PRESCRIBING PRACTICE IN DELIRIUM

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Learning outcomes

- Modifiable medication risk factors for delirium
- An appreciation of contributing factors – modifiable with medicines
- Pharmacological treatment recommendations

ICU Delirium
Definition

"A disturbance of consciousness and cognition that develops over a short period of time (hours to days) and fluctuates over time"

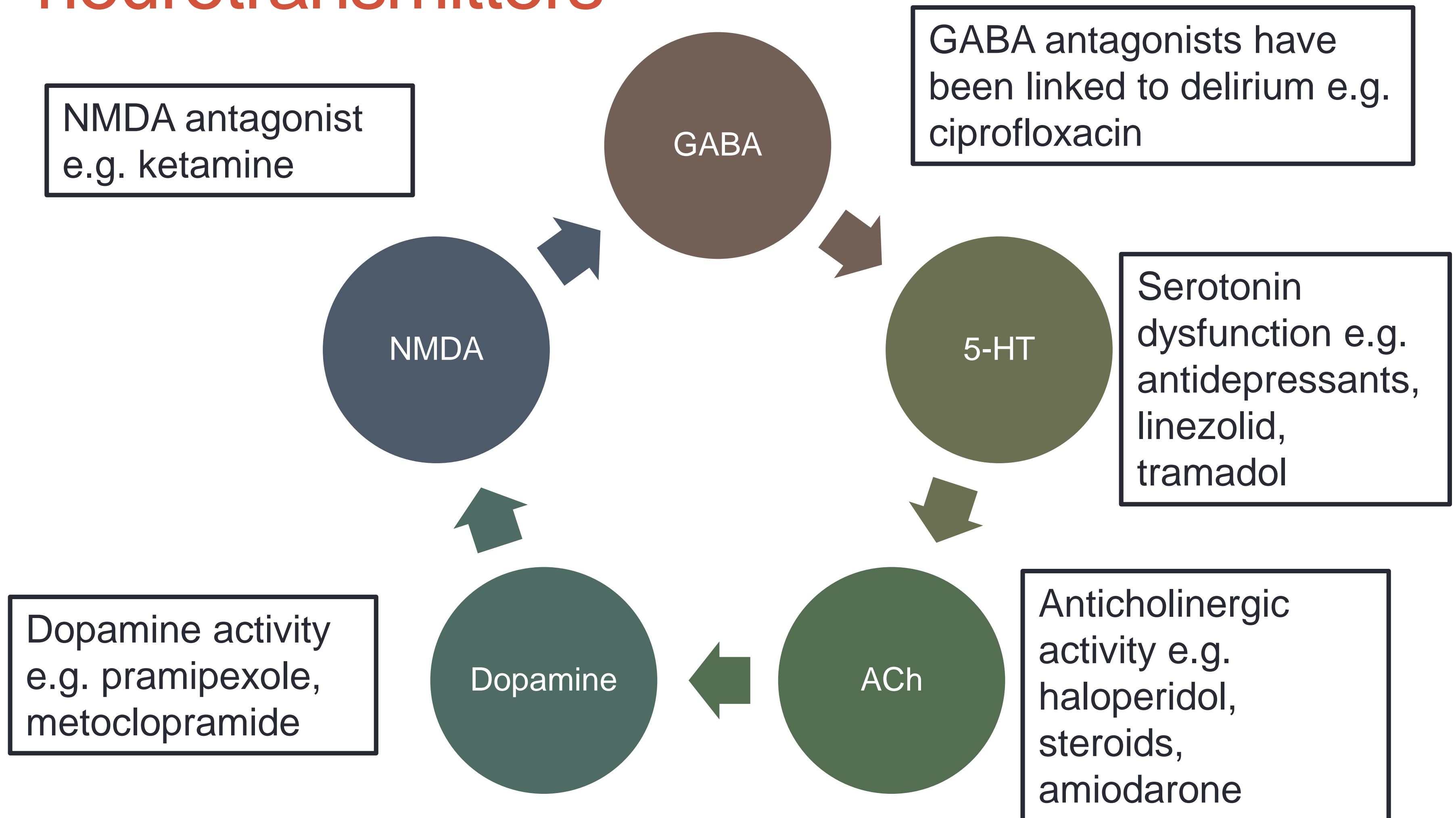
Pathophysiology of delirium…

and why medicines matter

Neurotransmitter imbalances that increase incidence of delirium:

