Tell Me Again

Tram Nguyen, MD - PGY2
Suhail Sheikh, MD

San Mateo County Behavioral Health and Recovery Services

Disclosures

- I have no financial and nonfinancial disclosures
- I have no actual or potential conflict of interest in relation to this presentation
- I will be discussing “off-label” uses of medications

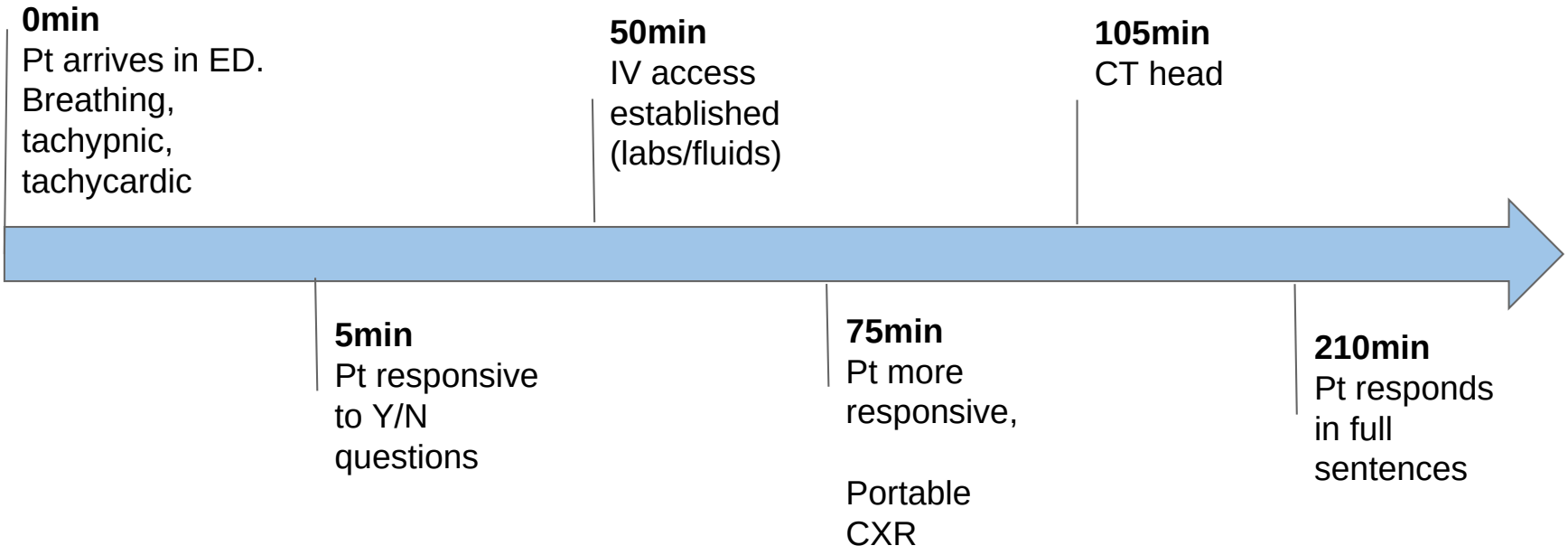
History of Present Illness

- A young male was found down for unknown amount of time by a friend in a hotel room
- Friend administered 4mg intranasal Narcan x2 without improvement
- Emergency personnel alerted and patient was brought into ED

Initial Physical Exam

- Constitutional: Appears distressed
- Neurological: oriented to person, awakens to voice, follows 1-step command, moving all 4 extremities
- Card: tachycardia, regular rhythm
- Pulm: tachypnea, effort normal, no wheezes/rales

ED Course


0min
Pt arrives in ED. Breathing, tachypnic, tachycardic
5min
Pt responsive to Y/N questions
50min
IV access established (labs/fluids)
75min
Pt more responsive,
Portable CXR
105min
CT head
210min
Pt responds in full sentences

Laboratory

BMP:

