Post Stroke Depression

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Disclosures

- No conflict of interest

Objectives

- Review the epidemiology of Post Stroke Depression (PSD)
- Understand the impact of PSD
- Develop an approach to assessment and management of PSD across the continuum of care

PSD: Prevalence

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

- PSD: Most frequent psychiatric complication following stroke

- Pooled prevalence of depression at any time after stroke
  - In population studies 22%
  - In hospital studies 30%
  - In rehabilitation studies 30%

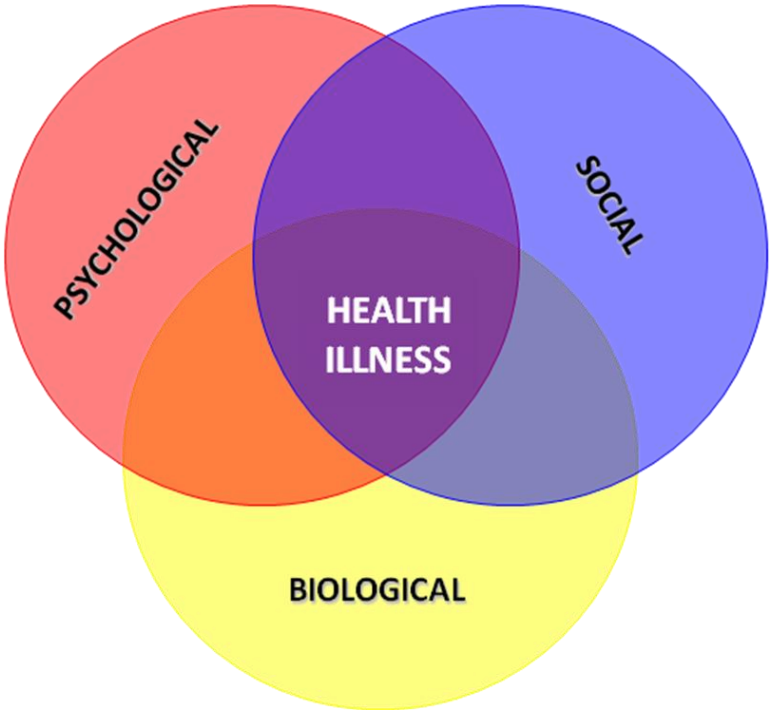
1. Chollet 2014
2. Ayerbe 2013

PSD: Under diagnosed

- Under diagnosed :
  - Prospective observational study of 13 centers in Ontario from Registry of the Canadian Stroke Network showed that 4.8% of stroke patients were diagnosed with depression while 6.7% treated were with a new antidepressant[1]
- However, stroke units identify and treat PSD more often as compared to other units:
  - 5.2% vs 4% diagnosed with PSD
  - 7.8% vs 4.5% received a new prescription for an antidepressant

1. Herrman Int J Geriatric Psychiatry 2011

PSD: Etiology



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

1. Fang, J., Cheng, Qi. Neurological Research, 2009
2. Hayhow, B., et al. The Behavioural Consequences of Stroke Ch 25, 2014

PSD: ETIOLOGY

- Biogenic amine theory:
  - Injury to biogenic amine axons decreases 5HT and NE1
  - Lower levels of 5HIAA in CSF of PSD patients [2]
- Cytokine Hypothesis[3]:
  - Increased production pro-inflammatory cytokines in stroke (IL-1β, TNF-α and IL-18)→ amplification inflammatory pathway → activation IDO enzyme → decrease in 5HT→ PSD
- Lesion location and relation to PSD

1. Robinson Biological Psychiatry 1977
2. Bryer J Neuropsychiatry and Clinical Neurosciences 1992
3. Spalletta Molecular Psychiatry 2006
4. Carson The Lancet 2000
5. Wei J Neurology 2015

