Affective disorders in late life

Mania
Depression & depressive symptoms

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Aims

- To explore affective disorders in old age with regard to:
  - Epidemiology
  - Aetiology
  - Clinical Presentation
  - Differential Diagnosis
  - Investigation
  - Treatment
  - Prognosis
<table>
<thead>
<tr>
<th>Well known people with Depression</th>
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<tbody>
<tr>
<td>Buzz Aldrin</td>
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<tr>
<td>Christian Bale</td>
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<tr>
<td>Frank Bruno</td>
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<tr>
<td>Alistair Campbell</td>
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<tr>
<td>Agatha Christie</td>
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<td>Winston Churchill</td>
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<td>Charles Darwin</td>
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<tr>
<td>Bob Dylan</td>
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<tr>
<td>Harrison Ford</td>
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<td>Beyoncé Knowles</td>
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<tr>
<td>Hugh Laurie</td>
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<tr>
<td>Bill Oddie</td>
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<td>Ronnie O’Sullivan</td>
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<td>Denise Welch</td>
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Mania

• uncommon in the elderly
• most are ‘graduates’
  – 95% have first affective episode by 26
  – Peaks for mania: <30 (all), late 40s (♀), 80s/90s (♂)
• 85% (at least) have had previous depression
• ECA study (80s)
  – 1.4% adults had mania in previous year
  – 0.1% >65s
• ‘secondary mania’
  – ie 2° to physical disorder / drugs / no prev Hx affective disorder (NB ‘manic symptoms’ v bipolar disorder)
Treatment of Mania

• As for working age adults but need caution with drug doses, etc, acutely
  – Less evidence for many drugs than in w. age adults
  – eg Haloperidol can accumulate → prolonged EPSE
  – watch for iatrogenic delerium
  – Li toxicity at lower plasma levels; possible impaired renal function; Diuretics
  – 80% respond to ECT
  – In dementia, atypicals → ? risk

• Similar cautions apply to prophylactic Rx
Depressive *Episode* v Depressive *Symptoms*
43 Million Antidepressant Prescriptions in England in 2011
Epidemiology

<table>
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<tr>
<th>Prevalence</th>
<th>Symptoms</th>
<th>Episode</th>
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<tr>
<td>Gurland, 1983</td>
<td>13 %</td>
<td>1.3 %</td>
</tr>
<tr>
<td>Copeland, 1987</td>
<td>11 %</td>
<td>3 %</td>
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</tbody>
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- Female : male = 70:30

- Rates in 64-75s approx = >75s (Morgan 1987)

- Being > 90yrs seems to mean less risk of depression
Location of ‘patients’

• Prevalence of significant depressive Symptoms

  – Community: 10%  (Alexopoulos, 92)
  – GP attenders: up to 33%
  – Hospitalized elderly: 12-45%
  – Nursing/Residential homes: 14-42%
Diagnostic classification points

- DSM IV
  - > 2 wks & need either depressed mood or loss of interest / pleasure
    (i.e. depressed mood not a prerequisite)
  - physical illness may preclude diagnosis
  - bereavement
    - unless > 2/12; marked functional impairment; suicidal ideation; psychosis.
ICD-10 criteria for depressive disorder

A. General criteria for depressive episode (essential):
   - at least 2 weeks
   - No prior manic/ hypomanic episodes
   - No psychoactive substances/ organicity

B. Depressed mood/ Loss of interest/ Decreased energy

C. Loss of confidence/ Guilt
   - Recurrent thoughts of death/ suicide
   - Diminished concentration
   - A change in psychomotor activity
   - Sleep disturbance/ Change in appetite

Mild: A and 2 B criteria and 4 C criteria
Moderate: A and 2 B criteria and 6 C criteria
Severe: A and 2 B criteria and 8 C criteria
Comorbidity

- Alzheimer’s D (AD): up to 63% dep. symptoms
- Prevalence of depressive d/o in Vascular Dementia (VD) higher than AD
- Depression more prevalent in CVA & Parkinson’s D (controlling for level of disability)
- Depression in dementia:
  - VD 19% (Ballard et al, 2000)
  - DLB 19% (Aarsland, McKeith et al, 2001)
  - AD 8% (Ballard et al, 2000)

NB: Depression = risk factor for dementia
Differences in Older People

- less likely to complain of low mood
- more likely to experience: physical symptoms, anxiety, memory complaints (Baldwin et al, 2002)
- in dementia, depression may lead to behavioural disturbance (Dwyer and Byrne, 2000)
- Increased agitation/retardation
# Pseudodementia

<table>
<thead>
<tr>
<th></th>
<th>Dementia</th>
<th>Depression</th>
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<tr>
<td>History</td>
<td></td>
<td>Acute</td>
</tr>
<tr>
<td>Previous Depression</td>
<td></td>
<td>More likely</td>
</tr>
<tr>
<td>Subjective Memory</td>
<td></td>
<td>More common</td>
</tr>
<tr>
<td>Problems</td>
<td></td>
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<tr>
<td>Cognitive Tests</td>
<td></td>
<td>Patchy</td>
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Range of Presentations

