Post Stroke Depression

PSD

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Objectives

1. Discuss the connection between stroke and depression
2. List significant risk factors for post-stroke depression (PSD)
3. Identify common symptoms of post-stroke depression
4. Describe treatment for depression after stroke

The Connection Between Stroke and Depression

Physical Connection

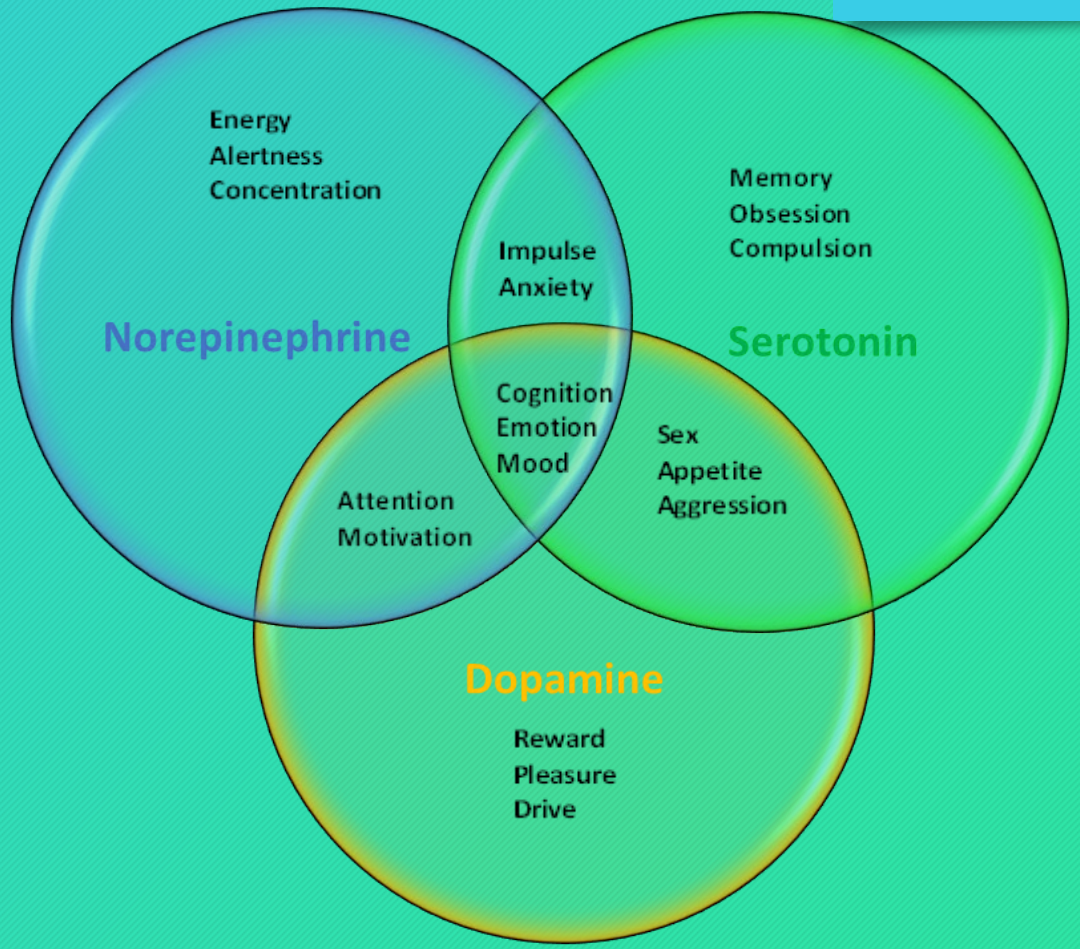
A stroke causes biochemical changes in the brain, which can affect emotions

Emotional Connection

A stroke often changes an individual's abilities (physical, emotional and cognitive), which can lead to depression

Physical Connection: Neurophysiology and PSD

- The main biological theory of PSD is the amine hypothesis.
- Researchers studying stroke patients have found a strong association between impairments in a network of the brain involved in emotional regulation and the severity of post-stroke depression



Brain
Derived
Neurotropic
Factor

: a neuropeptide that regulates the growth, survival, and differentiation of neurons and that affects synaptic plasticity especially by mediating long-term potentiation
Brain-derived neurotrophic factor … is critical for axonal growth, neuronal survival, and synaptic plasticity, and its levels are affected by stress and cortisol.
—R. H. Belmaker and Galila Agam, The New England Journal of Medicine

BDNF plays an important role in learning, memory, and behavior. As a result, BDNF has broad influence on mood, sleep patterns, eating habits, and appetite.

