Challenges in delirium

Anna Sobel
Itunu Ayeni
Timetable

• Overview
• Small group case studies
• Phenomenological differences: psychiatric presentations vs delirium
• Audit presentation
• Video: patient experience
• summary
Prevalence

- 1 in 8 hospital inpatients (Maclullich 2013)
- Medical inpatients:
  - 11-42% (Siddiqi et al 2006)
  - 50% elderly inpatients (Cole 2004)
- 20% those in long term care
- Under-detected:
  - 79% (Collins et al 2010)
  - 33-66% (Siddiqi et al 2006)
Consequences

- **Mortality**: \( \uparrow \) HR 1.95 (CI, 1.51-2.52) (Witlox et al 2010, Siddiqi et al 2006)

- **Institutionalization**: \( \uparrow \) OR 3.19 (CI, 1.33-7.64) (Bourdel-Marchasson 2004)
  - Increased risk at 2 years f/u - OR 2.45 (CI, 1.2-4.9) (Pitkala 2005)

- **Developing dementia**: \( \uparrow \) OR 12.52 (CI, 1.86–84.21) (Witlox 2010)

- **Length of stay**: \( \uparrow \) HR 1.2 (CI, 1.1-1.3) (Ely 2004)

*association exists independently of dementia*
Consequences

• Functional decline: $\uparrow$ RR 1.9 (95% CI, 1.3-2.8) (Rudolph et al 2010)

• Persistent delirium: Persistent delirium = worse outcomes (Cole et al 2009)

• Associated with adverse events: restraint, pressure areas, falls..
Synonyms

- Acute confusional state
- Organic brain syndrome
- Acute brain syndrome
- Toxic – metabolic encephalopathy
- Septic encephalopathy
- Organic brain syndrome
- Post operative confusion
- Acute cerebral insufficiency
- Terminal agitation
- Terminal restlessness
- ICU psychosis
- ICU delirium
- Altered mental status change
- Subacute befuddlement

....there are more
Fig. 1 The differential diagnosis of delirium reflects its broad symptom profile

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>In order to be diagnosed with delirium, as a consequence of a general medical condition a patient must show all of the four features listed below:</td>
<td>For a definite diagnosis, symptoms, mild or severe, should be present in each one of the following (five) areas:</td>
</tr>
<tr>
<td>1. A disturbance of consciousness (i.e. reduced clarity of awareness of the environment) is evident, with reduced ability to focus, sustain or shift attention</td>
<td>a) Impairment of consciousness and attention (on a continuum from clouding to coma; reduced ability to direct, focus, sustain, and shift attention)</td>
</tr>
<tr>
<td>2. There is a change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing or evolving dementia.</td>
<td>b) Global disturbance of cognition (perceptual distortions, illusions and hallucinations – most often visual; impairment of abstract thinking and comprehension, with or without transient delusions, but typically with some degree of incoherence; impairment of immediate recall and of recent memory but with relatively intact remote memory; disorientation for time as well as, in more severe cases, for place and person)</td>
</tr>
<tr>
<td>3. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.</td>
<td>c) Psychomotor disturbances (hypo- or hyperactivity and unpredictable shifts from one to the other; increased reaction time; increased or decreased flow of speech; enhanced startle reaction)</td>
</tr>
<tr>
<td>4. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.</td>
<td>d) Disturbance of the sleep-wake cycle (insomnia or, in severe cases, total sleep loss or reversal of the sleep-wake cycle; daytime drowsiness; nocturnal worsening of symptoms; disturbing dreams or nightmares, which may continue as hallucinations after awakening)</td>
</tr>
<tr>
<td></td>
<td>e) Emotional disturbances, e.g. depression, anxiety or fear, irritability, euphoria, apathy, or wondering perplexity.</td>
</tr>
</tbody>
</table>
Clinical subtypes (motoric)

• Hyperactive delirium: (least common)
  – Restlessness, agitation, hypervigilance, aggression, hallucinations, delusions (more commonly)

• Hypoactive delirium:
  – Lethargy, sedation, slow response, little spontaneous movement, withdrawn, apathy
  – More in elderly
  – Often missed or misdiagnosed as depression

• Mixed (most common)

• Significance?
Important in Psychiatry?