- Reduced ACh
- Over/ under activity of dopamine
- Increased/ decreased serotonin activity
- Reduced GABA activity

The effect of drugs on implicated neurotransmitters

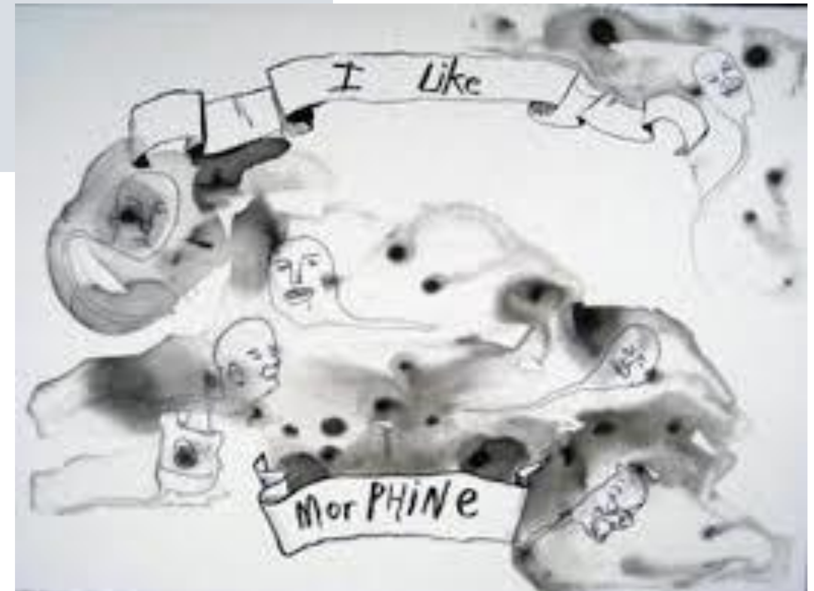


Delirium, Medicines and the literature

- PADIS guidelines
- NICE CG103
  - Not ICU specific
- ICUdelirium.org
  - ABCDEF
- ICS
  - Detection, Prevention and Treatment of Delirium in Critically ill Patients
- GPICS

A medication focus to delirium…

1. **Review** medication causes
2. **Optimise** therapeutic strategies to prevent contributing factors
3. Consider pharmacological **treatments**
4. **Collaborate** with all aspects of the overall delirium plan