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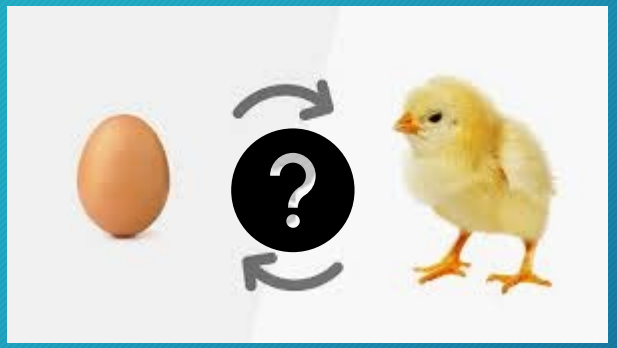


The neurotrophic hypothesis of depression is heavily based on the correlation between lower levels of BDNF and a higher frequency of depression, depressive symptomatology, neuronal loss, and cortical atrophy, and the restoration of the BDNF effect is linked to antidepressants

In PSD patients, the presence of stroke may contribute to the development of depression, including affecting the expression of BDNF. However, the mechanisms of BDNF in the development of PSD remain largely unknown. Lower BDNF levels may have existed in some patients before stroke onset, making them vulnerable to develop depressive symptoms.

Physical Connection: The Inflammatory Process and PSD

A considerable body of evidence has shown that inflammation plays an important role in the process of stroke rehabilitation and development of poststroke depression (PSD).

- For instance, an investigation revealed that anti-inflammatory treatment, such as acetylsalicylic acid, non-steroidal anti-inflammatory drugs, and statins decrease the risk of PSD, and inflammation contributes to PSD depending on the onset of PSD

Physical Connection: Neuroanatomy and PSD

- Early-onset depressions (i.e, those apparent within a few weeks after stroke) may be associated with left frontal lesions and serotonin receptor changes, while delayed-onset depressions may be associated with right-hemisphere strokes and a mechanism not related to serotonin receptors.
- *Am] Psychiatry 145:8, August 1988*

Behavioral neurology classically associates poststroke depression (PSD) with left frontal infarcts and pseudobulbar symptoms of emotional incontinence (PSEI) with bifrontal lesions

Study results (2000) were consistent with a number of previous studies in which anterior lesions were more closely associated with PSD and with a study in which left hemisphere lesions were associated with poststroke PSD but not with subacute or chronic PSD.

Kim JS and Choi-Kwon S. Poststroke depression and emotional incontinence: Correlation with lesion location. Neurology 2000 May 9 54 1805 1810

Pathophysiological Mechanisms Correlated with Post Stroke Depression

Glutamate Toxicity

High levels of Glutamate,(excitatory neurotransmitter) lead to glutamate-mediated excitoneurotoxicity (neuronal damage and/or death), particularly in the frontal cortex.

In a study, it was determined that chronic stress increases the vulnerability of neurons in the rat cortex and it was concluded that cortical neuronal apoptosis should be added to a list of events that have been proposed to explain loss of neuronal function and viability seen in depressive disorders.

Increased Inflammation / HPA Axis Dysregulation

Abnormal inflammatory response after a stroke has been linked to dysregulation of the HPA Axis. Increased inflammation and HPA axis products hinder neurotropic activity in the hippocampus and in the frontal cortex. These processes also reduce the availability of serotonin in the frontal cortex.

The hypothalamic-pituitary-adrenal axis (HPA) is the main stress response system. It is the neuroendocrine link between perceived stress and physiological reactions to stress (Breedlove and Watson, 2013).

Excessive stimulation of HPA has been implicated in depression

Abnormal Neurotropic Response

Brain-derived neurotrophic factor (BDNF) plays an important role in neuronal survival and growth, serves as a neurotransmitter modulator, and participates in neuronal plasticity, which is essential for learning and memory.

Inadequate neurotropic response after a stroke leads to impairment in the development and maturation of neurons in the hippocampus and in the frontal cortex.
In patients with PSD, their serum BNDF level is lower than in those without depression

Lower Levels of Monoamines

Ischemia of ascending monoaminergic neurons that originate in the brainstem causes lower levels of monoamines in the limbic system and in the frontal cortex.

Emotional Connection to PSD

- Having a stroke is a life-changing event. It can change how one feels about their identity and can cause worry about the future. Changes to responsibilities, relationships, work and finances can result in stress and sadness. The impact of stroke on the brain can also cause personality, mood and emotional changes.
- One in three people experience depression at some point during the five years after their stroke. Depression is most common in the first year after a stroke, however it can happen at any time. Anxiety may also occur, either by itself or together with depression.