- Commonly referred - frequently misdiagnosed
- 10% of deliriums in hospital see a psychiatrist
- In elderly change in mental state often earliest sign of serious physical illness
- Emotional and behavioural changes of delirium easily mistaken for adjustment reactions
- 42% pts referred for depression have delirium
- Hyperactive delirium can mimic anxiety disorders, agitated depression or mania.
Figure 7.30: risk factors for incidence of delirium

### 19.1.1 GDG confidence
- Vision impairment
- Infection
- Age over 65
- Illness severity (APACHE)
- Age over 80
- Cognitive impairment
- Fracture on admission

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Odds Ratio IV, Fixed, 95% CI</th>
<th>Odds Ratio IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vision impairment</td>
<td>0.530628</td>
<td>0.264309</td>
<td>1.70 [1.01, 2.85]</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>1.085189</td>
<td>0.373927</td>
<td>2.96 [1.42, 6.16]</td>
<td></td>
</tr>
<tr>
<td>Age over 65</td>
<td>1.108563</td>
<td>0.476525</td>
<td>3.03 [1.19, 7.71]</td>
<td></td>
</tr>
<tr>
<td>Illness severity (APACHE)</td>
<td>1.24990174</td>
<td>0.43769</td>
<td>3.49 [1.48, 8.23]</td>
<td></td>
</tr>
<tr>
<td>Age over 80</td>
<td>1.5524974</td>
<td>0.353647</td>
<td>5.22 [2.61, 10.44]</td>
<td></td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>1.84054963</td>
<td>0.397948</td>
<td>6.30 [2.89, 13.74]</td>
<td></td>
</tr>
<tr>
<td>Fracture on admission</td>
<td>1.88251383</td>
<td>0.550933</td>
<td>6.57 [2.23, 19.34]</td>
<td></td>
</tr>
</tbody>
</table>

### 19.1.2 GDG weak confidence
- Vascular surgery
- Comorbidity >3 disease

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Odds Ratio IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular surgery</td>
<td>0.99325177</td>
<td>0.230729</td>
<td>2.70 [1.72, 4.24]</td>
</tr>
<tr>
<td>Comorbidity &gt;3 disease</td>
<td>2.76883167</td>
<td>0.634413</td>
<td>15.94 [4.60, 55.27]</td>
</tr>
</tbody>
</table>

### 19.1.3 GDG uncertainty
- Sex
- Polypharmacy >7 drugs
- Dehydration BUN/creat
- Electrolyte disturbance
- Depression
- Bladder catheter
- Polypharmacy >3 drugs

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Odds Ratio IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.307486</td>
<td>0.385459</td>
<td>1.36 [0.64, 2.89]</td>
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<tr>
<td>Polypharmacy &gt;7 drugs</td>
<td>0.541854</td>
<td>0.272408</td>
<td>1.90 [1.11, 3.24]</td>
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<tr>
<td>Dehydration BUN/creat</td>
<td>0.70309751</td>
<td>0.5239</td>
<td>2.02 [0.72, 5.64]</td>
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<tr>
<td>Electrolyte disturbance</td>
<td>0.875469</td>
<td>0.401122</td>
<td>2.40 [1.09, 5.27]</td>
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<tr>
<td>Depression</td>
<td>0.887891</td>
<td>0.49003</td>
<td>2.43 [0.93, 6.35]</td>
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<tr>
<td>Bladder catheter</td>
<td>0.993252</td>
<td>0.319582</td>
<td>2.70 [1.44, 5.05]</td>
</tr>
<tr>
<td>Polypharmacy &gt;3 drugs</td>
<td>3.51452607</td>
<td>1.464535</td>
<td>33.60 [1.90, 592.86]</td>
</tr>
</tbody>
</table>
Barriers to detection

- Heterogeneity of presentation
- Variety nomenclature
- Hypoactive presentations
- Comorbid neuropsychiatric / functional disorders
- Detection tools
- Assessment
Management: non pharmacological

Support and orientation

Unambiguous environment

Maintaining competence

Non-pharmacological treatment
Management: pharmacological

• Antipsychotics:
  – Effective in hyperactive and hypoactive delirium
  – Improve cognition
  – Improve agitation and psychotic symptoms
  – Rapid onset of action (hours – days)
  – Superior to benzodiazepines (except ETOH withdrawal)
<table>
<thead>
<tr>
<th></th>
<th>Haloperidol</th>
<th>Risperidone</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
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<tbody>
<tr>
<td>studies</td>
<td>9 studies 7 All</td>
<td>7 studies 3 1</td>
<td>5 studies 3</td>
<td>4 studies 1</td>
</tr>
<tr>
<td></td>
<td>comparison 7</td>
<td>comparison 1</td>
<td>comparison 1</td>
<td>comparison 1</td>
</tr>
<tr>
<td></td>
<td>randomised</td>
<td>randomised</td>
<td>randomised</td>
<td>randomised</td>
</tr>
<tr>
<td>Total</td>
<td>153</td>
<td>138</td>
<td>161</td>
<td>66</td>
</tr>
<tr>
<td>participants (N)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean dose mg/day</td>
<td>3.9</td>
<td>1.7</td>
<td>5.8</td>
<td>102</td>
</tr>
<tr>
<td>Dose range mg/day</td>
<td>0.5-10</td>
<td>0.5-30</td>
<td>2.5-20</td>
<td>25-300</td>
</tr>
<tr>
<td>response</td>
<td>64% after a</td>
<td>82% after a</td>
<td>69% after a</td>
<td>82% after a</td>
</tr>
<tr>
<td></td>
<td>mean of 3.6 days</td>
<td>mean of 4.7 days</td>
<td>mean of 3.3 days</td>
<td>mean of 6.5 days</td>
</tr>
<tr>
<td>Adverse effects n/N</td>
<td>Sedation: 6/113</td>
<td>Sedation 8/138</td>
<td>Sedation 16/161</td>
<td>Sedation 6/66</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 Seizure</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EPS: 2/138 (1/84)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Management: pharmacological