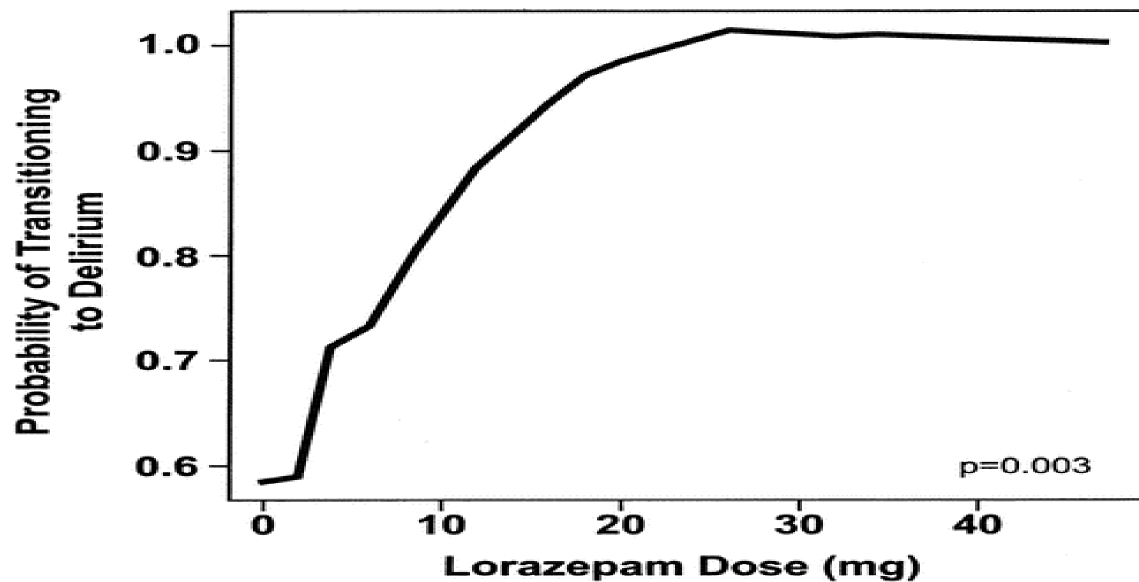


Medication risk factors

- Analgesics:
  - Codeine
  - Tramadol
  - Fentanyl
  - Pethidine
- Antidepressants
  - Amitriptyline
  - Paroxetine
- Anticonvulsants
  - Phenytoin
  - Phenobarbital
- Antihistamines
  - Chlorphenamine
  - Promethazine
- Anti-emetics
  - Prochlorperazine
- Antimuscarinics
  - Atropine
  - Hyoscine
- Miscellaneous
  - Furosemide
- Cardiovascular:
  - Atenolol
  - Digoxin
  - Dopamine
  - Lidocaine
- Steroids:
  - Dexamethasone
  - Hydrocortisone
  - Prednisolone
- Hypnotics:
  - Diazepam
  - Lorazepam
  - Chlordiazepoxide

Medication risk factors

- Medicines associated with a higher incidence of delirium:
  - Benzodiazepines –Lorazepam and midazolam

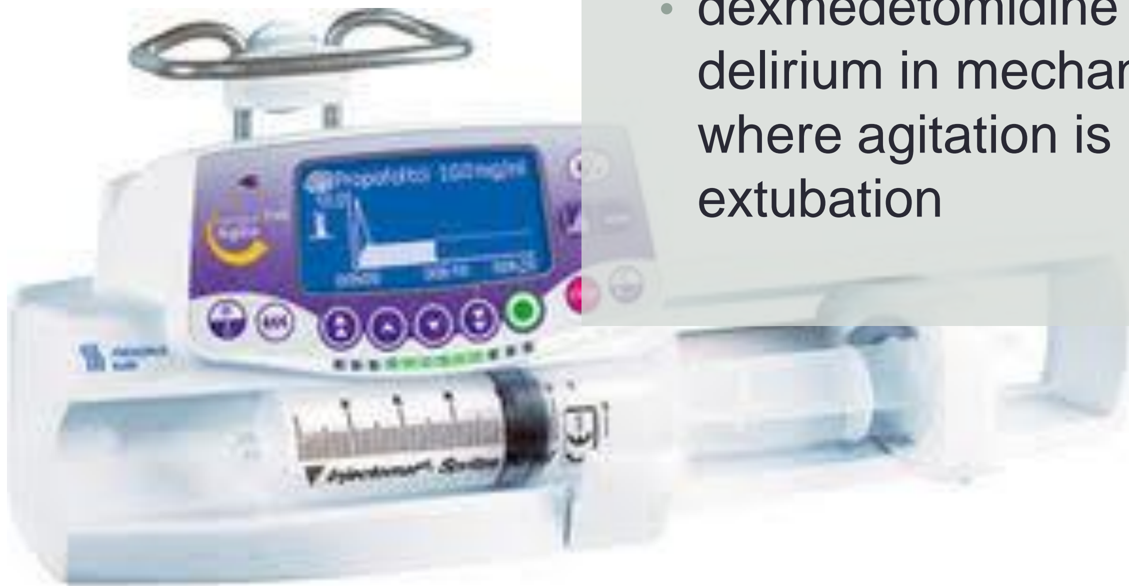


Modifiable risk factors -medicines

- Sedation
- Analgesia
- Withdrawal syndromes
- Bowel management –constipation
- Urinary retention
- Sleep
- Underlying psychiatric condition