Na 140
K 5.2
Cl 100
Cr: 2.06

LFT:

AST 408
ALT 324

CBC:

WBC 19.1
Hgb 15.1
Plt 229

Ck: 10,041

Toxicology:

(+) benzo, opioid, meth

(-) salicylate, acetaminophen, ethanol

- ➔ Acute Kidney Injury
- ➔ Metabolic Acidosis
- ➔ Rhabdomyolysis
- ➔ Transaminitis

Imaging/Procedures

CT Head: Negative for acute intracranial process

EKG: unremarkable

CXR: ? L infiltrate, otherwise remarkable

EEG: unremarkable

Repeat physical exam - 24hrs

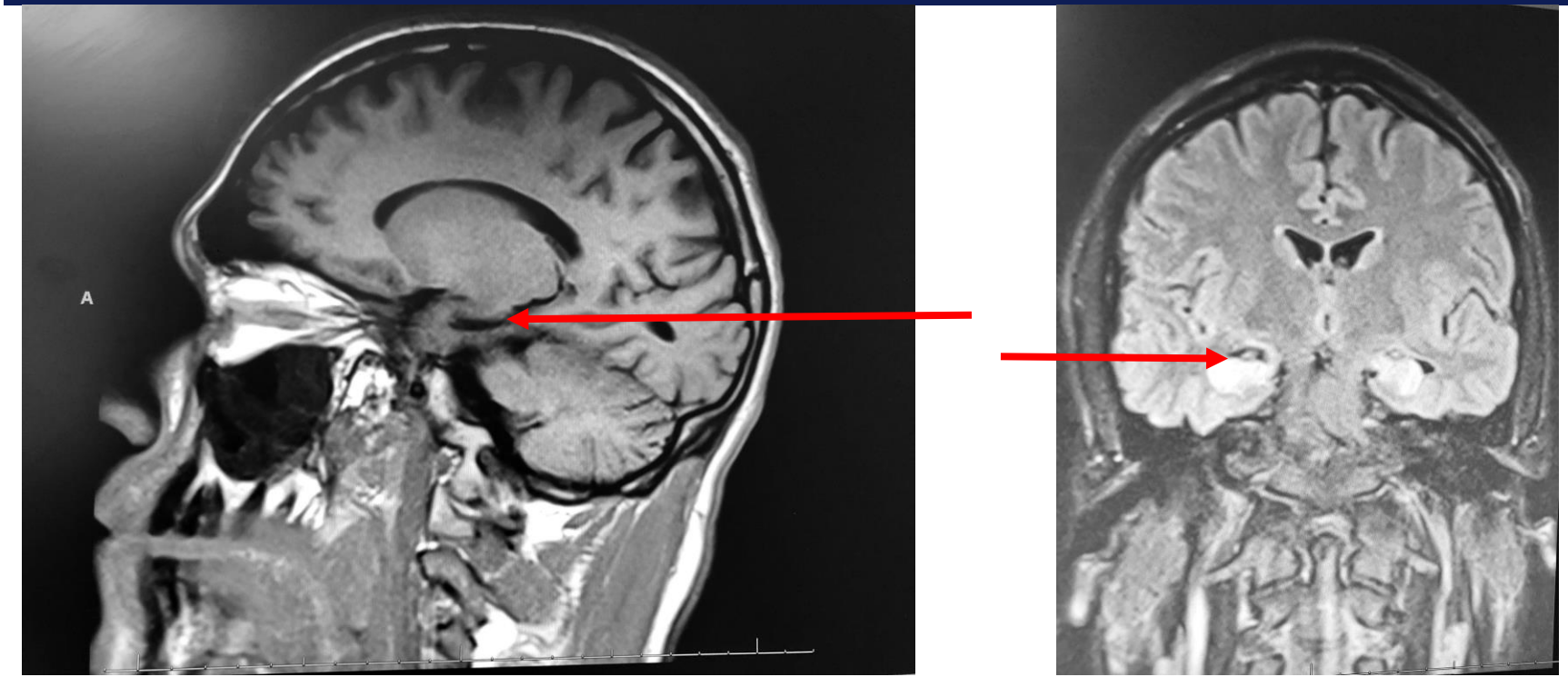
Constitutional: No acute distress, alert & oriented to person, appears confused and repeatedly asked where he was every 2-3mins

