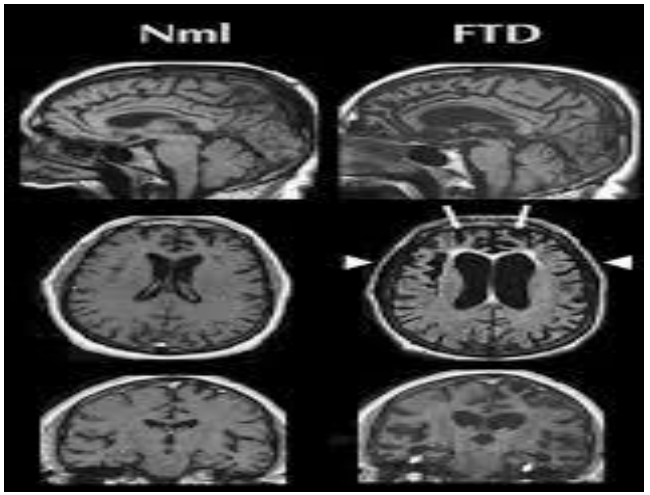
Evidence for neurobiological basis over situational psychological factors

- Catastrophic reactions occur more with left hemispheric lesions and aphasia
- Greater in strokes involving structures heavily connected to the amygdala and paralimbic regions
- May be seen as abnormal reflexes rather than conscious responses evoked by lesion related damage, hypoperfusion and edema in acute phase of stroke

Frontotemporal Dementia

- Behavioural changes in personality including apathy, inappropriate social conduct and language disturbance with memory deficits
- Asymmetric frontal and anterior temporal atrophy





Issues in use of self-report screening tools for PSD Gaete, et al. 2008)

- Self report measures are quite sensitive to the presence of depressive symptoms but lack specificity to differentiate from other comorbid or confounding factors.
- Somatic symptoms on self assessment measures may plan a role in reduced specificity
- Anosognosia – lack of awareness may affect sensitivity and specificity of instruments.
- Physical and cognitive deficits may make use of these tools prohibitive.

Self-report screening tools for patients without communication barriers

Hospital Anxiety and Depression Scale (HADS)

- Well tolerated
- Somatic symptoms excluded
- 14 items
- Relatively good date on its use in PSD screening

Self-report screening tools for patients without communication barriers

Geriatric Depression Scale (GRS)

- Designed for screening for depression in older individuals
- Low reliance on affective symptoms
- Good sensitivity and specificity in stroke patients but reports it is not well tolerated in hospitalized medical patients in part due to 30 items.
- Short form not evaluated in stroke population.

Self-report screening tools for stroke patients with communication barriers

Visual Analogue Mood Scale (VAMS)

- Eight cartoon face and verbal descriptions
- For stroke patients with communication disorders
- Not affected by neglect
- However, not validated yet in stroke population

Observational rating scales

Post-stroke Depression Rating Scale (PDRS)

- Ten items
- Specifically designed to assess depression in stroke patients
- No clear cut-off score
- Training and experience required to administer
- Not validated in stroke clinical or research settings

Observational scales

Stroke Aphasia Depression Questionnaire (SADQ-H 21 or SADQ-H 10)

- Completed by health care professional
- Observable behavior associated with depression
- Short version recommended for clinical applications though longer version was developed for hospital application and is better validated.

Observational scale

Aphasic Depression Rating Scale (ADRS)

- Designed to diagnose and monitor depression in patients with aphasia
- Training required to use instrument
- Cut off score of 9 of 32 items provides good sensitivity and specificity for depression in patients with Aphasia.

Nursing observational scale

Signs of Depression Scale (SODS)

- Six items
- Easy to administer
- Yes/no response format
- Adequate sensitivity and specificity in identifying depression in older individuals who are medically ill and in stroke patients without significant communication problems.

Considerations for treatment with antidepressant medication

- Goal is to choose agent with lease potential for side effects and titrate slowly to improve tolerability and compliance with treatment.
- Some agents, such as mirtazapine, may be preferential to treat poor appetite or other vegetative symptoms in some patients.
- In patients with apathy and significant psychomotor retardation, consider initiating treatment with psychostimulant and then convert to SSRI/SSNRI.

Non-pharmacological Intervention

- Psychotherapy most helpful in patients with milder cognitive and functional impairments.
- Psychotherapy more effective in patients with minor depression.
- Research is mixed on effectiveness of community based outreach and support programs.