Sedation practices and delirium

- Recommendations for avoiding or improving delirium:
  - Light sedation recommended (RASS > -2)
  - Non-benzodiazepine sedatives improve short term outcomes including delirium
  - dexmedetomidine could be used for delirium in mechanically ventilated adults where agitation is precluding weaning/ extubation



Other considerations: withdrawal

Opioid withdrawal

- Incidence 17% (approx)
- In patients diagnosed with opioid withdrawal 44% have been found to be CAM-ICU positive
- Predicting onset
- Objective assessment
- Principles:
  - Replace
  - Substitute
  - Weaning
  - Monitoring throughout

Clinical opioid withdrawal scale **COWS**

Nicotine withdrawal

- Altered neurotransmitter balance
  - Dopamine, glutamate, GABA
- Insufficient evidence to support routine use of replacement therapy
- Reserved for those experiencing agitation attributable to nicotine withdrawal
- Side effects
- Options available

Alcohol withdrawal

- The difficulties of diagnosis
- Symptom triggered withdrawal
- Management:
  - Benzodiazepines
  - Pabrinex

PHARMACOLOGICAL TREATMENT OF DELIRIUM

Recommendations from PADIS and elsewhere…

Pharmacological treatment recommendations

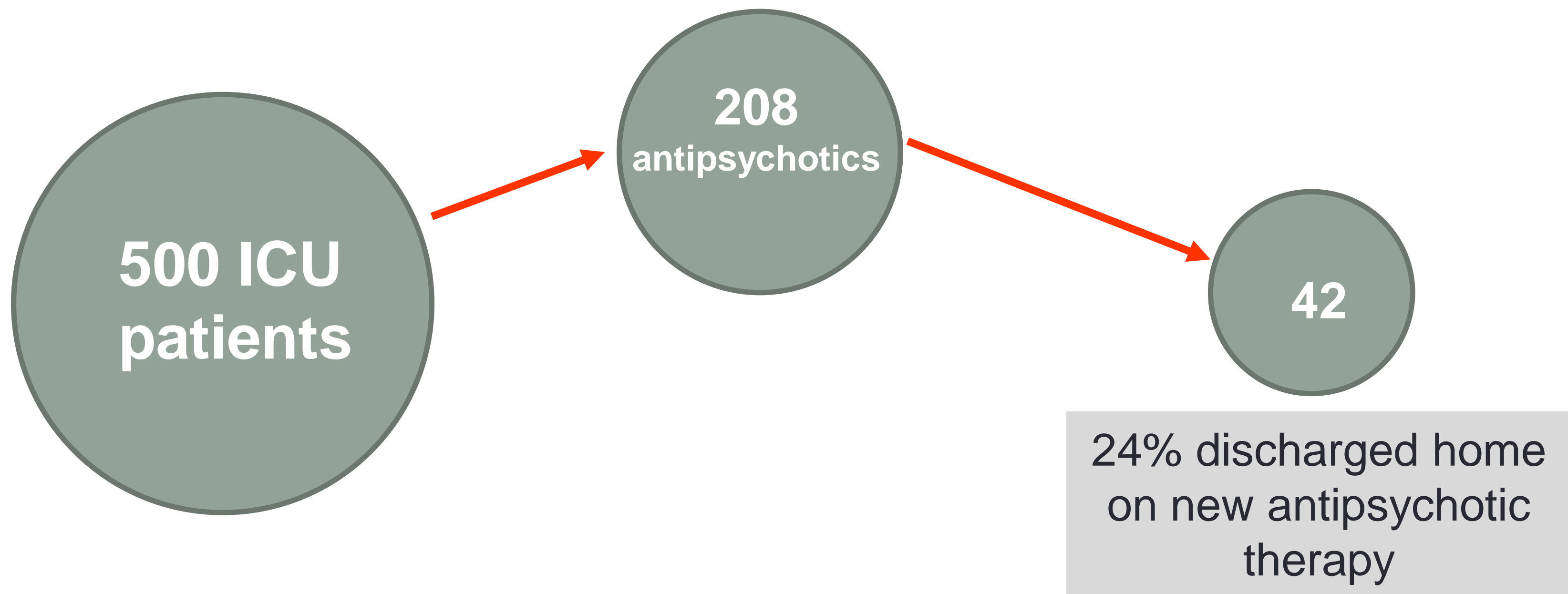
- Pharmacological agents should not be used routinely to prevent delirium

