Exploring how two classes of antidepressants influence neuronal survival and stroke outcomes

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Session outcomes

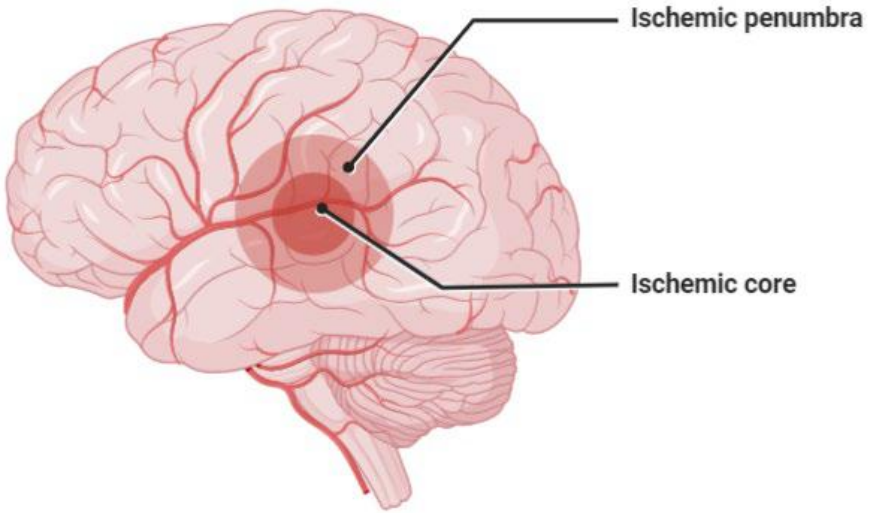
- 1. Stroke recovery is an ongoing biological process.
- 2. Mood and participation are critical drivers of recovery.
- 3. Emerging neuroscience may help us better understand how medications and rehabilitation work together to influence outcomes.

Why stroke recovery still matters?

- One of the leading causes of death and disability in Canada
  - ~62,000 Canadians
  - 1 in 10 recover completely
- *Why do two people with seemingly similar strokes sometimes experience very different recovery trajectories?*
  - Many factors impact recovery

The Canadian Stroke Best Practice Recommendations
improve care, save lives and promote recovery.

Acute Ischemic Stroke (AIS)



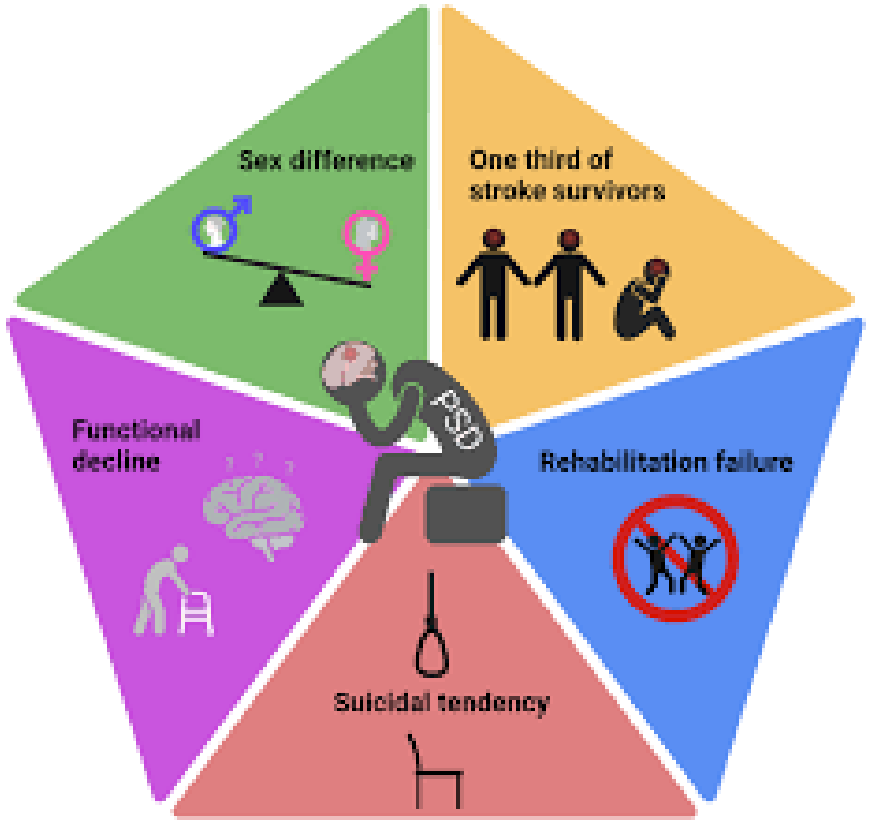
- **Ischemic stroke:** caused by a clot (thrombus) that blocks the flow of blood to the brain
  - Core = necrotic tissue
  - Penumbra = “at-risk” tissue
    - Ischemic cascade (excitotoxicity, oxidative stress, neuroinflammation)