Neurological:

- Concentration fair
- CN II-XII intact
- 5/5 motor strength bilaterally
- Intact to pinprick sensation b/l
- Speech within normal limits
- Word recall: ⅗ after 1 min, 0/5 after 3 min
- Planning/sequencing/judgement intact
- Naming intact
- Episodic memory intact
- *Procedural memory not tested*

Pure anterograde amnesia

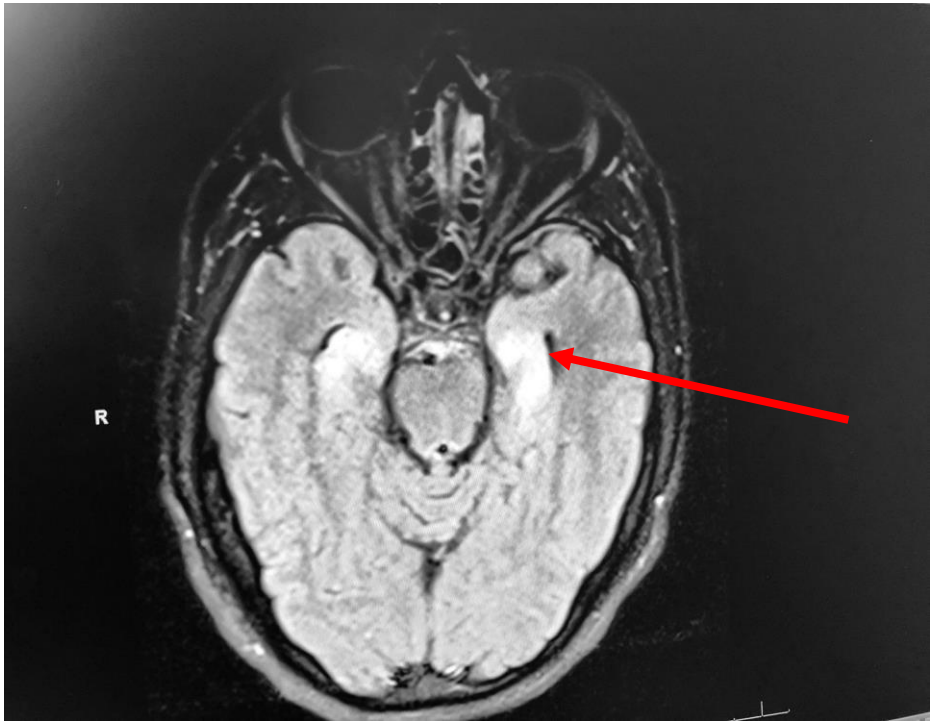
Imaging - MRI



SAG T1 FLAIR

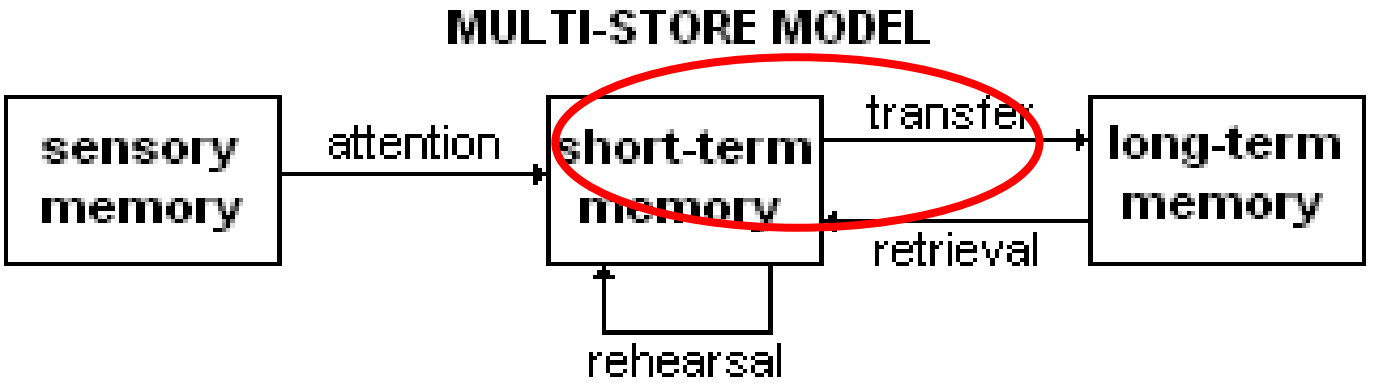
CORT T2 FLAIR

Imaging - MRI



AXIAL DWI

Discussion - Memory



- Semantic/episodic
- Procedural

Atkinson-Shiffrin memory Model , Jurzon 16:18, 2007 March

Discussion - Hippocampus

- Essential for learning new information
- Helps to consolidate short-term to long-term memory
- Damage causes:
  - Short attention span and disorientation
  - Anterograde amnesia
- Specifically susceptible to damage via hypoxic/excitotoxic injury (Sommer's Sector)
  - Highly metabolic
  - High concentration of NMDA glutamate receptors

Laboratory

Urine Toxicology:

(+) Opioid → **Hypoxic**

(+) Benzodiazepines

(+) Methamphetamines → **Excitotoxic**

Opioid & Hypoxia

- Central nervous system -
  - Ventrolateral medulla - inspiration is inhibited by opioid
  - Expiration is insensitive to opioid
  - Results in decrease inspiration and irregular breathing pattern in opioid overdose

- Peripheral nervous system –
  - Opioid receptors in smooth muscles of bronchi and intestines
    - Cough suppression

Methamphetamine & Excitotoxicity

- Acts on dopamine, serotonin, and NMDA glutamate receptor
