Post-Stroke Depression (PSD)

NIH StrokeNet Grand Rounds, April 26, 2018
Pamela H. Mitchell, PhD, RN, FAAN, FAHA
Objectives

- Describe the scope of the problem of depression and stroke
- Evaluate the evidence base for pharmacologic and non-pharmacologic treatment in post-stroke depression

Take Home Message

- PSD is prevalent worldwide
- PSD can be rapidly assessed
- PSD can be treated
Stroke as a leading cause of disability

- ~795,000 new or recurrent strokes per year (US)
- 4\textsuperscript{th} leading cause of death in US and 2\textsuperscript{nd} worldwide
- A leading cause of long-term serious disability
  - Blacks more than whites
  - Women more than men

Heart Disease and Stroke Statistics – 2018 update
DOI: 10.1161/CIR.0000000000000558.)
Global Stroke Incidence

3566 Stroke December 2015

Age-Standardized Stroke Incidence (per 100,000), 2010

stroke. 2015;46:3564-3570. DOI: 10.1161/STROKEAHA.115.008226.)
Global Stroke Disability Adjusted Life Years (DALY) Lost
Health Burden of Depression

- Depression is the *leading* global cause of years of life lived with disability
- Major contributor to the overall global burden of disease - disability-adjusted life-years (DALY).
  - Reduction in an individual’s productive life
  - Takes into account premature mortality

*Depression coupled with stroke is thus a double burden*

Impact of Depression and Chronic Illness
Change in the rank order of disease burden for 15 leading causes worldwide, 1990–2020 (as measured by DALYS)

<table>
<thead>
<tr>
<th>1990</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease or injury</td>
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</tr>
<tr>
<td>Lower respiratory infections</td>
<td>1. Ischemic heart disease</td>
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<tr>
<td>Diarrheal diseases</td>
<td>2. Unipolar major depression</td>
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<tr>
<td>Conditions arising during the perinatal period</td>
<td>3. Road traffic accidents</td>
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<tr>
<td>Unipolar major depression</td>
<td>4. Cerebrovascular disease</td>
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<tr>
<td>Ischemic heart disease</td>
<td></td>
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<tr>
<td>Cerebrovascular disease</td>
<td></td>
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<tr>
<td>Tuberculosis</td>
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<td>Measles</td>
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<td>Road traffic accidents</td>
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<tr>
<td>Congenital anomalies</td>
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<tr>
<td>Malaria</td>
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<tr>
<td>Chronic obstructive pulmonary disease</td>
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<tr>
<td>Falls</td>
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<tr>
<td>Iron-deficiency anemia</td>
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<tr>
<td>Protein-energy malnutrition</td>
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(Baseline scenario)

- Lower respiratory infections
- Diarrheal diseases
- Conditions arising during the perinatal period
- Unipolar major depression
- Ischemic heart disease
- Cerebrovascular disease
- Tuberculosis
- War
- Diarrheal diseases
- HIV
- Conditions arising during the perinatal period
- Violence
- Congenital anomalies
- Self-inflicted injuries
- Trachea, bronchus and lung cancer
Frequency of depression after stroke

• 35% in > 65 year olds (Kelly-Hayes et al, J Stroke Cerebrovas Dis 12, 119-126, 2003)

  – Pooled estimate was 33% (95% confidence interval, 26% to 39%) of all stroke survivors experiencing depression.
  – Range – 10% to 55%
  – Differences in case mix, method of mood assessment explains variation across studies
  – Reflects both incidence and prevalence
An alternative view

**FIGURE 1. The Prevalence of Depression in Various Clinical Settings Following Stroke**

- **Community-based Setting**: N=2,108
  - Major Depression: N=297, N=192
  - Minor Depression: N=598, N=553

- **Acute or Rehabilitation Hospitals**: N=2,769
  - Major Depression
  - Minor Depression