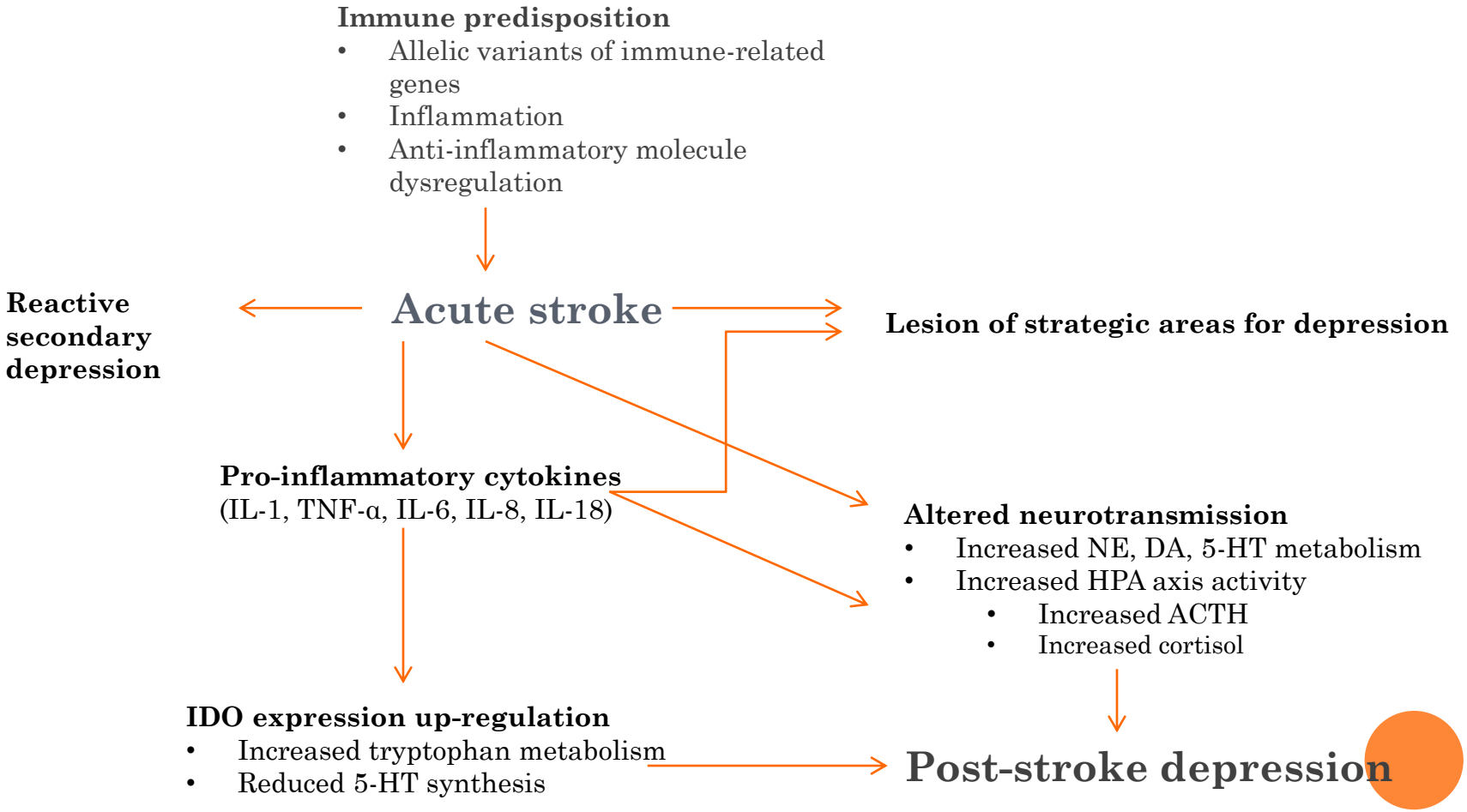
5HT= Serotonin
NE= Norepinephrine
5HIAA= 5 Hydroxyindoleacetic acid
IDO= Indoleamine 2,3 dioxygenase

PSD: ETIOLOGY

- Lesion location
  - Frontal, subcortical, basal ganglia lesions have been implicated
  - Other studies show left hemisphere, proximity to the frontal pole
  - Systematic reviews do not confirm role of lesion location
  - 'Silent infarcts' have also been linked to depression

1. Carota, A 2013
2. Fang, J 2009
3. Wei, N 2015
4. Whyte, E.M 2 015

PSD: ETIOLOGY



1. Spalletta, G., et al. Molecular Psychiatry, 2006

PSD: Risk Factors

- Disability secondary to stroke
- History of depression predating stroke
- Cognitive impairment
- Anxiety
- Social Isolation
- Risk increases exponentially if more than one risk factor is present
- Conversely, depression itself is a risk factor for the occurrence of stroke with a prospective population based cohort study reflecting a RR=1.73