- *What determines whether vulnerable neurons survive or die?*

Astrocytes

- Maintenance and support team
  - Regulate neurotransmitters
  - Maintain ionic balance
  - Support metabolism
  - Protect blood-brain barrier
  - Coordinate inflammatory response
- Kir4.1: potassium spatial buffering
  - Normal condition: 1mM increase following action potential
  - AIS: 10-12mM increase following

Post-Stroke Depression



- Most common medical complications post-stroke
  - Early diagnosis = better prognosis
  - Gold standard treatment = antidepressants
- Depression impacts participation in rehabilitation
  - More meaningful practice = more opportunities for adaptation (neuroplasticity)
  - High repetition with low intensity

Antidepressants and Motor Recovery

Fluoxetine (SSRI)

- Neuroprotection
- Increased cell viability
- Reduced infarct size
- No significant improvements in:
  - Motor recovery
  - Neurological outcomes

Nortriptyline (TCA)

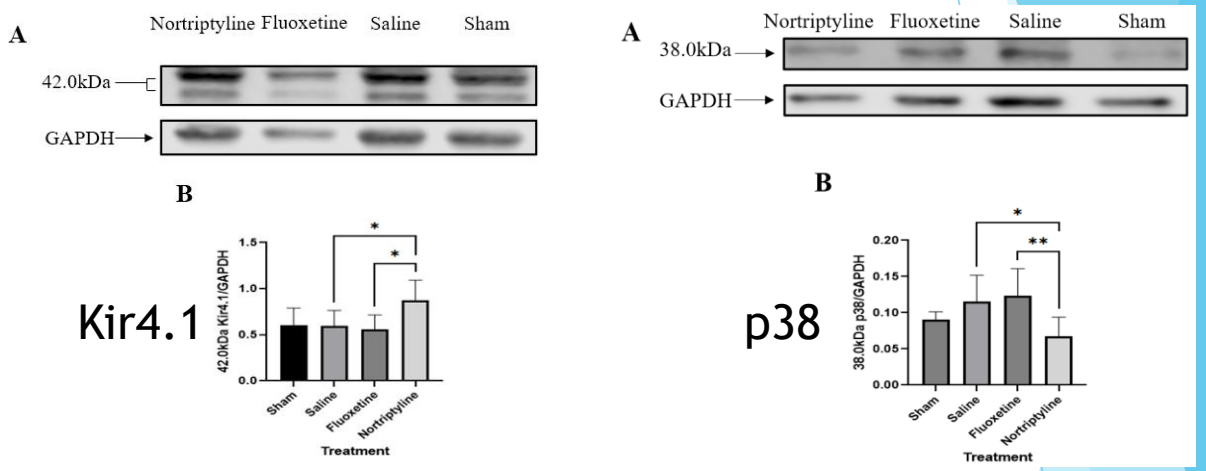
- Inhibit neuronal death
- Reduce lesion size (post-stroke)
- Improve neurological recovery
- Promote motor recovery

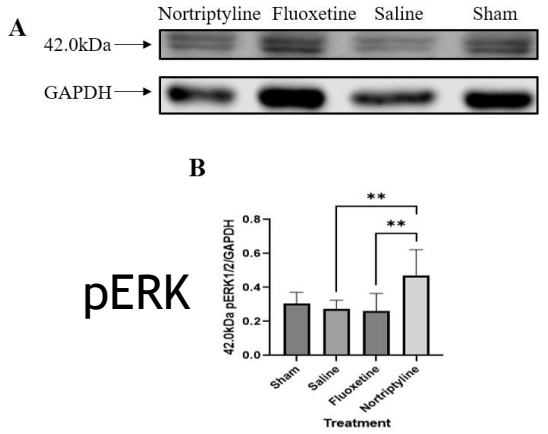
Research Question

Do these medications influence biological pathways involved in neurorecovery differently?