- Hua et al, 2006
  - RCT haloperidol vs olanzapine vs non-drug treatment in elderly
  - Response rates: haloperidol (87.5%) vs olanzapine (82%) vs non-drug treatment (31%)

- Meagher et al, 2013
  - Systematic review treatment of delirium with antipsychotics
  - Response rates: olanzapine (73%) vs haloperidol (74%) vs risperidone (78%) vs quetiapine (84%)
  - Quetiapine only antipsychotic included in placebo controlled trial and had highest response rate
  - EPSEs in atypicals (3-4%) vs haloperidol (22%)
  - Haloperidol associated with lowest sedation rates

  - Drug and non-pharmacological interventions better than non-pharmacological alone
Clinical scenarios
Case 1

• Ms R 65 yo Afrocaribbean female - presented with one week history of agitation and aggression. She was observed talking to herself and appeared to be experiencing ‘visions’. She was also expressing bizarre persecutory ideas – someone had spiked her food, she was not alive and her family were not real.
• There were fluctuations in her mental state. At times she was mute and motionless and other times she would smile, laugh inappropriately or become aggressive.
• 2 months prior to admission she had begun using heroin again and started to complain of forgetfulness.
• Her family took her to A&E and she was detained under S2 of the MHA and admitted to a psychiatric ward.
Case 1

• Past psych hx:
  – IV opiate use since 18 yo – previously known to Drug and alcohol services. On methadone last few years.

• Past medical hx:
  – Hepatitis C carrier
  – Bilateral leg DVTs
  – Carcinoma left breast 2008 (mastectomy, radiotherapy with tamoxifen)

• Meds on admission:
  – Methadone 75mg od
  – Amitryptilline 25mg on

• Family hx: censored family hx, younger sister and three children 20, 18, 11 all well.

• Social hx: 2 bed housing association. Son lives with her sister. ETOH not excessive. IVDU heroin.

• Personal hx: difficult to establish. NVD and normal milestones. Left school 16 to work in hospitality. Stopped working with her 1st child. Two significant relationships. Nil forensic hx
Case 1


• O/E:
  – Vitals 110/60, P80, RR 19, apyrexial, sats 98% OA
  – Left sided mastectomy
  – Needle track marks right arm
  – No positive signs on physical examination (although difficult concordance)
  – neurological exam within normal limits

What else would you like to know /do?
What investigations?
Differential diagnosis?
Management plan?
Question