1. Ayerbe Stroke 2011
2. Morrison J Psychosom Res 2005
3. Caeiro J Psychiatry Neurosci 2006
4. Jonas Psychosomatic Medicine 2000
5. Allan BJPsych 2013

Impact and 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 ; suicidal death
- Increased mortality risk

1. Carota, A., Paolucci, S. The Behavioural and Cognitive Neurology of Stroke, Ch 29, 2013
2. Hayhow, B., et al. The Behavioural Consequences of Stroke Ch 25, 2014

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Factors associated with post-stroke suicidal death

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ARTICLE INFO

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Stroke
Suicide
Depression
Lesion location

ABSTRACT

Background and purpose: The aim of this study was to estimate the relative risk of suicidal death compared to the general population and to identify risk factors for suicidal death among stroke patients.
Methods: Our sample consisted of 7175 patients who were diagnosed with stroke and admitted at Asan Medical Center from January 2005 to December 2012. Information on suicidal death was obtained from the database of the Korean National Statistical Office. The standardized mortality ratio (SMR) for post-stroke suicide was estimated. Additionally, we conducted a 1:6 case-control study using patients who did not commit suicide.
Results: Thirty patients committed suicidal death, with the mean time interval between hospital admission and suicide being 1.9 ± 1.8 years. The SMR for suicide was 2.14 (95% confidence interval [CI], 1.44–3.05). Case-control analysis revealed that diabetes mellitus, depression, and large ischemic lesions in the subcortex and brainstem were significantly associated with suicidal death.
Conclusions: The risk of suicidal death is approximately 2 times higher than that in the general population. Depression, diabetes, and large lesions in specific locations should be considered in the implementation of suicide prevention strategies in stroke patients.

PSD: Screening

- All patients with stroke should be screened for depression using a validated tool (Evidence Levels A)[1]
- Screening should take place at various stages throughout the continuum of stroke care [Evidence Level C]:
  - during acute care stay
  - following hospital discharge to an outpatient or community-based healthcare setting
  - throughout rehabilitation
  - periodically, following discharge to the community

PSD: Assessment

- All patients with stroke have to be screened for depression
- Patient interview, mental status examination, collateral from caregivers
- Some suggested validated tools (Best practice guidelines)

1st line	Additional Tools	Aphasic patients
PHQ 9	BDI	SADQ-10
HADS	CES-D	ADRS
GDS		

PHQ: Patient Health Questionnaire; HADS: Hospital Anxiety and Depression Scale; GDS: Geriatric Depression Scale

BDI: Beck Depression Inventory; SADQ: Stroke Aphasic Depression Questionnaire; CES-D: Center Epidemiological Studies Depression Scale; ADRS: Aphasia Depression Rating Scale

Canadian Best Practice Recommendations for Stroke Care 2015
Williams Stroke 2005

PSD: Assessment

	PHQ-9	HADS	GDS	SADQ-10
Rater	Self-Rated or Interviewer Administered	Self-Rated or Interviewer Administered	Self- Rated or Interviewer Administered	Observer/ Caregiver Rated
Time in minutes	2-4	2-5	8-10	2-4
Population	Adults Older adults	Adults Older adults	Developed in Older adults	Stroke Population
Cost	Free	$	Free	Free
Misc	Based DSM-IV	Both D + A	Possible use aphasia	Rater: Family vs. health professional

PSD: Assessment

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____

=Total Score: _____

PHQ-9 Questionnaire and scoring

Total Score
Depression Severity
0-4 None
5-9 Mild depression
10-14 Moderate depression
15-19 Moderately severe depression
20-27 Severe depression

PSD IN PATIENTS WITH APHASIA

- Pooled estimates of depression in studies including patients with aphasia vs. those that did not include patient with aphasia show no significant difference in overall prevalence

Hackett 2014

APHASIA IN STROKE PATIENT

The impact of stroke: are people with aphasia different to those without?

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Abstract

Purpose. Stroke rehabilitation programmes aim to improve functional outcomes and quality of life. This study explored long-term outcomes in a cohort of people admitted to two acute stroke units with stroke. Comparisons were drawn between people with aphasia (PWA) and people without aphasia.