- **Outpatient Populations**: N=2,191
  - Major Depression: N=526, N=524

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*Patients were examined using a standardized mental status examination and DSM-IV diagnostic criteria for depression following stroke with major depressive-like features or minor depression defined as more than two but less than five symptoms of major depression. Meta-analyses stating that the prevalence of poststroke depression is 31% miss these important clinical variables.*
Depression preceding stroke

Depression and Risk of Stroke: A Meta-Analysis of Prospective Studies
Jia-Yi Dong, Yong-Hong Zhang, Jian Tong and Li-Qiang Qin

Stroke 2012, 43:32-37: originally published online October 20, 2011
doi: 10.1161/STROKEAHA.111.630871
Consequences of post-stroke depression

- Poorer rehabilitation outcomes
- Reduced quality of life for stroke survivor and significant others
- Possibly increased risk of subsequent stroke, other CVD, death
Top 10 Things I want friends and family of stroke survivors to know about PSD

• 10: I don’t have the words to tell you what’s wrong. I really don’t and I feel bad about it.
• 9: I’m not in control and I’m confused.
• 8: I feel like a burden. I was independent. I’m not now and it makes me sad.
• 7: I don’t know what would help me feel better. But keep loving me.
• 6: I feel unlovable. I don’t love myself. Touch heals. Hug me.
• 5: I don’t recognize myself in the mirror.
• 4: I am working harder than you can imagine, at everything.
• 3: Are you afraid of me or are you afraid of having your own stroke? Stroke is scary. But I am not scary. Stay near.
• 2: Life can’t go back to the way it was and neither can I. I’m changed. I didn’t choose to change. I don’t want to change. I can’t deal with any more change.
• 1: I didn’t survive a stroke to be miserable. I can be magnificent. But I need help and I need HOPE!

Rachel Scanlon Henry, Stroke Connection, Spring 2018
Postulated mechanisms linking depression and cardio-cerebrovascular disease

• Biological
  – Tissue injury (stroke)- damage to neural circuits regulating mood
  – Serotonin signaling disruption (genetic propensity?)
  – Inflammation – cytokines
    • Stroke leads to changes in the levels of pro-inflammatory cytokines which has been associated with depression in humans and in animal models

• Psychological
  – Stroke as stressor, ‘reactive’, chronic CVD as stressor OR life stresses lead to inflammatory response

• Bio-psycho-social
  – Combination of above
Premorbid Personal, Genetic & Psychosocial Characteristics

Pathologic Factors: Initial Impairment

Perceived Social & Emotional Support

Post-Stroke Depression

Morbidity Outcomes

Functional Outcomes – Limits in Ability, Stroke Impact

Social Outcomes – Limits in participation

Treatment
Identifying PSD – ask the patient!

• Clinically simple one question screen (Yale – Watkins et al 2001; Lachs et al 1990)
  – “Do you often feel sad or depressed?”

• Or two question -PHQ-2 (Kroenke et al 2003)
  – Over the last 2 weeks, how often have you been bothered by 1) “little interest or pleasure in doing things” and 2) “feeling down, depressed, or hopeless.”
  – Rated: “not at all,” “several days,” “more than half the days,” or “nearly everyday” (scored as 0, 1, 2, and 3, respectively)
Formal Screening Tools

- Formal screening
  - Geriatric Depression Scale (GDS) – 30 or 15 items
  - Patient Health Questionnaire (PHQ-9)
  - Beck Depression Inventory (BDI) – 21 items

- DSM-IV criteria
  - Major depressive disorder: 5 or more of 10 depressive symptom; present at least “more than half the days” in the past 2 weeks, including depressed mood or anhedonia.
  - Other depressive disorder: 2 – 4, including mood or anhedonia
  - Suicidal ideation always counts as one
Understanding How Post-Stroke Depression Affects Your Loved One

Just because someone is home from the hospital does not mean that all is normal and they are running on all cylinders. Their brains have been injured, and it takes time and the compassion and patience of friends and family for them to recover.

It is important to let survivors respond to this situation in their own way, without trying to meet the expectations of others who have not experienced a brain injury. It may not be possible to understand how they feel.