• Screening methods currently used?
Possible tools

- 4 As test
- Nursing Delirium Screening Scale
- Delirium Observation Screening Scale
- OSLA
- RASS
- DRS R98
- CTD
- CAM
- CAM-ICU
- SQiD
- MMSE
- ACE-R
- Frontal assessment battery
- Praxis tests
- AMTS
- Digit span
- Serial 7s ....
<table>
<thead>
<tr>
<th>Study name</th>
<th>Comments</th>
<th>Test operator</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>LR+</th>
<th>Pre-test probability</th>
<th>Post-test probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cole 2003</td>
<td>CAM &gt; 6 symptoms vs DSM III-R for patients with dementia</td>
<td>Nurse</td>
<td>97.7</td>
<td>75.0</td>
<td>84.0</td>
<td>4.0</td>
<td>57.7</td>
<td>84.5</td>
</tr>
<tr>
<td>Cole 2003</td>
<td>CAM &gt; 6 symptoms vs DSM III-R for patients without dementia</td>
<td>Nurse</td>
<td>95.0</td>
<td>83.3</td>
<td>79.0</td>
<td>5.7</td>
<td>40.0</td>
<td>79.2</td>
</tr>
<tr>
<td>Laurila* 2002</td>
<td>CAM vs DSMIII-R</td>
<td>Geriatrician</td>
<td>81.0</td>
<td>71.7</td>
<td>50.0</td>
<td>2.9</td>
<td>25.9</td>
<td>50.0</td>
</tr>
<tr>
<td>Pompei 1995</td>
<td>CAM vs DSMIII-R without 4 patients for whom no results</td>
<td>Research Assistant</td>
<td>45.9</td>
<td>92.1</td>
<td>49.0</td>
<td>5.8</td>
<td>14.3</td>
<td>49.1</td>
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<tr>
<td>Rockwood 1994</td>
<td>CAM vs DSMIII-R raw data estimated based on sensitivity and specificity</td>
<td>Study physician</td>
<td>63.0</td>
<td>93.0</td>
<td>88.2</td>
<td>8.7</td>
<td>46.15</td>
<td>88.2</td>
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<tr>
<td>Rolfson 1999b CAM nurse</td>
<td>Nurse</td>
<td>12.5</td>
<td>100.0</td>
<td>100.0</td>
<td>NA</td>
<td>26.7</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Rolfson 1999b CAM [physician] vs DSM III-R [geriatrician]</td>
<td>Physician</td>
<td>69.6</td>
<td>100.0</td>
<td>100.0</td>
<td>NA</td>
<td>32.4</td>
<td>100.0</td>
<td></td>
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<tr>
<td>Rolfson 1999b MMSE</td>
<td>MMSE vs DSM III-R</td>
<td>Nurse/physician</td>
<td>34.8</td>
<td>81.2</td>
<td>47.0</td>
<td>1.9</td>
<td>32.4</td>
<td>47.0</td>
</tr>
<tr>
<td>Rolfson 1999b Clock Drawing</td>
<td>Clock-drawing test vs DSM III-R</td>
<td>Nurse/physician</td>
<td>8.7</td>
<td>97.9</td>
<td>67.0</td>
<td>4.2</td>
<td>32.4</td>
<td>66.7</td>
</tr>
</tbody>
</table>

NCGC 2010 Delirium: diagnosis prevention and management
Short CAM

I. ACUTE ONSET AND FLUCTUATING COURSE
1 a) Is there evidence of an acute change in mental status from the patient’s baseline?
1 b) Did the (abnormal) behaviour fluctuate during the day, that is tend to come and go or increase and decrease in severity?

II. INATTENTION
2) Did the patient have difficulty focusing attention, for example, being easily distractible or having difficulty keeping track of what was being said?

III. DISORGANIZED THINKING
3) Was the patient’s thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

IV. ALTERED LEVEL OF CONSCIOUSNESS
4) Overall, how would you rate the patient’s level of consciousness? –
-- Alert (normal)
-- Vigilant (hyperalert)
-- Lethargic (drowsy, easily aroused)
-- Stupor (difficult to arouse)
-- Coma (unarousable)

If yes to 1a, 1b and 2 and either 3 OR 4 a diagnosis of delirium is suggested.

Case 1

**Diagnosis**: acute psychotic episode with catatonic features / opioid related psychotic disorder.

Management: 1:1, clonazepam 1mg tds, risperidone 2mg bd, haloperidol 2.5mg bd (added)

**Progress on ward**:

**Physical health concerns**:
Mute and motionless for long periods with bradycardias and hypothermia
5/12 into admission – bradycardic and unresponsive following clopixol acuphase
6/12 one episode of loss of consciousness – awaiting 24 hour ECG
7/12 Emergence extrapyramidal symptoms – difficulty walking and abnormal limb movements
(d/w consultant neurologist – 2° antipsychotics)

8/12 into admission – loss of consciousness. Transferred medical hospital.
Anti-NMDAR encephalitis

- Immune mediated encephalitis
- NMDA R: ionotrophic glutamate cation channel
- crucial in synaptic transmission, plasticity and memory
- 72%– 83% psychiatric symptoms alone
- Recognition of symptom complex key to diagnosis:
  - Progressing from bizarre behaviour, psychosis, depression, mania, anxiety to memory defects, visual or auditory hallucinations.
  - seizures, dyskinesia, autonomic instability and catatonia.
- F>M (80%)
- Cause is ovarian teratoma in 50% F
- Potentially lethal but reversible, treatment responsive
- prognosis is good with early recognition and treatment
Phenomenological differences: delirium vs psychosis

Functional psychoses
- Disturbances thought / perception - complex well systematised.
- Consciousness, attention & memory less impaired (except acute phase)
- Thought content, hallucinations and thought disorder closely linked - relationship not found in delirium (Meagher et al, 2007)
- Behaviour goal directed not random interactions with environment

Delirium
- Disturbances thought / perception fragmentary & fluctuant.
- Thought content & perceptual disturbance – themes from immediate environment and circumstances
- FTD typically poverty and illogicality
- Presence of delusions / hallucinations did not correlate with thought process abnormalities
- Delusions and thought disorder correlate with affective lability (Meagher et al, 2007)
- Psychosis associated with degree and rate cognitive decline (Levy et al, 1996; Aalten et al 2005, Meagher et al, 2007)
Case 2