Pharmacological treatment recommendations

- Haloperidol, atypical antipsychotics and statins should not be used routinely to treat delirium (with a caveat)

Pharmacological treatment recommendations

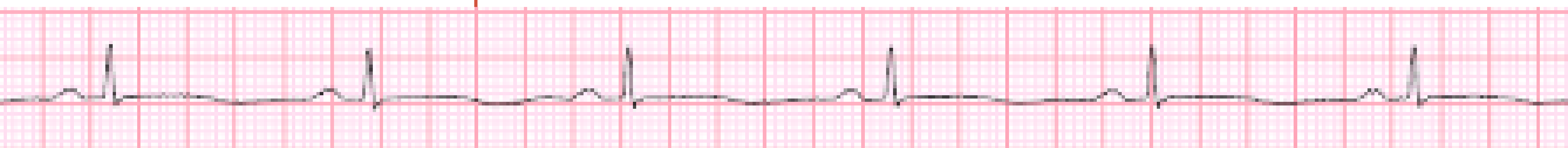
- Antipsychotics should be reviewed regularly and be stopped as soon as appropriate to do so



Tomichek et al. Antipsychotic prescribing patterns during and after critical illness: a prospective cohort study. Crit Care. 2016 Nov 24;20(1):378.

Haloperidol

- Dopamine receptor antagonist
- Clinical considerations:
  - Avoid completely in Parkinson's
  - Licensing considerations
  - QTc prolongation
  - Ventricular arrhythmias
  - Extrapyramidal side effects
  - Neuroleptic malignant syndrome
- Dose: 2-10mg 6 hourly

