Substance use and cognitive disorders in later life

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Alcohol related brain injury

• Covers a wide range of presentations
  – Mainly impaired memory, executive function, judgement

  – Umbrella term

Wernicke-Korsakoff Syndrome   “Alcohol related Dementia”

  - Thiamine deficiency
  - Alcohol induced toxicity

Other persistent alcohol-related cognitive impairment
  - TBI, CVD, depression, effects malnutrition / end organ dysfn etc
Alcohol related brain injury

• There are different considerations in older patients

• Numbers admitted UK with amnestic syndromes a/w alcohol by age
  – 15-59 yrs  ▲  <10%
  – 60+ yrs  ▲  140%
Alcohol – 56% dementia cases. But is it alcohol or poor diet, lifestyle, concomittant smoking, CVS disease, depression, social isolation, or failure to comply with medical management? **greatest modifiable risk factor.**
• Compare the projected effect size of the last slide with effect of ApoE4 status in late onset dementia:
  – Estimated around 7%.
Table 1. Alcohol drinking status, frequency and consumption among older Australians and all Australian adults, 2013 [5]

<table>
<thead>
<tr>
<th>Age group</th>
<th>Abstainers (%)</th>
<th>Drink daily (%)</th>
<th>Risky drinking (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>19.0</td>
<td>9.0</td>
<td>20.1</td>
</tr>
<tr>
<td>60-69</td>
<td>24.4</td>
<td>12.4</td>
<td>18.6</td>
</tr>
<tr>
<td>70+</td>
<td>40.3</td>
<td>14.7</td>
<td>10.1</td>
</tr>
<tr>
<td>All ages 18+</td>
<td>22.6</td>
<td>6.9</td>
<td>19.1</td>
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</tbody>
</table>

* at a level to be at risk of alcohol-related harm over a lifetime [4]
Baby Boomers are ageing:
more liberal attitudes to substance use.....
Alcohol in older patients

• Less does more
  Higher sensitivity to effects
  Decreased ability to metabolise

  Balance – Comorbidities, risks, cognitive reserve
The problem of comorbidities

• Often no single presenting problem cf. younger patients
• Frailty
• Increased risk for cognitive change
• Falls
• Iatrogenic harm – polypharmacy / hosp
• Metabolic changes

... Same goes for our brains as the rest of us
Benefits mainly confined to CHD

Countries where CHD risk low, Little or no benefit

Recent studies Dementia / alc : mixed
What are ‘safe’ levels of alcohol then?

- NHMRC guidelines (2009) for younger groups
  - UK guidelines
    - <14g = 1.5 units/d
    - <11 units per week
  - Binge defined as
    - >4.5 units for men
    - >3 units for women
Alcohol - comorbidities

- Alcohol affects many organ systems, not just CNS
- Neurological
  - Cerebellar dysfunction, Myopathy, Seizures, cognitive, peripheral neuropathy
- Cardiomyopathy
- Anaemia
- Hypoglycaemia, pancreatitis, hepatic dysfunction
- Nutritional deficiency – thiamine, piridoxine, etc
- Foetal alcohol syndrome
- Secondary – sleep disorders, stroke, depression, suicide

What is cause and what is effect can be unclear
So what is ‘old’ then?

Depends on drug misuse and comorbidities

Different ages depending on services

– Aged care >75
– MH services >65*
– D&A services 50+
– Medical wards UK studies

– General practitioners
The Silver Tsunami

By 2030 there will be 72.1 million older Americans
AOD use, depression, and suicide

• Older people self report drinking for pain, meaningless life, anxiety / mood, loneliness, sleep problems

• Psychological autopsy 261 suicides aged 35+ and 73 aged 70+  
  De Leo and Draper 2013
  – 22% alcohol abuse
  – 18% other substances
Pattern of use in later life

• Long history which persists into older age ("survivors"), 2/3 of US problem drinkers
  – Often mult comorbidities
  – Less intact relationships, more likely depression etc
  – Might have better understanding of psych / AOD services but less success utilising these on their own
Pattern of use in later life

• About 1/3 commence in later life ("reactors")
  – Adjustment (retirement, bereavement, illness)
  – Collateral info from families – often unaware
  – Underestimate harms given older age
  – May forget amounts if early dementia

• Cf survivors – less knowledge of available help but better prognosis
Pattern of use in later life

- Previously “unproblematic” use continues into older age but now with complications – “maintainers”