- “Trivial” DSH
- Accentuation of problematic personality traits
- Late onset alcohol dependency
- Depression in dementia (X- Y%)
- Somatisation, hypochondriasis & disproportionate concern w minor physical Sx
- ‘Neurotic’ Sx of recent onset
- *Sudden* change in sleep pattern
Depression induced cognitive impairment

- Almost all episodes of major depression have reduced cognitive function, but
  - **not higher functions** (aphasia/ apraxia/ agraphia)
  - deficits in memory & cognitive slowing
  - memory improves with cueing (cf AD)
- prognosis poor
  - 5x Relative risk of AD
  - 1/3 persisting cog. probs when dep. ‘resolved’
Assessment (1)

• Hx - patient & informant
  – may clarify many otherwise problematic cases
    • prev / family Hx, etc
    • prev Rx response
    • recent changes/ “upheaval”/ Physical health
    • bereavements / losses - family, assetts
    • High achievers
    • Suicide Risk: Age, isolation, Depression

• MSE
  – incl cog function to allow later comparisons
• Physical exam
  • Depression triggered by overt physical illness
  • Occult illness presenting as depression
    • metabolic (hypoT4, hyperCa, Cushing’s)
    • drugs (steroids, B-blockers, nifedipine, digoxin, L-dopa, tetrabenazine)
    • infection (post-viral, “ME”)
    • organic brain disease (SOL, degenerative)
    • Cardiac failure
    • Ca (lung, pancreas, abdomen)
Investigation (1)

• Haematology (inc B12/ folate for 1st episode)
• U&E, LFT, Ca, TFT, HbA1C/ Glucose (if not in last 12/12 on recurrent episode)
• Syphilis (not routinely)
• Repeat of those prev done if clinically indicated
• CT (MRI/SPECT/EEG if clinically indicated)
Investigation (2) - Rating scales

- GDS (Geriatric Depression Scale; Yesavage, 1983) – sens 79-100%, spec 67-80%, self-rated, mainly cognitive aspects of depression. 15 questions.
- Beck
- Hamilton
- Cornell (depression in dementia; inc. collat info)

**NB:** all scores must be taken in context of presentation.
Aetiology

- Genetic
- Demographics
- Personality
- Social
- Physical health
  » Neurobiological
  » Structural brain changes
Aetiology (1)

- **Genetic** (well established)
  - **early onset** risk to 1st degree relatives is 20%
  - **late onset**: risk is only 8%

- **Demographic/Social**
  - female>male (70:30)
  - more common in widowed/divorced
  - Social isolation / lack of confidante
  - Substance use

- **Personality**
  - evidence for dependent, passive-aggressive, avoidant & obsession-compulsive types
  - lack of capacity for intimacy
Aetiology (2)

- **Physical health**
  - hearing impairment (depression most common psych illness in this group)
  - Parkinson’s Disease
  - Stroke (esp Left basal ganglia; Left frontal)
  - Cardiovascular dis (20-25% serious heart dis depd)
  - Occult illness (as previously)
  - Illnesses as life events

- **Life events**
  - 48% depressives (cf 23% controls) at least 1 major life event in 12/12 preceding depression (Murphy 1982)
  - often losses.
  - BUT: may be red herrings in some cases!
Aetiology (3)

Neurobiological and Structural Brain Changes

- Amine theories of depression
  - changes in normal ageing similar to depression
    - reduced NA, 5HT, DA
    - increased MAO-B activity
  - Endocrine changes
    - HPA axis dysregulation: associated with depression in all ages
    - TRH/-TSH: little research in elderly depressives
Aetiology (4)
HPA axis changes

- **DST:**
  - 86% elderly (>72) depressed = non-suppressors, v 58% (<72). (Alexopoulos 1986)
- **Glucocorticoid cascade hypothesis** (Sapolsky):
  - Stress ↑ cortisol
  - ↑ cortisol may be toxic to hippocampal (HC) neurones
  - HC has effect of downregulating HPA axis
  - So ↑ cortisol dysregulates HPA axis
  (HC has high concentration of glucocorticoid & mineralocorticoid receptors)
Fronto-subcortical circuits
Aetiology (5)
Fronto-subcortical circuit disruption

- White matter lesions
  - Deep WML associated with late-onset depression.
  - DWML of particular interest re circuit disruption.
  - Pathology: some evidence from depression

- Subcortical grey matter lesions (B Ganglia)
- Stroke
- L Frontal, L Basal Ganglia
White matter disease (WML) or leukoaraiosis: "surrogate marker for vascular damage"
Neurobiology of Depression