RISK FACTORS FOR STROKE

Nonmodifiable

- Increasing age: risk doubles every 10 years after the age of 55 years
- Gender: women have a higher lifetime risk for stroke than men
- Race and ethnicity: incidence is higher in African Americans, Hispanics, American Indians, and Alaska natives than Whites or Asians
- Family history: possibly related to genetics and shared environmental and lifestyle influences
- Prior stroke: 10-year risk of recurrence is 43%

Modifiable

- Hypertension: systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg
- Hypercholesterolemia: low-density lipoprotein ≥100 mg/dL
- Obesity: body mass index ≥30 kg/m^2
- Physical inactivity: <30-60 minutes of aerobic activity 3-5 times per week
- Diabetes
- Smoking
- Heavy alcohol consumption: >2 drinks for men and >1 for women per day

Risk Factors for Post Stroke Depression

- Female gender
- Age 60 or under
- Divorced
- Substance abuse
- Non-fluent aphasia
- Major deficit in motor function or cognition
- Lack of social support
- Pre-stroke depression
- Pre-stroke cognitive or neuromuscular impairment

Common Symptoms of Depression

- Persistent sad, anxious or “empty” mood
- Restlessness, frustration, fear, irritability, anger
- Feelings of hopelessness, pessimism, guilt, worthlessness or helplessness
- Loss of interest or pleasure in hobbies and activities, including sex
- Decreased energy and fatigue, and feeling “slowed down”
- Difficulty concentrating, remembering and making decisions
- Insomnia, early-morning awakening or oversleeping
- Appetite and/or weight changes
- Thoughts of death or suicide, or suicide attempts

Symptoms Specific to PSD

Post-stroke depression is characterized by:

- Feelings of sadness
- Hopelessness or helplessness
- Irritability
- Changes in eating, sleeping and thinking

Other common emotional reactions include:

- Frustration
- Anxiety
- Anger
- Apathy or not caring what happens
- Lack of motivation
- Depression

THE EMOTIONAL IMPACT OF STROKE

- "The emotional side of stroke is a wasteland. Many of the emotional issues arrive not at the time of the stroke, when all you are doing is trying to get well again physically, but it's months later when the reality hits that you will never be the person you once were." A stroke survivor
- "I would not wish what I've been through on my worst enemy. I've battled with depression and fatigue, but I no longer consider suicide on a daily basis. I can talk and I make myself do things. Life is a constant daily struggle." A stroke survivor

"I was offered tablets for depression, when I wanted therapy and verbal support to deal with the changes in my role." A stroke survivor

"I wish people would realise that stroke is not an illness that can be treated and then you are well again, but a major life event that usually has lifelong effects." A stroke survivor

"My husband's stroke has been the most devastating experience of my, and his, life. First you have to rebuild the survivor and their life. Then your joint lives together and, if you have any energy left, you can have a go at remembering who you are." A caregiver

THE EMOTIONAL IMPACT OF STROKE

Depression following a stroke/poststroke depression (PSD) has been newly recognized as one of the most common complications after stroke

A total of 76 cases were recruited for the study and out of which 44 were available for the analysis after six months. Patients were divided into three groups according to severity of depression: Group A (without depression), Group B (mild-to-moderate depression), and Group C (severe depression) on the basis of Patient Health Questionnaire-9 (PHQ-9) scale scores. All patients were assessed for depression by PHQ-9, and for quality of life by Stroke Specific Quality of Life (SSQOL) scale. Neuroplasticity was assessed by measuring levels of serum brain-derived neurotrophic factor.

Quality of life was observed to be significantly affected by depression ($P \leq 0.05$). The most commonly affected characteristics were energy, family roles, mobility, self-care, social roles, upper extremity function, and work productivity. Serum BDNF levels were also affected significantly by depression