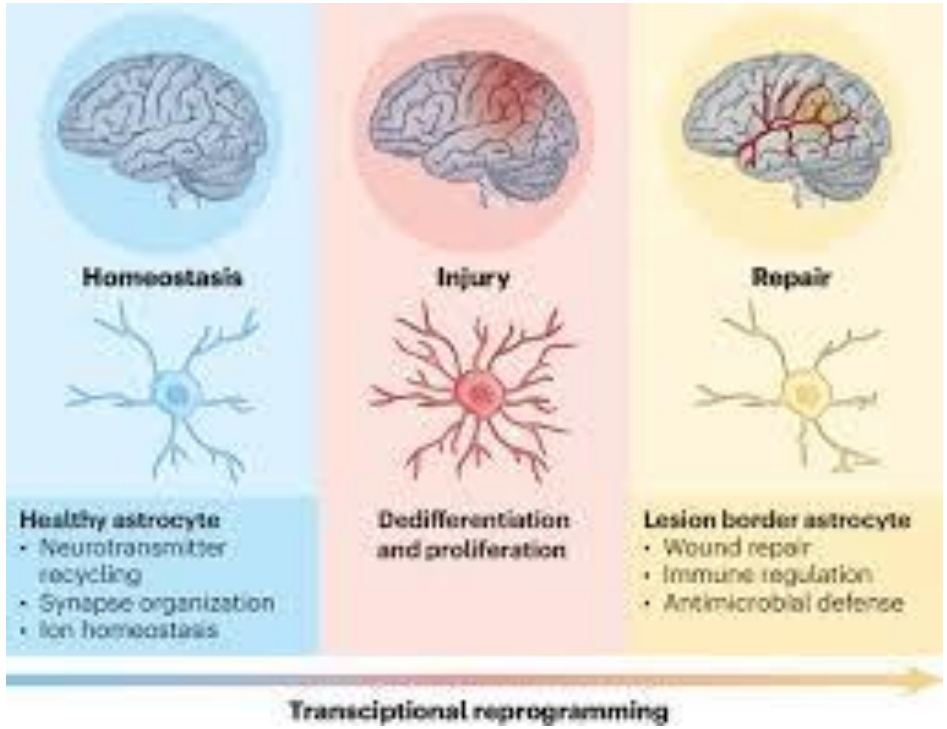
Research Findings

- Nortriptyline administration post-stroke produced:
  - Increased Kir4.1 expression
  - Increased activation of cell-survival signaling pathways (pERK)
  - Reduced activation of pathways associated with inflammation and cellular stress (p38)
- Fluoxetine did not produce same cellular changes post-stroke
- Does NOT mean that it is time to change prescriptions!





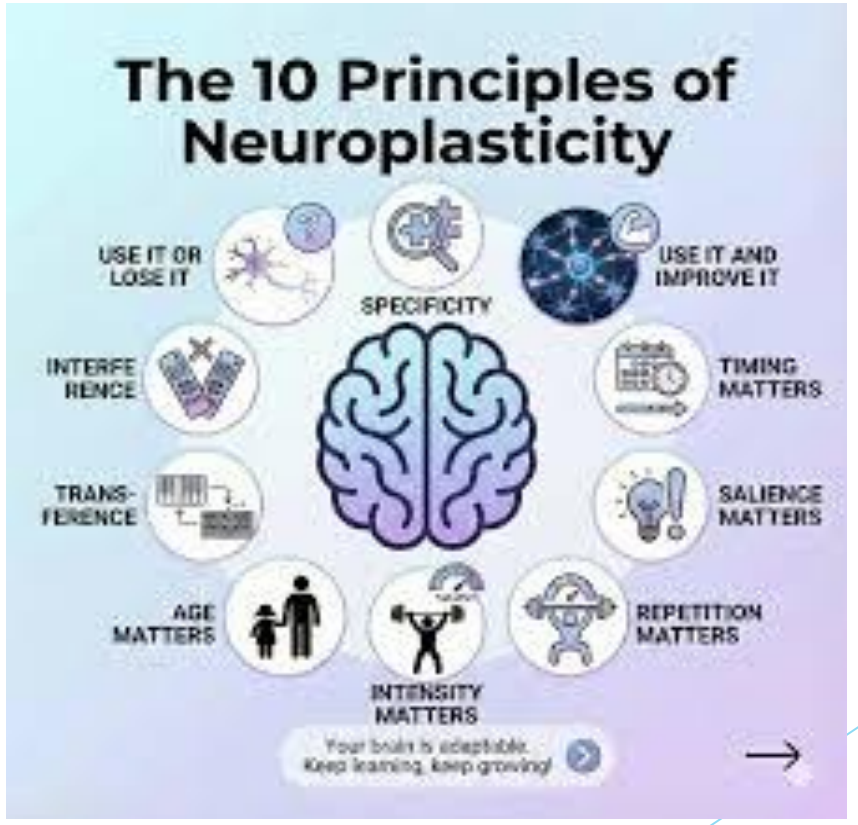
Why This Matters to Everyone in This Room?



- Recovery emerges from interactions between
  - Neurobiology
  - Medication
  - Rehabilitation
  - Mental health
  - Social support
- *What biological environment exist for recovery? Can we optimize that environment?*

A Practical Example

- Two different stroke survivors
  - One = severe depression, struggles to engage
  - Second = highly motivated, active participant
- Most would predict different outcomes
- *What if we could create a favourable biological environment for neuroplasticity?*



Future Directions

1. Do these molecular changes translate into meaningful improvements in function?
2. Can certain medications enhance responsiveness to rehabilitation?
3. Can we personalize treatment based on biological recovery profiles?
4. *How can we integrate neuroscience discoveries into everyday stroke care?*

Take-Home Messages

1. Stroke recovery is an ongoing biological process that extends far beyond the acute event
2. Post-stroke depression is common and has major implications for participation and recovery
3. Antidepressants may influence recovery through mechanisms that extend beyond mood management
4. Research findings suggest that different antidepressants may affect different recovery-related biological pathways
5. Future of stroke care will likely involve greater integration of neuroscience, pharmacology, rehabilitation, and person-centered care

Thank you for coming!

Any questions?