- 75 yo caucasian male transferred under S3 from a general adult psychiatric ward to your old age ward.
- 6 yr hx of mixed disease (Alzheimer’s and Vascular Dementia). 1 yr hx of aggressive behaviour – hitting his wife who he believed was having an affair, resulting in admission to a psychiatric ward. During the previous admission he had been violent to nursing staff and has kicked down doors and destroyed furniture in his room. He is severely dysphasic and disorientated to time, place and person. He shouts out at night and has been witnessed “putting himself on the floor” so that he now sleep on a mattress in his room. At times he appears to be picking at his bedclothes. His symptoms improved on the general adult ward with the use of two different antipsychotics and regular benzos. You have not witnessed any violence on the ward and he seems able to settle as long as he has the freedom to wander. The plan is to manage and monitor behaviour in order to assess for a suitable placement.
Case 2

- No past psych. hx of note.
- Past medical hx of hypercholesterolaemia, BPH, hypothyroidism, cataracts. Hypertension.
- Fhx: father postal worker died prostate cancer in his 80s, mother housewife died in RTA in her 40s. Has one brother (estranged) lives in US. Married with two sons who are well. No fhx history of dementia / neurological illness.
- Shx: ex smoker 10 year pack hx, previous excessive alcohol use. Tendency not to confide in others / little social support.
- Meds on admission:
  - thyroxine 75mcg od, amlodipine 10mg od, donepezil 10mg od, simvastatin, quetiapine 300mg on, Risperidone 1mg od + 2mg on, lorazepam 0.5mg bd, clonazepam 1mg on.
Case 2

• MSE: Mod kempt, well built, shuffling slow gait wandering around the room during assessment then walked out of room, no eye contact, unable to follow instruction, no social awareness. Incomprehensible spontaneous speech. Unable to access mood or thought content, non reactive affect with no range. At times responding to visual hallucinations. Not orientated, unable to comply with cognitive testing. Insightless.

• O/E
  – Would not comply with full physical exam – refusing to come into treatment room. Nursing staff managed to take vitals while briefly in the corridor sitting on a chair. Vitals within normal range.

What else would you like to know /do
Investigations?
Differential diagnosis?
Management plan?
Case courtesy of Dr Frank Gaillard, Radiopaedia.org
Case courtesy of Dr Frank Gaillard, Radiopaedia.org
## Phenomenological differences: delirium vs dementia

<table>
<thead>
<tr>
<th>DRS-R98 item</th>
<th>Controls (n = 40)</th>
<th>Delirium (n = 40)</th>
<th>Comorbid delirium-dementia (n = 40)</th>
<th>Dementia (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Sleep-wake cycle disturbance</td>
<td>0.7 ± 0.7</td>
<td>1.6 ± 0.8†</td>
<td>1.5 ± 0.7†</td>
<td>1.0 ± 0.6¶</td>
</tr>
<tr>
<td>2. Perceptual disturbances and hallucinations</td>
<td>0.1 ± 0.3</td>
<td>0.8 ± 1.2*</td>
<td>0.7 ± 1.0*</td>
<td>0.1 ± 0.3¶</td>
</tr>
<tr>
<td>3. Delusions</td>
<td>0.0 ± 0.0</td>
<td>0.2 ± 0.7</td>
<td>0.6 ± 1.0†</td>
<td>0.1 ± 0.5¶</td>
</tr>
<tr>
<td>4. Lability of affect</td>
<td>0.2 ± 0.4</td>
<td>0.9 ± 0.8‡</td>
<td>0.7 ± 0.7†</td>
<td>0.2 ± 0.4¶</td>
</tr>
<tr>
<td>5. Language</td>
<td>0.3 ± 0.5</td>
<td>1.3 ± 0.7</td>
<td>1.0 ± 0.8</td>
<td>0.9 ± 0.6</td>
</tr>
<tr>
<td>6. Thought process abnormalities</td>
<td>0.4 ± 0.5</td>
<td>1.9 ± 1.0‡</td>
<td>§1.1 ± 0.8*</td>
<td>0.6 ± 0.9¶</td>
</tr>
<tr>
<td>7. Motor agitation</td>
<td>0.1 ± 0.4</td>
<td>1.6 ± 3.4‡</td>
<td>0.9 ± 0.8‡</td>
<td>0.2 ± 0.4¶</td>
</tr>
<tr>
<td>8. Motor retardation</td>
<td>0.4 ± 0.5</td>
<td>1.3 ± 0.8‡</td>
<td>0.9 ± 1.0*</td>
<td>0.4 ± 0.5¶</td>
</tr>
<tr>
<td>9. Orientation</td>
<td>0.1 ± 0.2</td>
<td>1.4 ± 0.7*</td>
<td>1.4 ± 0.7*</td>
<td>0.9 ± 0.7</td>
</tr>
<tr>
<td>10. Attention</td>
<td>0.2 ± 0.4</td>
<td>2.2 ± 0.9*</td>
<td>2.1 ± 0.9*</td>
<td>1.6 ± 1.1</td>
</tr>
<tr>
<td>11. Short-term memory</td>
<td>0.2 ± 0.5</td>
<td>1.9 ± 1.0</td>
<td>2.0 ± 1.0</td>
<td>1.5 ± 1.2</td>
</tr>
<tr>
<td>12. Long-term memory</td>
<td>0.3 ± 0.5</td>
<td>1.3 ± 0.9</td>
<td>1.7 ± 1.0</td>
<td>1.1 ± 1.1</td>
</tr>
<tr>
<td>13. Visuospatial ability</td>
<td>0.3 ± 0.6</td>
<td>1.9 ± 1.0</td>
<td>2.3 ± 1.9</td>
<td>1.8 ± 1.0</td>
</tr>
<tr>
<td>14. Temporal onset of symptoms</td>
<td>0</td>
<td>1.5 ± 0.6‡</td>
<td>1.6 ± 0.7‡</td>
<td>0.1 ± 0.2¶</td>
</tr>
<tr>
<td>15. Fluctuation in symptom severity</td>
<td>0</td>
<td>1.1 ± 0.5‡</td>
<td>1.0 ± 0.6‡</td>
<td>0.0 ± 0.0¶</td>
</tr>
<tr>
<td>16. Physical disorder</td>
<td>1.0 ± 0.2</td>
<td>1.5 ± 0.5‡</td>
<td>1.7 ± 0.5‡</td>
<td>1.0 ± 0.1¶</td>
</tr>
</tbody>
</table>