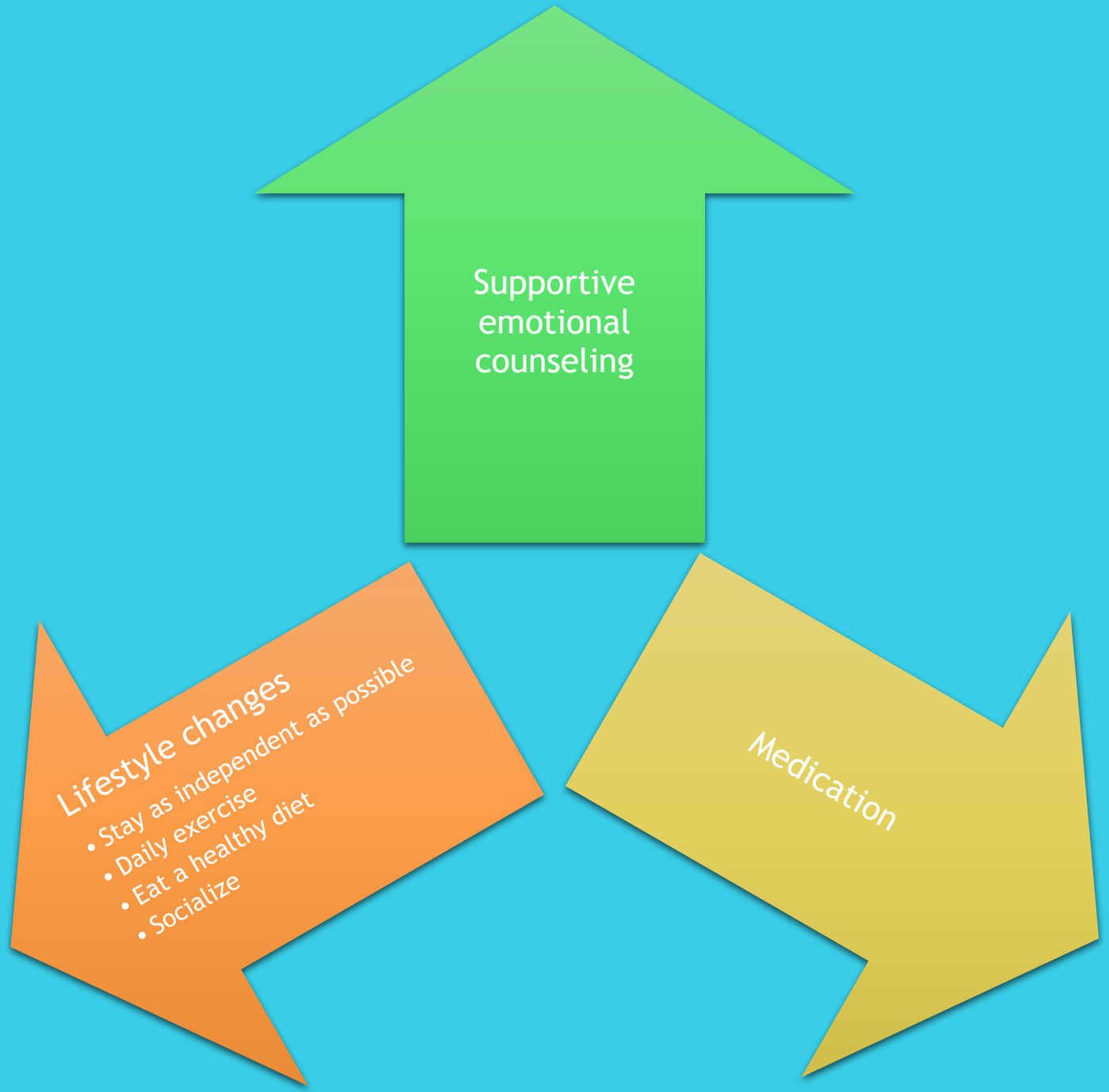
Conclusion:

PSD is a serious complication, affecting quality of life and neuroplasticity (BDNF) in patients. Decreased neuroplasticity further may affect functional improvement.

Effect of PSD on Recovery

- Depression can affect a persons quality of life
- Depression increases the risk of cardiovascular disease and therefore increases the risk of another stroke
- Depression may jeopardize a person's ability to meet functional goals and to reintegrate into society
- The incidence of complications (skin breakdown, urinary tract infections), hospital length of stay, and medical costs expenses may all increase because of depression
- PSD has been linked with higher mortality rates

Treatment for PSD



Supportive Counseling

Psychotherapy has shown to be more effective as adjustment issues emerge later in post-stroke recovery

Early intervention with structured group problem-solving interventions can be effective in improving quality of life and functioning in both patients and significant others/caregivers

Psychotherapy with significant others has been shown to significantly improve functional outcomes for patients and can reduce PSD

Medication

Selective Serotonin Reuptake Inhibitors (SSRIs)

Tricyclic Antidepressants (TCAs)

Stimulant Medication

Selective Serotonin Reuptake Inhibitors

- Fluoxetine (Prozac)
- Sertraline (Zoloft)
- Paroxetine (Paxil)
- Escitalopram (Lexapro)
- Fluvoxamine (Luvox)
- Citalopram (Celexa)
- Volazodone (Viibrid)
- Vortioxetine (Trintellix)