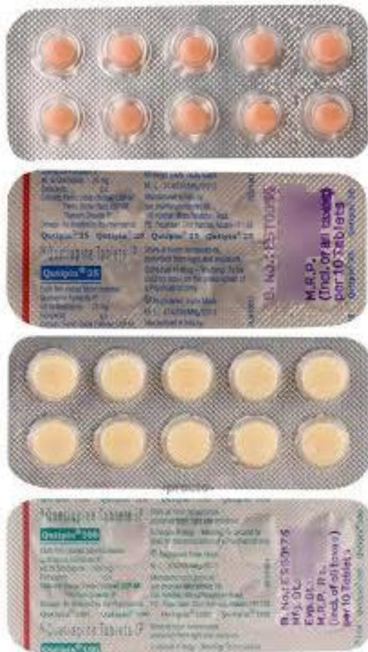


Atypical antipsychotics

Quetiapine

Olanzapine

Risperidone

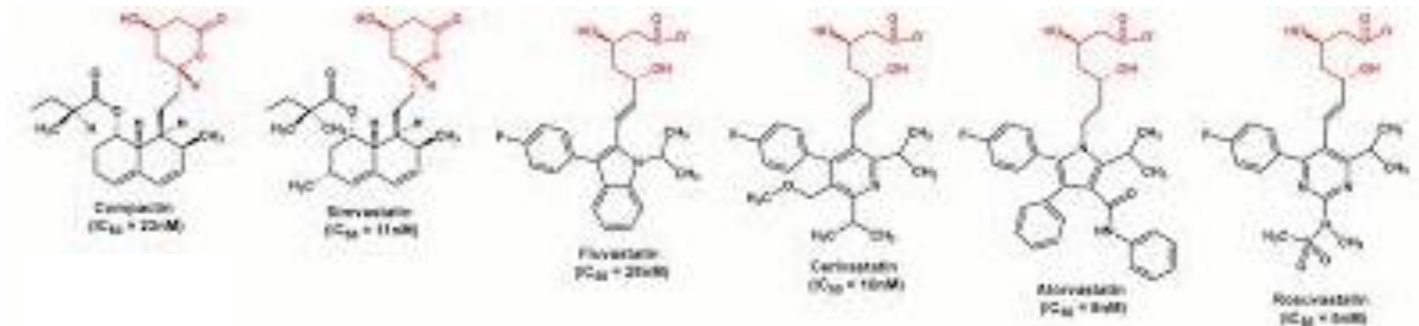


- Different profiles:
  - Route
  - Dose
  - Side effect profiles (lower risk option)
    - Seizures (Risperidone)
    - QT prolongation (Aripiprazole)
    - Cardiovascular disease (Quetiapine)
    - Hepatic impairment (Haloperidol)
    - Parkinson’s (Quetiapine)

Statins?

- Hypothesis: Statins have effects on inflammation and coagulation that may interrupt delirium pathogenesis

- The evidence so far:
  - Ongoing statin use associated with a lower risk of delirium
  - Addition of statins seems to reduce delirium risk also
  - Statin users experienced reduced delirium (odds ratio 0.47) [Simvastatin > Pravastatin > Atorvastatin]



Methyl-phenidate

- Often used as a stimulant for treating ADHD (Ritalin®)
- Considered for hypoactive delirium
  - Very limited evidence
  - Shown to improve mini-mental state performance in cancer patients with hypoactive delirium
- Starting dose 10mg twice daily (0800 and 1200)
- Titrated in 5mg increments

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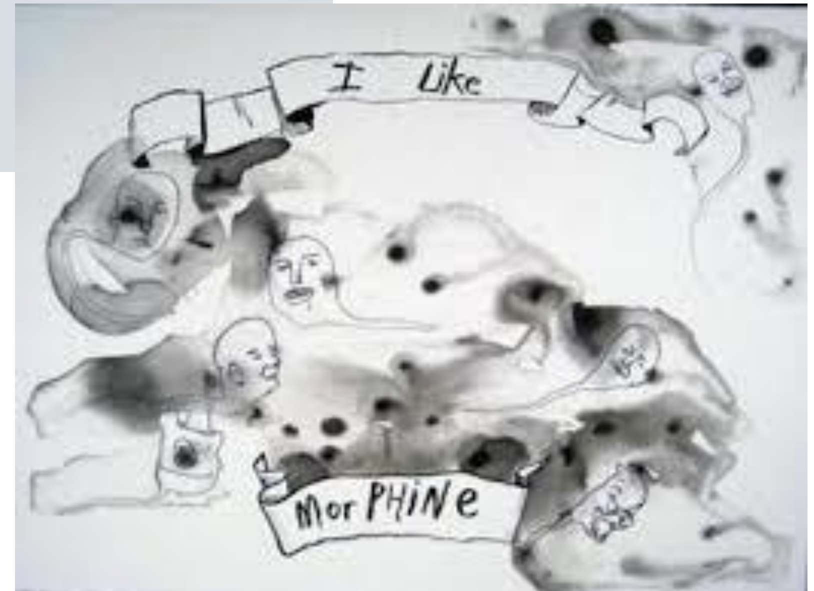

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