*More impaired than dementia at p<0.05; †more impaired than dementia at p<0.01; ‡more impaired than dementia at p<0.001; §more impaired than delirium-dementia at p<0.001; ¶no difference between dementia and controls.
Phenomenological differences: delirium vs dementia

Figure 2  Boxplots of distribution of scores on the Cognitive Test for Delirium (CTD) spatial span item forwards (SSF) and backwards (SSB) for diagnostic groups.

Meagher et al, 2010
Phenomenological differences: delirium vs dementia

• All patients with apparent BPSD should be investigated for delirium
• Symptoms of delirium will dominate the clinical picture
• 3 core domains: inattention (cog deficits) – sleep-wake cycle disturbance and change in motor activity
• Delirium responds better to antipsychotics than do similar symptoms in BPSD
Case 3

• 74 yo caucasian male with an established history of BPAD under care of the CMHT. Previously had admissions for manic presentations and severe depression. For the last 5 years he has been well, on a small maintenance dose of risperidone. 4 months ago his wife died with breast cancer. His mood has been lowering since. You therefore added valproic acid (depakote) 500mg bd for combination therapy.

• Presenting with a 2/52 history of self-neglect. Eating only small amounts and not self-caring otherwise. Son manages to ensure he takes his medication. Spends his day lying in bed, reduced volume of speech – mainly monosyllabic in response, poor motivation and concentration. Denies any problems with sleep. Incontinent of urine.
Case 3

- His CPN notes psychomotor retardation and poor eye contact. She has never seen him so withdrawn. He continually closed his eyes and either would not listen or could not attend to her questions.
- Concerned about the presentation, new onset incontinence and acute history you request a medical assessment before considering admission to your ward. He is seen in A&E. His observations are unremarkable, there is nothing on examination, routine bloods are within range, urine dip was normal and an ECG was in NSR with no acute changes. He is “medically cleared”.
- You assess him on the Old Age Psychiatric ward.

What else would you like to do/ know?
Investigations?
Differential diagnosis?
Management plan?
Case 3

- PMhx: Type II DM, hypertension, GORD, COPD, pacemaker in situ - bradyarrhythmia
- Fhx: father died 80s dementia, mother died old age, hx depression mother. Married with one son.
- Shx: Occasional alcohol, smoker (20 pack year)
- Dhx:
  - omeprazole 20mg od
  - amlodipine 10mg od
  - Tiotropium TT bd inh
  - Salbutamol PRN
- MSE: lethargic, poorly kempt, inattention. Poor concentration. Psychomotor slowing. Able to follow instructions. Speech sparse and often monosyllabic in answers with long pauses. No formal thought disorder. Mood subjectively described as “I feel bad” objectively flat with decreased responsiveness. No psychotic symptoms elicited. Not orientated to time but aware he is in a hospital. States he is unwell. Unable to further elaborate.
- O/E
  - Vitals 112/60, p60 (paced rhythm) RR 14, apyrexial
  - Pacemaker scar
  - Chest clear
  - No positive neurological findings
Case 3