Methods. People admitted to hospital with a first stroke were assessed at 2-weeks, 3-months and 6-months post-stroke. Measures included: the Barthel Index for Activities of Daily Living (ADL), the Frenchay Aphasia Screening Test, the General Health Questionnaire-12 for emotional well-being and the Stroke and Aphasia Quality of Life Scale-39g. Extended ADL and social support were also measured at 3 and 6 months, with the Frenchay Activities Index and the Social Support Survey, respectively.

Results. Of 126 eligible participants, 96(76%) took part and 87(69%) were able to self-report. Self-report data are reported here. Although outcomes improved significantly across time, at 6 months people continued to experience substantial functional limitations (16% aphasic; 32% dependent on basic ADL); participation limitations (79% $\leq$30 on the FAI); high psychological distress (45%) and compromised quality of life (54% $\leq$4 on the SAQOL-39g). Levels of social support remained relatively stable. Though at 3-months post-stroke PWA were significantly more likely to experience high psychological distress (93% *versus* 50% for those without), across time, there were no significant differences between PWA and those without on psychological distress and also ADL and social support. There were, however, significant differences on extended ADL ($F(1,68) = 7.80$, $p < 0.01$) and quality of life ($F(1,69) = 6.30$, $p < 0.05$).

Conclusion. PWA participated in fewer activities and reported worse quality of life after stroke than people without aphasia, even when their physical abilities, well-being and social support were comparable. Implications for clinical practice and future research are discussed.

Keywords: *Stroke outcome, aphasia, health-related quality of life*

PSD vs. Post stroke emotional incontinence (EI)

- EI: Pathological laughing or crying usually incongruent with mood
- Treatment :
  - Small RCT with Citalopram showed 50% reduction in pathological crying
  - RCT with Nortriptyline 50-100mg showed significant improvement of EI as reflected by the validated Pathological Laughing and Crying Scale
  - Fluoxetine also shown to improve EI

1.Andersen The Lancet 1993
2.Robinson Am J Psychiatry 1993
3.Choi-Kwon Stroke 2006

Post stroke emotional incontinence (EI)

- In cases of severe, persistent or troublesome tearfulness, patients may be given a trial of antidepressant medication [Evidence Level A]. Side effect profiles suggest that some selective serotonin reuptake inhibitors may be preferred over others for this patient population.[1]

Canadian Best Practice Recommendations for Stroke Care 2015

PSD: Treatment

- Non-pharmacological and Adjunct Treatments
- Pharmacotherapy

Canadian Best Practice Guidelines for Stroke Care: Psychological Management

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

Canadian Best Practice Guidelines for Stroke Care: Antidepressants

- **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)
  - Continuous outcomes: SMD -1.02 (-1.80 - -0.23, p 0.01)
- Cochrane
  - A small but significant effect of pharmacotherapy on treating depression and reducing depressive symptoms was found, as was a significant increase in adverse events.

1. Price 2011
2. Hackett 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

1. Paolucci, Neuropsychiatr Dis Treat. 2008
2. Karaiskos, J Neuropsychiatry Clin Neurosci 2012

Antidepressants and Risk of Intracerebral Hemorrhage

- Antidepressants increase the risk of bleeding related adverse events:
  - Upper GI bleeds, perioperative bleeding
  - Mediated through anti-platelet aggregation effects of serotonergic antidepressants
- Risk of intracerebral hemorrhage with SSRIs:
  - RR: 1.42 (95% CI: 1.23 – 1.65)
  - RR: 1.5 for antidepressants combined with oral anticoagulants (above anticoagulants alone)
  - Absolute risk: 1/10,000 treated for 1 year

Hackam 2012

Antidepressants for Stroke Recovery

- RCT of fluoxetine (20 mg daily) vs. placebo for adults with acute ischemic stroke (5-10 days post stroke) treated for 3 months, all patients received physiotherapy[1]
  - Excluded patients with depression
  - Fluoxetine group had significant improvement in motor recovery on Fugl-Meyer Motor Score (9.4 point difference, p=0.003), effect only observed at 90 days
- RCT of problem solving therapy vs. escitalopram in prevention of depression demonstrated cognitive benefit of escitalopram on Repeatable Battery for Assessment of Neuropsychological Status (RBANS)[2]