- E.g. 66 yo lady, 6 years bereaved, always 2 glasses wine /d over 40 years, lives by self, now p/w falls while at social functions. GP finds abnormal liver function and hypertension, poor balance
Acute alcohol use disorders

Think of if confused / agitated, sleep/wake disturbance, hallucinations

• Intoxication / withdrawal
• Wernicke’s
• Delirium - DT’s or delirium due to another medical illness
• Treat as urgent, high rates morbidity / mortality
• Other - Hallucinosis
  • AH, VH, paranoid delusions
    – Higher morbid jealousy
Wernicke’s

• Severe thiamine deficiency: malnutrition, persistent vomiting, GIT / bariatric surgery, anorexia
  – Caine’s criteria (1997): at least 2 of
    • Dietary deficiency
    • Oculomotor signs (nystagmus, palsies)
    • Cerebellar dysfunction
    • Either altered mental state or mild memory impairment
  – Increases diagnostic sensitivity from 20% to 85%
Wernicke’s

• Only a minority suspected during life: 20%
• 10 – 20% only with classic triad of signs
• Of those cases suspected,
  – 30% alcohol dependent
  – 6% non-alcohol dependent
• Untreated: up to 20% mortality, 85% survivors develop KS

• Developed world: decreasing population prevalence (thiamine in bread); increasing frequency in patients with previous AUDs (e.g. 19% forensic patients)
Korsakoff’s psychosis

Originally described in 30 patients alcohol abuse, and 16 cases unrelated to alcohol

• Spectrum with ARBD
• Arises from WE
• Confusion, oculomotor abnormalities, ataxia
• MRI – graded volume loss
  – “uncomplicated” alcoholism: milder; frontal cortical volume loss
  – WE: Neuronal loss and haemorrhagic lesions periaqueductal grey matter and paraventricular lesions, mamillary bodies
  – KS: thalamus as well
• Heterogenous group so incidence unclear
63 yo man, Normal control

59 yo man, alcoholism

63 yo man, WKS
Alcohol related dementia

Rare by itself; more common in YOD – 4th most common
• Recognised in ICD 10 / DSM 5
• But debate whether it is separate entity or not
  – Course often fluctuates
  – Effects alcohol neurotoxicity rare in isolation cf effects thiamine / vasc / HI / liver disease
  – ECA study : OR 1.5 or Liverpool longitudinal study OR 4.5 for cog disorders in general
  – Outpatient consecutive diagnoses neurdegen clinic : 1.1%
  – Draper 2011 : 20000 consecutive dementia admissions for patients > 50 yo : 1.4%
  – YOD – between 5 - 10 % of cases; “reversible dementias” 5%
Draper et al 2011: Dementia diagnosis by age in NSW hospitals – 2006/7

ARD 1.4% of total
Not all alcohol dependent people develop lasting cog impairment

• Bouts of thiamine deficiency likely in 80% alcoholics yet only about 13% of these develop WKS

• Female : increased vulnerability
  – Males × 1.7 despite 3 – 4 increased rates dependence
  – Women – greater frontal grey matter loss on MRI
  – After detox : do men do better??
  – Reduced tolerance and different body composition

• Correlation between WE and per capita alc consumption not found

• Genetic differences tolerating borderline $B_1$ deficiency, metabolising, $B_1$ transport, ApoE4...
Outcomes

• ARBD can improve, rule of quarters:
  – ¼ complete recovery
  – ¼ significant recovery
  – ¼ slight recovery
  – ¼ no recovery

• If abstain and good nutrition over 2 years in NH care, only AD or VaD patients had degenerative course
Is there ‘pure’ alcohol dementia?

• Incidence with age
• Pathology: primary ‘toxicity’ (effects of alcohol), or thiamine deficiency?
• ARBD can improve with time in some patients
• In ‘older’ patients cognitive changes likely comorbid with VaD, AD
• The problem is one of comorbidities and what is the main problem in this patient
So...

