Opioids and cognitive impairment and dementia

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UNDER THE STEWARDSHIP OF MARY AIKENHEAD MINISTRIES

Definitions

Dementia

Chronic disorder of at least two mental processes

Caused by disease or injury

Characterized by memory deficit, personality change, impaired reasoning

Cognitive impairment

Can be acute or chronic

Impairment in one or more processes

Including remembering, learning, concentration, making decisions

Risk factors for dementia

- Approximately 40% of dementia cases are attributable to a combination of potentially modifiable risk factors
  - Hypertension
  - Mid-life obesity
  - Diabetes
  - Physical inactivity
  - Hearing loss
  - Late-life depression
  - Social isolation
  - Early life low educational attainment
  - Smoking
  - Mid life alcohol (>21 standard drinks/week)

  (Early life <45yo, Mid-life 45-65yo, Later life >65yo)

- The strongest (non-modifiable) risk factor dementia is age – the incidence of Alzheimer's doubles every 10 years after the age of 60

Do opioids *per se* contribute to dementia syndromes?

Dementia syndromes

- Multiple distinct syndromes with specific clinical, diagnostic and pathological aspects
  - Alzheimer's disease (most common, 50-80% of dementia)
  - Vascular dementia (2nd most common, metabolic risk factors)
  - Dementia with Lewy bodies and Parkinson's disease
  - Frontotemporal dementia
  - Mild cognitive impairment

Do opioids contribute to any or all of these forms of dementia syndromes?

Opioids and cognitive impairment (1)

- Longstanding postulation that illicit intravenous opioid use is associated with neuropathological effects
  - Evidence of IV drug use being linked to hypoxic brain injuries (lack of oxygen) [1]
  - Evidence of activation of microglial cells (supportive cells in central nervous system) [2] *hence CNS inflammation*

- One study in 2005 compared post mortem evaluations of drug-related deaths in young adults (n=34) to age-matched non-drug users (n=16) [3]
  - Detailed immunohistochemical analysis of hippocampus, brainstem and basal ganglia for signs of pathology: *hyperphosphorylated tau, β-amyloid, β-amyloid precursor protein, ubiquitin and neurofibrillary tangles*

  - Demonstrated excess of neuropathogenic process in drug-use population with prevalence of 59% compared to 23% in control (p=0.0012)

BUT

Opioids and cognitive impairment (2)

No suggestion of cognitive impairment was displayed in either cohort

[1] https://pubmed.ncbi.nlm.nih.gov/10423852/

[2] https://pubmed.ncbi.nlm.nih.gov/10564526/

[3] https://pubmed.ncbi.nlm.nih.gov/16008828/

Opioids and cognitive impairment (3)