- Inflammation
- Stress/HPA Axis
- Metabolic Syndrome

- Atherosclerosis
- Neurodegeneration

- Depression
Vascular Depression

- Evidence for a proposed subtype of old age depression (Alexopoulos, 1997)
  - Association of WML with vascular risk factors & causes of death in general population (but still more WML in late onset dep when vasc RFs controlled for)
  - Neuropath. evidence for vascular basis to WML in late life depression
Vascular Depression Hypothesis Schematic

Krishnan et al, 1995

Risk factors:
- Age
- Hypertension
- Hyperlipidemia
- Smoking
- Diabetes mellitus

Artherosclerosis

Deep white matter lesions (vulnerability to LOD)

Negative life events

Lack of social support

Vascular depression with executive dysfunction
Neuropsychological deficits

• Found to persist between episodes in significant number of cases
  – Memory deficits fit with hippocampal damage though as yet no proof of hippocampal cell loss
  – Deficits in frontal functions fit with hypothesis of disrupted fronto-subcortical circuitry
Late onset v Early onset

- Genetics
  - FHx much less likely in LO
- WML
  - related to LO but not EO
  - DWML in excess probably predict poorer response to Rx & poorer short and long-term outcome
- Points to possible differing aetiological processes
Other areas of interest

- EEG
  - Increase in waking alpha rhythm amplitude in depression
  - Sleep EEG in depression similar to normal ageing (can be distinguished from dementia)
Treatment

- **Mild:**
  Monitoring/ Sleep hygiene/ CBT/ Exercise/
  Peer Group support

- **Moderate-severe:**
  - Antidepressant:
    1\textsuperscript{st} line: SSRI
    2\textsuperscript{nd} line: Mirtazapine or venlafaxine or duloxetine
  Check response: 4 weeks/ 6 weeks

  - Psychological Therapy (High Intensity)
Treatment

- At least 2 months/ at least 2 yrs.
- Indefinite prophylaxis
- TCAs 50% improve (cf 20% on placebo)
- SSRIs of equal efficacy - fewer dropouts
- NaSSAs – mirtazapine – can be helpful
- NARIs reboxetine - not recommended in UK in elderly
MAOIs Rx-resistance – NB interactions & s/effects

Moclobemide - as effective as TCAs, generally well tolerated

SNRIs: **Venlafaxine** efficacious but postural drop in BP can occur – NB CV disease, need for ECG;

Duloxetine – option esp. with comorbid anxiety

Lithium augmentation – aim for lower part of therapeutic range in intractable illness

Combinations.....
Treatment of special groups

- **Dementia:**
  treat depression if evident.

- **Physical illness:**
  - SSRIs preferable to TCAs (side effects).
    - NB citalopram & sertraline have little effect on CyP450 system
  - **Post CVA** - Citalopram
  - **Post MI** - Sertraline
Side effects

• TCAs - caution
  • (anticholinergic, antihistaminic, adrenergic)
    – avoid in
      • tachy- or bradyarrhythmia/ BBB
      • Abnormal QT interval
      • poorly controlled heart failure
    – Relative problems
      • postural hypotension
      • Delirium/ sedation (driving!)
ECT

- **Indications**
  - As younger adults: life threatening
    - Guilt/ psychotic Sx/ agitation/ stupor/ neglect/ risk
    - Neuro-vegetative symptoms
  - All may predict good response, except anxiety
  - NICE guidelines
  - Good response in 70-90% of Major D. Cases
  - Unilateral < confusion (Can be given in dementia)
Psychological Treatments

- Shorter sessions
- Explicit goals
- More active therapist
- Include
  - bereavement counselling (CRUSE)
  - CBT (Arean and Cook, 92)
  - Interpersonal therapy
  - Family & marital therapy
  - Life review
- Issue: Therapist mobility
Prognosis

- 60% inpatients well or relapse with good recovery
- mortality = 2.5 x age/sex/health matched
- Poor prognostic indicators
  - coarse brain changes
  - subtle brain changes (e.g., diffuse DWML)
  - physical ill health
  - major adverse life events
Case Example

- 78 yr old man
- Lives with his wife
- Medical history: arthritis, type 2 diabetes mellitus
- Previously ran business- now retired, sense of loss.
- 2 month history “I can’t get out of this dark place”, “can’t be bothered”, guilt, mild sleep disturbance, tired/ “ache”, reduced energy/ concentration, financial ruin. Memory problems.
- Sertraline 200mg- 3 weeks- no response
- Now hopeless, agitated, suicidal ideas- no plans
Case Management

- CMHT urgent
- Risk assessment/management
- ? Psychotic
- Medication review
- Pros/cons of alternative antidepressants: Venlafaxine, Duloxetine, Mirtazapine
References

- Byrne A in in Curran S & Wattis J 2008. Pharmacological management of Depression in Older People. Practical Management Of Affective Disorders In Older People; 2008, Chapter 4. Radcliffe; Oxford,. (http://books.google.co.uk/books)
References


THANK YOU

Any Questions?