1. Chollet 2011
2. Jorge 2010

Antidepressants for Stroke Recovery

- Cochrane review of 52 RCTs[2]
  - Reduced dependency, neurological deficits, depression
  - No benefit in cognitive status and death
  - Insufficient evidence to recommend routine use
- Routine use of prophylactic antidepressants is not recommended in post-stroke patients at this time [Evidence Level A]

Mead 2013

Prevention of Post Stroke Depression

- Antidepressants
  - No clear effect of pharmacological therapy on the prevention of depression in a Cochrane review[1]
  - AD prophylaxis was associated with a significant reduction in the occurrence rate of newly developed poststroke depression in another meta-analysis[2]

1. Hackett 2008
2. Chen 2007

Psychotherapy to Prevent PSD

- Problem-solving therapy administered over 12 months (12 sessions)
- PST adapted for use in stroke population, psychotherapy well adapted to use in populations with executive dysfunction
- PST more effective in preventing development of depression when compared to placebo:
  - HR = 2.2 (95% CI: 1.4 – 3.5, P<0.01)

Robinson 2008

PSD: OTHER TREATMENT OPTIONS

Contents lists available at ScienceDirect

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Review article

Repetitive transcranial magnetic stimulation for the treatment of post-stroke depression: A systematic review and meta-analysis of randomized controlled clinical trials

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ARTICLE INFO

Keywords:
Post-stroke depression
Transcranial magnetic stimulation
Meta-analysis

ABSTRACT

Background: Every year, more than fifteen million people worldwide experience a stroke, nearly 30% of stroke survivors are likely to experience post-stroke depression (PSD). Repetitive transcranial magnetic stimulation (rTMS) is one of the emerging techniques which assist in targeting rehabilitation after stroke. Although deterioration of PSD greatly affects the recovery and quality of life of stroke sufferers, the effect of rTMS therapy has not been systematically studied.

Objective: A systematic review and meta-analysis was conducted to determine the effect of rTMS on PSD.

Methods: We carried out a systematic review and meta-analysis of randomized controlled trials (RCTs) of rTMS for the treatment of PSD. Primary outcome was severity of depression measured by the Hamilton Depression Rating Scale (HAMD). Secondary outcomes were response rates, remission rates, stroke severity and ability to perform daily activities.

Results: 22 RCTs studies (n=1764 patients) were included. The results demonstrated that rTMS was beneficial on PSD using three scales: HAMD (MD=−6.09, 95% CI: −7.74, −4.45, $P < 0.001$); response rates (OR=3.46, 95% CI: 2.52, 4.76, $P < 0.00001$); remission rates (OR 0.99, 95% CI: 0.56, 1.75, $P < 0.00001$); National Institutes of Health Stroke Scale (NIHSS) (MD=−2.74, 95% CI: −3.33, −2.15, $P < 0.001$); Activities of daily living (ADL) (SMD=−1.20, 95% CI: 0.68, 1.72, $P < 0.001$); Montgomery-Asberg Depression Scale (MARDE) (MD=−6.21; 95% CI: −9.34, −3.08; P=0.0001);