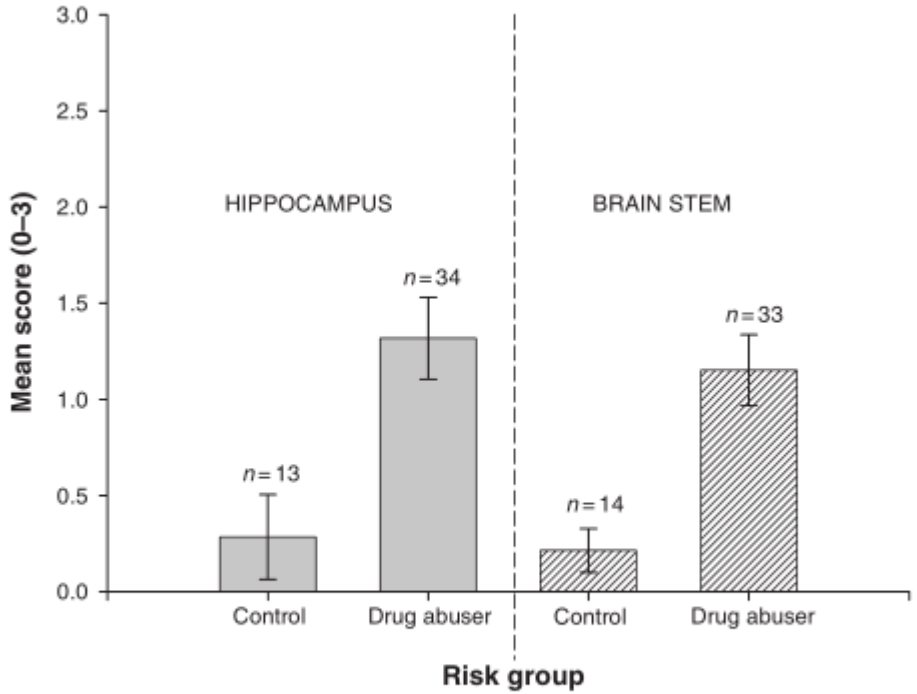

Figure 3. β-amyloid precursor protein immunohistochemistry in controls and drug abusers.

Table 4. Scoring system for immunopositive features

Score	*Tau (NFT and pre-tangles)*	*Tau (NTh)*	*βAPP*	*Ubiquitin*
0	Negative	Negative	Negative	Negative
1	1–2 tangles	1–5 NTh	Trace	Mild
2	2–5 tangles	5–20 NTh	1–10 foci	Moderate
3	5+ tangles	20+ NTh	10+ foci	Severe

βAPP, β-amyloid precursor protein; NFT, neurofibrillary tangles; NTh, neuropil threads.

[3] https://pubmed.ncbi.nlm.nih.gov/16008828

Opioids and cognitive impairment (3)

- Well established short term effects of opioids on cognitive function
  - Impaired concentration
  - Sedation
  - Slowing of information processing
  - Tracking impairment and dynamic visual acuity changes
- Limited evidence to suggest long term opioid use associated with cognitive impairment
- One cohort study reviewing safety of driving whilst on long term opioid agonist therapy reflected no difference in accidents or traffic violation rates (with suboxone having lower rates than methadone) [4]
- One cross sectional analysis of 41 participants on opioid agonist therapy revealed better psychomotor performance amongst participants on suboxone therapy compared to methadone [5]

[4] https://pubmed.ncbi.nlm.nih.gov/26256593/
[5] https://pubmed.ncbi.nlm.nih.gov/11748323/

Opioids and cognitive impairment (4)

- **Case** series of 20 patients with opioid dependence treated with suboxone longitudinally monitored over 6 months reported **improved neuropsychological function** (particularly in domains of learning and memory) with ongoing adherence [6]

Table 4 Participant neuropsychological (NP) characteristics at baseline and follow-up ($N = 20$)

	Time 1 T-score *M*(*SD*)	Time 2 T-score *M*(*SD*)	sRCS *M*(*SD*)
NP Domains			
Global	41.8 (6.4)	44.5 (6.2)	−.01 (.46)
Learning	36.2 (11.7)	37.8 (9.3)	−.22 (.50)
Memory	36.9 (12.2)	38.5 (11.4)	−.12 (.89)
Verbal Fluency	46.3 (9.0)	47.3 (12.0)	−.13 (.94)
Processing Speed	49.5 (8.6)	52.2 (8.8)	−.09 (.88)
Attention/Working Memory	44.3 (8.0)	46.9 (9.2)	.04 (.98)
Motor	39.2 (9.9)	42.9 (9.0)	.09 (.68)
Executive Functioning	41.7 (6.7)	46.2 (8.8)	.41 (.92)

Notes. sRCS summary regression-based change scores

[6] https://pubmed.ncbi.nlm.nih.gov/29141650/

Confounders

Concurrent issues common in opioid dependent population

- Polypharmacy (prescribed and illicit)
- Malnutrition
- Depression *(common mimic for cognitive impairment)*
  - Patients with depression are more likely to complain about memory loss than those with no depression
  - Depression is well established in cohort with opioid dependence
    - Cross sectional study revealed 50% of patients on opioid agonist therapy suffered from depression with concurrent risk factors including concurrent psychiatric diagnosis, use of psychotropic medication, benzodiazepine use/abuse and methadone dose >120mg/day [6]

[7] https://pubmed.ncbi.nlm.nih.gov/17055063/

References

[1] https://pubmed.ncbi.nlm.nih.gov/10423852/
[2] https://pubmed.ncbi.nlm.nih.gov/10564526/
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any
questions?