- Hippocampus - high concentration of NMDA glutamate receptors
- Excessive activation of the NMDA receptors leads to excessive glutamate release and excitotoxic injury

Follow Up

- Collateral:
  - Patient had been living in SLE, sober for approximately 4 weeks
- Discharge:
  - Patient's conditions improved
  - 3-min Recall: ⅖ compared to 0/5 on previous days
  - Memory evaluation and substance use rehabilitation
- 2 weeks later:
  - Patient was readmitted for similar episode
  - Physical exam shows return of anterograde amnesia with suspected reinjury of hippocampal region

Take Home Points

- Pure anterograde amnesia is suggestive of hippocampal injury
- Hippocampus is susceptible to both hypoxic and excitotoxic injury
- Methamphetamine (and psychostimulants) can cause long term excitotoxic injury
- Providing education regarding lost of tolerance in opioid relapse

References

Pattison, KT. Opioid and the control of respiration. BJA: British Journal of Anaesthesia, 2008 June 1. Vol 100 (6), 747-758

Paola D, Caltagirone c, Fadda L, Sabatini U, Serra L, Carlesimo GA. Hippocampal atrophy is the critical brain change in patients with hypoxic amnesia. Hippocampus 2008; 18 (7): 719-28

Halpin LE, Collins SA, Yamamoto BK. Neurotoxicity of Methamphetamine and 3,4-mehtyenedioxymethamphetamine. Life Sci. 2014 Feb 27: 97(1): 37-44

Methamphetamine and Trauma induced brain injuries: Comparative Cellular and Molecular Neurobiological Substrates

Krasnova In, Cadet JL. Methamphetamine Toxicity and Messengers of Death. Brain Res Rev. 2009 May; 60(2): 379-407