- Look out for comorbidities: apathy / depression / vascular change and subcortical impairment / end organ effects / frailty and risks of further morbidity e.g. falls
- Physiological changes in older people mean commonly quoted upper limits ‘safe’ consumption are NOT safe
- Treat recent unexplained confusion / mental state changes in an alcoholic as an emergency. Everyone should get thiamine if nutrition status in doubt
- With abstinence cognition can improve
- If on longitudinal assessment there is cog decline think of another primary neurodegenerative process
Benzodiazepines

- Prescribed for sleep, anxiety – often symptoms of depression
- Risk of dependence and withdrawal (seizures, depirium, tremors)
- Slow reduction : <10% /week
Benzos and cognition

- Bias of published results: the ‘file drawer’ problem
- Still, evidence of increased cognitive impairment with LT use

Barker et al 2004

Fig. 1. Weighted mean effect sizes and 95% CIs for the performance of patients who were taking benzodiazepines on tests of various cognitive function categories. A negative effect size indicates that patients were performing worse than controls upon assessment.
Opiates

- Increasing use in last 10 years, first rise in death rates in that time in Australia
- Deaths – 500 in NSW in 2008;
  - >700 in NSW in 2010, only 30% due to heroin
- Older: chronic pain management
  - RF: higher pain, depression scores with lower disability levels a/w opioid misuse
  - Living alone, unemployed, polysubstance use
  - Alcohol, Benzos, THC, other e.g. amphetamines

Draper 2014 and NDARC 2012

Park & Lavin 2010
Opiates – cognitive effects

• Both acute and chronic effects of opiate abuse on neuropsychology testing performance

• Attention, concentration, processing speed, spatial skills, recall. Greatest effect (LT) on executive function (flexibility, set shifting, inhibition)

• Chronic pain + LT opiate therapy: estimated cog effects in 20 – 62% of patients

• Predictors
  – Depression, degree of pain + distress
Opiates – cognitive effects

• Darke et al 2012: 125 opioid maintenance, mean age 30
• Impaired executive function, info processing, verbal and non verbal learning
• Lizentaris and Draper 2016 studied health needs of older D+A clients aged 50 – 71
  – Cog changes methadone > suboxone but less than alcohol using the Addenbrooke’s (small numbers)
• Predictors
  – depression
Cannabis

- Endocannabinoid system
  - Multiple end receptor effects, second messenger systems (cAMP, K+, Ca, prot-kinase, cFOS, cJun, etc, GABA transmission)
  - CB₁ – brain, lungs, liver, kidneys; CB₂ – immune / haematopoietic cells; there are more....

Can’t separate “beneficial” from “undesirable” effects
THC is perceived as not harmful, even healthy...
Cannabis and cognition in elders

- Attention and memory
- Impairments a/w earlier age of use / frequency / duration
- Studies mainly middle life, not elders
- Mixed findings
  - ECA study: 12 year f/up, no Δ MMSE under 65
  - Are cog changes related to personality? Sanchez-Torres 2013

  .... No :
THC and cognition (ctd)

- Comparing heavy users with recreational users
- Decreased grey matter volumes in nearly all areas / networks known to have CBD receptors
  - Motivation, emotion, emotional learning
  - i.e. hippocampus, insula, ventromed + orbitofrontal
- Either starting in adolescence or with heavy use
- Other studies: atrophy of white matter tracts
What about medicinal cannabis?

• Pharmacotherapy or potential drug interactions in elderly not known

• Different strains / mixes of CBD’s

• Largest study I found – 2700 pts, Israel

• Largely well tolerated, 18% discontinued

<table>
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<tr>
<th>Indication</th>
<th>Number of patients (N = 2736)</th>
</tr>
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<tbody>
<tr>
<td>Cancer associated pain</td>
<td>1001 (36.6%)</td>
</tr>
<tr>
<td>Nonspecific pain</td>
<td>821 (30.0%)</td>
</tr>
<tr>
<td>Cancer – chemotherapy treatment</td>
<td>661 (24.2%)</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>146 (5.3%)</td>
</tr>
<tr>
<td>Others</td>
<td>49 (1.8%)</td>
</tr>
<tr>
<td>Post-traumatic stress disorder</td>
<td>21 (0.8%)</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>10 (0.4%)</td>
</tr>
<tr>
<td>Amyotrophic lateral sclerosis</td>
<td>9 (0.3%)</td>
</tr>
<tr>
<td>Compassion treatment</td>
<td>7 (0.3%)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>5 (0.2%)</td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td>4 (0.1%)</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>2 (0.1%)</td>
</tr>
</tbody>
</table>
In summary

- Cognitive impairment is common anyway, with increased risk for elder substance users.
- Disentangling cause + effect – problem of comorbidity, underlying vulnerabilities.
- Diagnostic issues – think of pathology.
- With chronic use: apathy / depression / vascular change and subcortical impairment.
- And the effects of comorbid psych issues.

This will inform your engagement and future management for this particular patient.