Post-Stroke Depression
A Review

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Disclosures

• No conflict of interest
Objectives

Review:

• The prevalence, etiology and risk factors for Post-Stroke Depression (PSD)

• The impact of PSD

• Screening and assessment guidelines for PSD

• Non-pharmacological and pharmacological management strategies
Prevalence

- 62,000 people with stroke and TIA are treated in Canadian hospitals every year

- 1/3 of individuals who experience stroke develop PSD
  – Most frequent psychiatric complication following stroke

- Existing prevalence data may be difficult to interpret

Etiology

- Psychological reaction to critical illness
- Physiological consequence of stroke
  - Lesion location
  - Neurotransmitters
  - Inflammatory cytokines
  - Gene polymorphisms

1. Fang, J., Cheng, Qi. Neurological Research, 2009
Etiology

• Lesion location

  – Frontal, subcortical, basal ganglia lesions have been implicated
  – Greatest association: left hemisphere, proximity to the frontal pole
  – In hospitalized and < 28 days following stroke: left hemisphere
  – Community samples and after 1-4 months: right hemisphere
  – ‘Silent infarcts’ have also been linked to depression

2. Fang, J., Cheng, Qi. Neurological Research, 2009
Etiology

• Neurotransmitters

– Ischemia-induced enzyme inhibition leads to decreased monoamine synthesis

– Metabolite of serotonin is low in the CSF of post-stroke depression patients

2. Fang, J., Cheng, Qi. Neurological Research, 2009
Etiology

• Inflammatory Cytokines

  – Stroke induces an inflammatory response
  – Increase in IL-1β, TNF-α, and IL-18
  – Inflammatory cytokines alter serotonin function

1. Fang, J., Cheng, Qi. Neurological Research, 2009
Etiology

Immune predisposition
• Allelic variants of immune-related genes
• Inflammation
• Anti-inflammatory molecule dysregulation

Reactive secondary depression

Acute stroke

Pro-inflammatory cytokines (IL-1, TNF-α, IL-6, IL-8, IL-18)

IDO expression up-regulation
• Increased tryptophan metabolism
• Reduced 5-HT synthesis

Lesion of strategic areas for depression

Altered neurotransmission
• Increased NE, DA, 5-HT metabolism
• Increased HPA axis activity
  • Increased ACTH
  • Increased cortisol

Post-stroke depression

Risk Factors

- Increasing stroke severity
- Functional dependence
- Presence of cognitive impairment
- Previous history of depression

- Risk increases exponentially if more than one risk factor is present

Consequences

- Poor functional recovery
- Increased risk for dependence
- Poorer cognitive function
- Reduced social participation
- Increased hospital visits, length of stay in hospital
- Increased depression in family and caregivers (30-60%)
- Suicidal ideation (10-15%)
- Increased mortality risk

Screening

- Canadian Best Practice Recommendations for Stroke Care (4th Ed.)
  - Identification, diagnosis and treatment is associated with better outcomes
  - All patients considered at high risk
  - Screening should be done in all settings and at all stages, transitions
Screening

• Canadian Best Practice Recommendations for Stroke Care (4th Ed.)

• Screen using a validated tool
  – Hospital Anxiety and Depression Scale
  – Geriatric Depression Scale
  – Patient Health Questionnaire-9 (PHQ-9)
  – Stroke Aphasic Depression Questionnaire
  – The Hamilton Depression Rating Scale (HDRS)
  – The Beck Depression Inventory

Recommended
• Canadian Best Practice Recommendations for Stroke Care (4th Ed.)

– At risk patients should be managed by a healthcare professional with expertise in post-stroke depression
– DSM Diagnosis:
  • ‘Mood disorder due to a general medical condition’
– Overlap between stroke and depressive symptoms
Assessment

- Disorders of emotional expression vs. primary disorders of feelings
  - Pathological crying
    - Reflex crying, laughing after neutral stimuli
    - No congruent feelings
    - Bilateral lesions of the corticobular tracts
  - Emotionalism (11 – 35%)
    - Crying or laughing with little or no warning
    - After congruent stimuli, with congruent feelings
    - Associated with post-stroke depression
  - Catastrophic reactions
    - Disruptive emotional behaviour when confronted with unsolvable task
    - Associated with left hemisphere stroke and aphasia
    - At risk for developing post-stroke depression

Treatment

• Non-pharmacological and Adjunct Treatments
• Pharmacotherapy
• Patients should be given information and advice about the impact of stroke, and the opportunity to talk about the impact on their lives [Evidence Level B].

• Patients with marked anxiety should be offered psychological therapy [Evidence Level B].