What to Understand About Post-Stroke Depression

- It is extremely common. Studies document that between one-third and two-thirds of stroke survivors experience depression.
- It can result from the stroke lesion itself. It may also be a reaction to their stroke deficits. Or it may be both.
- It can stymie recovery because it may prevent them from participating in therapy.
- It increases risk of another stroke.
- It generally responds well to treatment, which typically is a combination of medication and talk therapy.
- It is not a character flaw or moral failing.
- It is unlikely to go away by itself.

Things your loved one may be thinking and feeling when experiencing post-stroke depression:

- “I don’t have the words to tell you what’s wrong. I really don’t, and I feel bad about it.”
- “I’m not in control and I’m confused.”
- “I feel like a burden. I was independent. I’m not now and it makes me sad.”

What Can Help

Family members and friends can help by coming from a position of compassion and understanding, rather than the expectation that everything should be better. Stroke support groups help both survivors and caregivers accept the new normal that stroke has brought to their family.
Treatment of PSD

• Pharmacologic (Hackett et al 2005, Stroke 36, 1098-)
  – Antidepressants
  – Psychostimulants

• Non-pharmacologic (Hackett et al 2004, Cochrane... CD003437)
  – Behavioral, psychosocial
  – Supportive therapy
  – Neuromodulation
Most recent scientific statement

AHA/ASA Scientific Statement

Poststroke Depression
A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Amytis Towfighi, MD, Chair; Bruce Ovbiagele, MD, MSc, MAS, FAHA, Vice Chair; Nada El Husseini, MD, MHSc; Maree L. Hackett, PhD; Ricardo E. Jorge, MD; Brett M. Kissela, MD, MS, FAHA; Pamela H. Mitchell, PhD, RN, FAHA; Lesli E. Skolarus, MD; Mary A. Whooley, MD; Linda S. Williams, MD, FAHA; on behalf of the American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; and Council on Quality of Care and Outcomes Research

(Stroke. 2017;48:e30-e43. DOI: 10.1161/STR.00000000000000113.)
Antidepressants and PSD

- Antidepressants
  - Tricyclics – (nortriptaline, clomipramine)
  - Serotonin Selective Reuptake Inhibitors – SSRI (citalopram, fluoxetine, paroxetine, sertraline)
  - Norepinephrine Reuptake Inhibitors – NRI (reboxetine)
  - Serotonin-Norepinephrine Reuptake Inhibitor – SNRI (venflaxine)
Primary prevention

• (Anderson et al, 2004, Cochrane review) - no effect
• Escitalopram, problem-solving (Robinson et al, 2008 JAMA) effective
• Towfighi et al, 2017
Non-pharmacologic Treatments

• Neuromodulation – repetitive transcranial magnetic stimulation rTMS (Deng et al, Scientific Reports, 2017, mostly in China)

• Behavioral, psychosocial (Towfighi et al, Stroke, 2017)
  – Cognitive Behavioral Therapy (+ effect)
  – Brief psychodynamic problem-solving (+ effect)
  – Motivational interviewing (+effect)
  – Collaborative care (+effect)
  – Stroke liasons (no effect on depression scores)
ASA Resources for Patients/Families