Tricyclic Antidepressants

- Amitriptyline.
- Amoxapine.
- Desipramine (Norpramin)
- Doxepin.
- Imipramine (Tofranil)
- Nortriptyline (Pamelor)
- Protriptyline (Vivactil)
- Trimipramine (Surmontil)

TCAs

Stimulant Medication

- Ritalin (methylphenidate)
- Concerta (extended release methylphenidate)
- Adderall (amphetamine)
- Strattera (atomoxitine hcl)
- Vyvanse (related to dextroamphetamine)
- Dexedrine (dextroamphetamine)

Medication Education

The Good

More effective than placebos in research studies

No blood levels needed

The Bad

Side effect profiles

Remaining on a schedule to avoid missing doses

Potential dietary restrictions (MAOIs)

The Ugly

Black Box Warnings

The choice of antidepressant is based on side-effect profiles, history of prior response, concurrent medical illnesses, concurrently prescribed medications, and antidepressant cost

Lifestyle Changes

- Home changes
  - Making items that are frequently used easy to reach from a chair
  - Using a microwave more often to cook
  - Replacing knobs and handles with levers that are easier to use
  - Installing grab bars in hallways, stairwells, and the bathroom
  - Widening doorways
  - Having doors open out instead of in
  - Keeping rugs and carpets in place to prevent falls
  - Installing a corded phone or keeping a fully-charged cell phone in case of an emergency

Lifestyle Changes

- Quit Smoking
  - Smoking can raise the amount of fatty buildup in the arteries. This can block blood flow to the brain. Nicotine can narrow blood vessels and raise the heart rate and blood pressure. It can also decrease the oxygen in the blood. If smoking continues after the first stroke, the chance of having second one is higher. After quitting, the risk of drops to that of a nonsmoker within 5 years.
- Limit Alcohol
  - Too much alcohol raises the risk of stroke. Limiting alcohol may reduce the risk. It may also lower the risk of heart attack. Alcohol may affect the efficacy of other medications in the system.

Lifestyle Changes

- **Eat a Healthful Diet**
  - A diet low in saturated fat , *trans* fat, and cholesterol, and rich in whole grains , fruits, and veggies will help lower cholesterol, blood pressure, and body weight. These are 3 stroke risk factors. Individuals should also add fish to the diet at least twice per week. This food group contains omega-3 fatty acids.
- **Workout Often**
  - After a stroke, follow medical advice about working out. Choose exercises that are enjoyable and safe. It is important to stick to an exercise program that helps to achieve fitness as well as a healthy weight. For most people, this could mean walking briskly or doing another aerobic activity for at least 30 minutes each day.

CAREGIVERS

- Depression doesn’t just affect the person with a stroke.
- Family caregivers in general already face a high risk of developing depression. Those who are caring for people recovering from stroke are not only dealing with challenges in mobility, care and communication, but a loved one’s depression adds an additional burden that can lead to the caregiver developing a depression of their own.
- Research from the American Stroke Association reveals that 30 to 33 percent of caregivers were depressed at their loved one’s 18-month post-stroke checkup appointments.

Pseudobulbar Affect (PBA)

- Pseudobulbar affect (PBA) is characterized by uncontrolled crying or laughing which may be disproportionate or inappropriate to the social context.
- PBA is a disinhibition syndrome in which pathways involving serotonin and glutamate are disrupted. The underlying mechanism in PBA appears to be a lack of voluntary control

Post Stroke Depression (PSD) vs. Pseudobulbar Affect (PBA)

PBA		PSD
Seconds to minutes	Duration	Weeks to months
None to minimal	Voluntary Control	Modulated by the situation
Unrelated to or independent of mood	Affect	Sad, worried, guilty, depressed
Does not change	Behavior	Fatigue, apathy, agitation
No misperceptions	Perception	Negative view of self, others, future
Usually not impaired	Insight	May be impaired
Nonspecific, minimal, or inappropriate	Stimulus	Specific mood-related situations

Treatment for PBA

- Antidepressants (TCAs, SSRIs) for the **treatment** of PBA are typically prescribed at doses lower than are those used to **treat** depression.
- Dextromethorphan hydrobromide and quinidine sulfate (Nuedexta). This is the only medication approved by the Food and Drug Administration that is designed to specifically **treat** PBA. A study on people with MS and ALS showed that those taking the medication had only about half as many laughing and crying episodes as did those taking the placebo.

NUEDEXTA®

(dextromethorphan HBr and quinidine sulfate) capsules 20 mg / 10 mg

QUESTIONS