• Patients and their caregivers should have their psychosocial and support needs reviewed on a regular basis as part of long-term stroke management [Evidence Level A].
Psychotherapy for PSD

• There is inadequate evidence at present to support the use of psychotherapy as monotherapy in the treatment of PSD [Evidence Level C].

• Reasonable to consider these therapies as one of the first line treatments for depressive disorders post-stroke, given demonstrated efficacy in primary depressive disorders (Evidence Level A).

• May be used as adjunctive therapies (Evidence Level B)
Psychotherapy for PSD

- Cochrane review: no evidence of effectiveness of psychotherapy to treat depression after stroke

- Group CBT for PSD pts and carers
  - Decreased depression scores, maintained at 1 but not 6 months
  - Decreased carer burden, depression & anxiety scores maintained at 6 months

Hackett, Cochrane 2008
Ward, Topics in Stroke Rehab 2016
Patients diagnosed with a depressive disorder should be given a trial of antidepressant medication, if no contraindication exists. No recommendation for use of one class of antidepressants over another; side effect profiles suggest that selective serotonin reuptake inhibitors may be favoured in this patient population [Evidence Level A].

Patients with mild depressive symptoms or those diagnosed with minor depression may initially be managed by “watchful waiting”* (Evidence Level B).

Treatment should be monitored; should continue for a minimum of six months if a good response is achieved [Evidence Level A].

Routine use of prophylactic antidepressants is not recommended in post-stroke patients [Evidence Level A].
Pharmacological Therapies

• Meta-analysis of antidepressants for post-stroke depression (10 studies)
  – 8 SSRIs, 2 TCAs, 1 trazodone
  – Recovery or remission of depression: OR: 2.58 (1.56 – 4.26, p=0.002)

• Cochrane
  – A small but significant effect of pharmacotherapy on treating depression and reducing depressive symptoms

1. Price, J Neurol Neurosurg Psychiatry, 2011
2. Xiao-min Xu Medicine 2015
3. Hackett, Cochrane, 2008
Pharmacotherapy

- Both TCAs and SSRIs effective for PSD
- Relatively little comparative information on how to make the choice of one AD over another\(^1\)

- SNRIs:
  - Duloxetine vs. Citalopram and Sertraline
  - Duloxetine more effective in reducing symptoms of depression and anxiety\(^2\)

- Benefits vs. risks of antidepressant use need to be considered

1. Paolucci, Neuropsychiatr Dis Treat. 2008
• RCT of Fluoxetine (20 mg daily) vs. placebo for non-depressed adults with acute ischemic stroke treated for 3 months, all patients received physiotherapy\(^1\)
  – Fluoxetine group had significant improvement in motor recovery; effect only observed at 90 days

• RCT of problem solving therapy vs. Escitalopram in prevention of depression demonstrated cognitive benefit of Escitalopram

2. Jorge, Arch Gen Psychiatry, 2010
Antidepressants for Stroke Recovery

• Cochrane review of 52 RCTs
  – Insufficient evidence to recommend routine use

• Routine use of prophylactic antidepressants is not recommended in post-stroke patients at this time
  [Evidence Level A]

• No clear effect of pharmacological therapy on the prevention of depression in a Cochrane review\textsuperscript{1}

• AD prophylaxis was associated with a significant reduction in the occurrence rate of newly developed post-stroke depression in another meta-analysis\textsuperscript{2}

1. Hackett, Cochrane, 2008
Psychotherapy to Prevent PSD

• Problem-solving therapy administered over 12 months (12 sessions)

• PST more effective in preventing development of depression when compared to placebo:\(^1\)
  \[ \text{HR} = 2.2 \ (95\% \ CI: \ 1.4 - 3.5, \ P < 0.01) \]

• Follow-up study: PST assoc. With decrease in mortality

1. Robinson, JAMA, 2008
Conclusions

• Depression is common following stroke and associated with significant disability
• There is limited evidence for psychotherapy in PSD at the present time
• Antidepressants are effective for PSD and anxiety symptoms, and may also provide cognitive and functional benefit for individuals without depression
Resources

• Geriatric Psychiatry Outreach Programs
• (Providence Care)
• Providence Care – Mood Disorders
• Canadian Coalition for Seniors Mental Health
  – [www.cccsmh.ca](http://www.cccsmh.ca)
  – Tools for Healthcare Providers → Depression
  – Guidelines, pocket card and family guide for depression
• Canadian Stroke Best Practice Recommendations: Mood, Cognition and Fatigue Following Stroke practice guidelines, update 2015; International Journal of Stroke
Thank you

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