Progress:

- Ix: FBC, U+Es, LFTs, CRP, ESR, Ca, Phos, TFTs, B12, folate, lipids, glucose
- ECG: paced 70bpm
- MSU: Proteus - trimethoprim sensitive

Brain CT: NAD
Stays in bed. Little interaction with ward staff. Cooperative with medication but unable to self-care.
Agitated at times and calling out his wife’s name. Day and night time sleep.
Case 3

Valproate level - therapeutic 75 mg/l (50-100mg/l)
Liver USS normal
Venous serum ammonia
level was checked and found to be 360 mcg/dl (reference range=15-45mcg/dl)
Valproate stopped and lactulose 60 mg given.
1/7 ammonia level was 158 mcg/dl
4/7 normal at 44 mcg/dl
Confusion resolving, less disorientated
Over next 1/52 more able to interact, engage with staff and less psychomotor slowing.
Able to access mental state more fully…..
Valproic acid induced hyperammonaemic encephalopathy

- Few studies in psychiatric setting
- 51.2% inpatients on VA asymmptomatic hyperammonaemia (Raja et al, 2002)
- Mental status changes: psychosis / mania / depression
- No symptoms or signs hepatic injury / failure
- Acute onset – LOC, lethargy, vomiting, perserveration, aggression, ataxia, focal neurological signs
- Occurs wt therapeutic and subtherapeutic levels of VA
- No reassurance in prior safe treatment wt VA
### TABLE 1. Characteristics of Case Reports of Symptomatic Hyperammonemia Due to Valproic Acid Therapy in a Psychiatric Setting

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Length of Valproic Acid Treatment</th>
<th>Maximum Daily Dose of Valproic Acid</th>
<th>Valproic Acid Level&lt;sup&gt;a&lt;/sup&gt; (μg/ml)</th>
<th>Ammonia Peak (Serum)&lt;sup&gt;b&lt;/sup&gt; (μg/dl)</th>
<th>Symptoms</th>
<th>Risk Factors</th>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Settle (3)</td>
<td>57</td>
<td>Bipolar disorder</td>
<td>7 days</td>
<td>Not given</td>
<td>108 μg/ml</td>
<td>134 μg/dl</td>
<td>Coma</td>
<td>Unknown</td>
<td>Intubation, no others described</td>
</tr>
<tr>
<td>Nicolai et al. (6)</td>
<td>33</td>
<td>Schizophrenia</td>
<td>4 years</td>
<td>1000 mg</td>
<td>30 μg/ml</td>
<td>991 μg/dl</td>
<td>Coma</td>
<td>Unknown</td>
<td>Intubation, lactulose, neomycin, valproic acid stopped</td>
</tr>
<tr>
<td>Sewart (7)</td>
<td>79</td>
<td>Schizophrenia, epilepsy</td>
<td>2 days</td>
<td>2250 mg</td>
<td>48,500 μg/ml&lt;sup&gt;c&lt;/sup&gt;</td>
<td>151,571 μg/dl</td>
<td>Lethargy, confusion</td>
<td>Unknown</td>
<td>Lactulose, protein restriction, valproic acid stopped</td>
</tr>
<tr>
<td>Raby (8)</td>
<td>24</td>
<td>Borderline personality disorder, major depression</td>
<td>10 days</td>
<td>1000 mg</td>
<td>12.9 μg/ml</td>
<td>173 μg/dl</td>
<td>Lethargy, nausea</td>
<td>Unknown</td>
<td>Vegetarian, valproic acid decreased</td>
</tr>
<tr>
<td>Kimmel et al. (9)</td>
<td>38</td>
<td>Bipolar disorder</td>
<td>6 months</td>
<td>1000 mg</td>
<td>10.5 μg/ml</td>
<td>172 μg/dl</td>
<td>Lethargy</td>
<td>Vegetarian</td>
<td>Vegetarian, valproic acid stopped</td>
</tr>
<tr>
<td>Elguaid et al. (10)</td>
<td>50</td>
<td>Schizoaffective disorder</td>
<td>4 years</td>
<td>1250 mg</td>
<td>88 μg/ml</td>
<td>242 μg/dl</td>
<td>Possible seizure, Coma</td>
<td>Polypharmacy</td>
<td>Lactulose, valproic acid stopped</td>
</tr>
<tr>
<td>Barreto and Hack (11)</td>
<td>41</td>
<td>Bipolar disorder</td>
<td>3 years</td>
<td>Not given</td>
<td>73.5 μg/ml</td>
<td>642 μg/dl</td>
<td>Coma</td>
<td>Unknown</td>
<td>Comitine, lactulose, valproic acid stopped</td>
</tr>
<tr>
<td>Eze et al. (12)</td>
<td>69</td>
<td>Bipolar disorder, type 2, benzodiazepine dependence</td>
<td>4 days</td>
<td>750 mg</td>
<td>107.2 μg/ml</td>
<td>244 μg/dl</td>
<td>Coma</td>
<td>Unknown</td>
<td>Intubation, lactulose, valproic acid stopped</td>
</tr>
<tr>
<td>Pannikkat and Gilman (13)</td>
<td>53</td>
<td>Bipolar disorder, alcohol dependence</td>
<td>5 days</td>
<td>1750 mg</td>
<td>107 μg/ml</td>
<td>135 μg/dl</td>
<td>Lethargy, confusion</td>
<td>Unknown</td>
<td>Valproic acid decreased</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>Schizoaffective disorder, alcohol dependence, cocaine abuse intermittent explo-</td>
<td>14 days</td>
<td>1500 mg</td>
<td>70–80 μg/ml</td>
<td>329 μg/dl</td>
<td>Contusion</td>
<td>Unknown</td>
<td>Lactulose, valproic acid stopped</td>
</tr>
<tr>
<td>Yehya et al. (14)</td>
<td>9</td>
<td>Bipolar disorder</td>
<td>7 months</td>
<td>1500 mg</td>
<td>113 μg/ml</td>
<td>127 μg/dl</td>
<td>Violence, Lethargy, aggression</td>
<td>Unknown</td>
<td>Valproic acid stopped</td>
</tr>
<tr>
<td>Carlson et al. (15)</td>
<td>11</td>
<td>Asperger’s syndrome, attention deficit hyperactivity disorder (ADHD)</td>
<td>A few days</td>
<td>750 mg</td>
<td>87–90 (units not given)</td>
<td>213 (units not given)</td>
<td>Polypharmacy</td>
<td>Risperidone and valproic acid stopped</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Converted to μg/ml for comparison.
<sup>b</sup> Converted to μg/dl for comparison.
<sup>c</sup> In the original article, these values were reported as 48.5 mg/ml of serum valproic acid and 88 mmol/liter serum ammonia, both of which are 1,000-fold above the standard range.