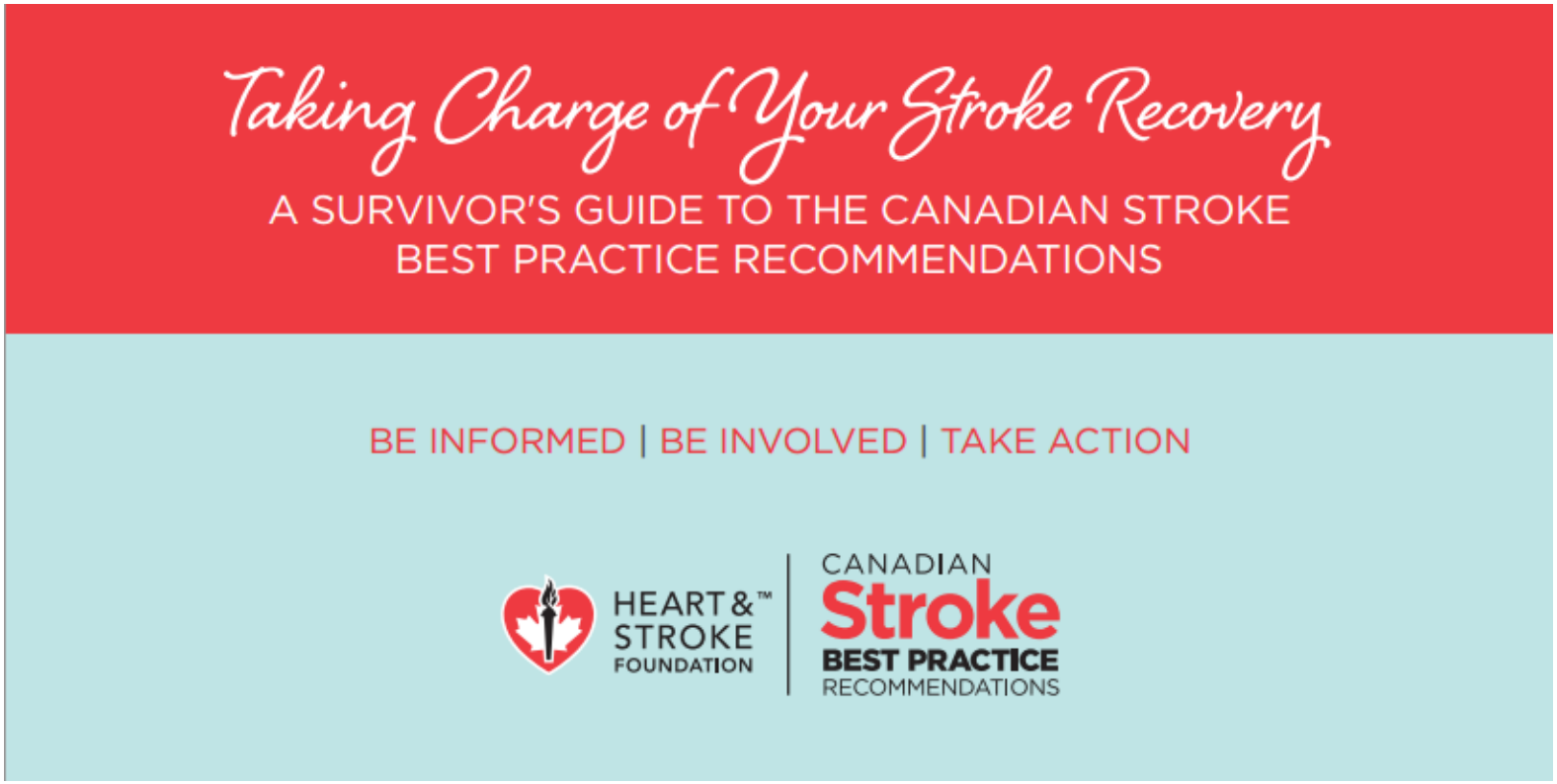
Conclusion: In present meta-analysis, the positive findings suggest rTMS has beneficial effects on PSD. However, those findings should be treated with caution because of heterogeneity and potential biases.

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 and Mood Disorder Program through Providence Care Hospital
- Canadian Coalition for Seniors Mental Health
  - www.ccsmh.ca
- Canadian Stroke Best Practices website (healthcare provider information and patient information):
  - www.strokebestpractices.ca, particularly:
  - http://www.strokebestpractices.ca/cognition-mood/post-stroke-depression/
- www.strokengine.ca


Taking Charge of Your Stroke Recovery
A SURVIVOR'S GUIDE TO THE CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS
BE INFORMED | BE INVOLVED | TAKE ACTION
HEART & STROKE FOUNDATION
CANADIAN Stroke BEST PRACTICE RECOMMENDATIONS

Academic Resources

- Canadian Stroke Best Practice Recommendations: Mood, Cognition and Fatigue Following Stroke practice guidelines, update 2015; International Journal of Stroke
- Robinson, R. G., & Jorge, R. E. (2015). Post-stroke depression: a review. American Journal of Psychiatry
- Price A, Rayner L, Okon-Rocha E, et al. Antidepressants for the treatment of depression in neurological disorders: a systematic review and meta-analysis of randomized controlled trials. *J Neurol Neurosurg Psychiatry*. Vol 82.2011:914-923.
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- Chollet et al. Fluoxetine for motor recovery after acute ischemic stroke (FLAME): a randomised placebo-controlled trial. Lancet Neurology 2011;10:123-130

Thank you

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