• [http://strokeconnectio
n.strokeassociation.or
g/Spring-
2018/Helping-Others-
Understand-Post-
Stroke-Depression/](http://strokeconnectio
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(Stroke. 2017;48:e30-e43. DOI: 10.1161/STR.0000000000000113.)
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<th>Topic</th>
<th>Summary of Findings</th>
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<tr>
<td>Epidemiology</td>
<td>Approximately one third of stroke survivors develop PSD at some point after stroke. The frequency is highest in the first year, at nearly 1 in 3 stroke survivors, and declines thereafter.</td>
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<td>Pathophysiology</td>
<td>The pathophysiology of PSD is complex and likely involves a combination of biological and psychosocial factors. Further research is needed to develop a better understanding of PSD pathophysiology with an aim to develop targeted interventions for prevention and treatment.</td>
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<td>Predictors</td>
<td>A multitude of studies have evaluated predictors of PSD, but because of differences in inclusion and exclusion criteria, statistical methods, and inadequate sample sizes for multivariate analyses, generalizability is limited. The most consistent predictors of PSD have been physical disability, stroke severity, history of depression, and cognitive impairment. Further studies are needed to develop a better understanding of predictors of PSD.</td>
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<td>PSD and functional outcomes</td>
<td>PSD is associated with poorer functional outcomes after stroke. Treatment with fluoxetine was associated with lower PSD occurrence rates and improvement in motor recovery in 1 RCT. Further research is needed to assess the effect of PSD on outcomes and to develop optimal strategies to counteract these effects.</td>
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<tr>
<td>PSD and QOL</td>
<td>A few studies suggest that PSD adversely affects QOL. Further research is needed to further elucidate the independent effect of PSD on QOL and to determine how to improve QOL in individuals with or at risk for PSD.</td>
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<td>PSD and healthcare use</td>
<td>A few studies have shown an association between PSD and healthcare use. Further studies are needed to evaluate the effect of treatment of PSD on subsequent healthcare use.</td>
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<tr>
<td>PSD and mortality</td>
<td>PSD is associated with higher mortality after stroke.</td>
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<td>Screening</td>
<td>Twenty-four studies (n=2907 participants) showed that the CES-D, HDRS, and PHQ-9 had high sensitivity for detecting PSD; however, the studies had several limitations, including generalizability. Systematic screening for PSD with the 9-item PHQ-9 is pragmatic, has high sensitivity for detecting PSD, and may improve outcomes, provided that processes are in place to assure accurate diagnosis, timely and effective treatment, and follow-up. Further research is needed to determine whether screening for PSD—in conjunction with collaborative care to ensure timely intervention, treatment, and follow-up—improves outcomes in diverse populations of stroke survivors.</td>
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<tr>
<td>Management: pharmacotherapy</td>
<td>Twelve trials (n=1121) suggest that antidepressant medications may be effective in treating PSD; further research is needed to determine optimal timing, threshold, and medications for treatment.</td>
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<tr>
<td>Management: neuromodulation</td>
<td>Further studies are needed to determine the efficacy of neuromodulation on treating PSD.</td>
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<tr>
<td>Management: psychosocial interventions</td>
<td>Seven trials (n=775) suggest that brief psychosocial interventions may be useful and effective in treatment of PSD. Whether antidepressant medication is a necessary or beneficial adjuvant cannot be established from these trials because of a lack of placebo controls.</td>
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<tr>
<td>Management: stroke liaison workers</td>
<td>Fifteen trials (n=2743) have not revealed a beneficial effect from stroke liaison workers on PSD; however, the trials included individuals without a diagnosis of PSD. Further studies are needed to determine the effect of liaison worker on those with established PSD.</td>
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<tr>
<td>Management: information provision</td>
<td>Seven trials (n=720) suggest that information provision provides a small benefit in depression scores; however, the clinical significance of this improvement is unclear.</td>
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<tr>
<td>Management: self-management</td>
<td>Few studies have assessed the effectiveness of self-management strategies on PSD; further studies are needed to determine whether these strategies are beneficial.</td>
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<tr>
<td>Prevention: pharmacotherapy</td>
<td>Eight trials (n=776) suggest that pharmacological treatment may be effective in preventing PSD; however, further studies are needed in more representative samples of stroke survivors, and additional study is required to determine the optimal timing and duration of treatment.</td>
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<tr>
<td>Prevention: psychosocial interventions</td>
<td>Five trials (n=1078) suggest that psychosocial therapies may prevent the development of PSD; however, the studies are not generalizable to all stroke survivors, given their narrow inclusion and exclusion criteria. Further research with more rigorous methods is needed to assess the effect of psychotherapy on prevention of PSD.</td>
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CES-D indicates Center of Epidemiological Studies-Depression Scale; HDRS, Hamilton Depression Rating Scale; PHQ, Patient Health Questionnaire; PSD, poststroke depression; QOL, quality of life; and RCT, randomized controlled trial.
Questions and Comments