VA hyperammonaemic encephalopathy

- Renal: VA effects uptake glutamine $\rightarrow$ $\uparrow$ NH3
- Liver: VA binds carnitine & CoA $\rightarrow$ $\uparrow$ NH3
- CNS: $\uparrow$ NH3 $\rightarrow$ $\uparrow$ glutamine in astrocytes $\rightarrow$ cerebral oedema & astrocyte dysfunction
- Risk factors: carnitine deficiencies
  - Genetic abnormalities
  - Dietary restrictions / nutritional intake
  - Polypharmacy
  - Other medical conditions
- Treatment: stop VA, lactulose, neomycin
Phenomenological differences: delirium vs depression

Depression

- Sustained alterations in mood more frequent in delirium than previously recognized
- Primary mood disorders rarely score significantly on formal measures of delirium severity (Leonard et al, 2008)
- Delirium less common in MDD than moderate (Leonard et al, 2009)
- Onset of depressive illness is generally less acute
- Mood disturbance dominates
- Cognitive impairment in depression resembles dementia (not delirium)
Audit presentation
Patient centred care

• After care:
  – 50% distressing memories of episode 6 /12 later (O’Keeffe, 2005)
  – psychological sequelae - depression and PTSD
  – Concerns about loss of mental faculties and independence.
  – Patients can be ashamed to admit to symptoms.
  – Persistent problems with attention and orientation
  – persistent delirium and dementia risk
Patient centred care

• After care:

  A follow-up visit with patients and, if possible, their carers.
15.7 Recommendations

Information and support

Offer information to people who are at risk of delirium or who have delirium, and their family and/or carers, which:

- informs them that delirium is common and usually temporary
- describes people’s experience of delirium
- encourages people at risk and their families and/or carers to tell their healthcare team about any sudden changes or fluctuations in behaviour
- encourages the person who has had delirium to share their experience of delirium with the healthcare professional during recovery
- advises the person of any support groups. [1.7.1]

Ensure that information provided meets the cultural, cognitive and language needs of the person. [1.7.2]
In summary…..

• Delirium is under diagnosed in elderly patients
• Delirium comprises a wide of range of symptoms
• Diagnosis can be improved by
  – awareness of hypoactive presentations
  – using simple screening instruments in normal practice
  – vigilance in those with risk factors
• Environmental strategies for treatment are effective but underutilised
• Short term use of neuroleptics are effective
• Continuous reassessment of causation may be warranted
Thank you for listening

a.sobel@nhs.net