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The Mind-Body Connection:
Understanding The Neurobiological Impact Of Stress And Enhancing Brain Health Through Wellness Strategies

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This program is paid for by Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC).

Speakers are employees and/or paid consultants of Otsuka Pharmaceutical Development & Commercialization, Inc.

Objectives

Brief overview of stress, its physiological impact on the body, and its connection to brain health

Introduce strategies for stress reduction and improving brain health

Discuss the effects of wellness practices

What Is Stress?

Stress is the response to any physical or psychological stimuli, resulting in physiological and behavioral changes[1]

- Stress can lead to adverse impacts on cardiovascular, respiratory, endocrine, gastrointestinal, nervous, muscular, and reproductive systems[1]

Chronic stress can induce neuroinflammation, characterized by the activation of glial cells and increased production of pro-inflammatory cytokines in the brain[2]

- This may contribute to the development of various mental health disorders

A, amygdala; HI, hippocampus; PAG, periaqueductal gray; PFC, prefrontal cortex; SSC, somatosensory cortex.

References:

1. Chu B, et al. Physiology, stress reaction. In: *StatPearls*. Treasure Island, FL; 2025.
2. Calcia MA, et al. *Psychopharmacology (Berl)*. 2016;233(9):1637-50.
3. Fülöp B, et al. *Brain Behav Immun Health*. 2025;44:100964.
4. Hassamal S. *Front Psychiatry*. 2023;14:1130989.

Neuroinflammation:
an inflammatory response within the brain and spinal cord[3,4]

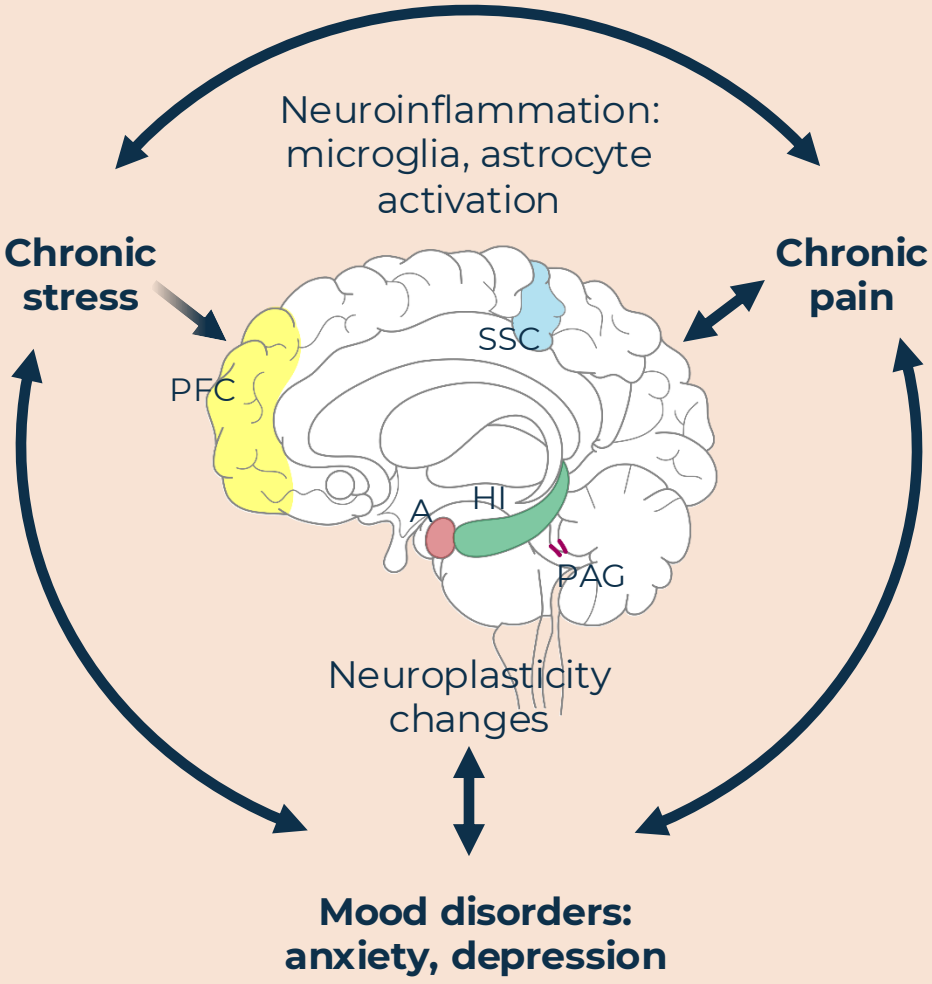

Image reference: Recreated infographic based on Fülöp B, et al. *Brain Behav Immun Health*. 2025;44:100964, with permission through the Creative Commons Attribution License (CC BY).

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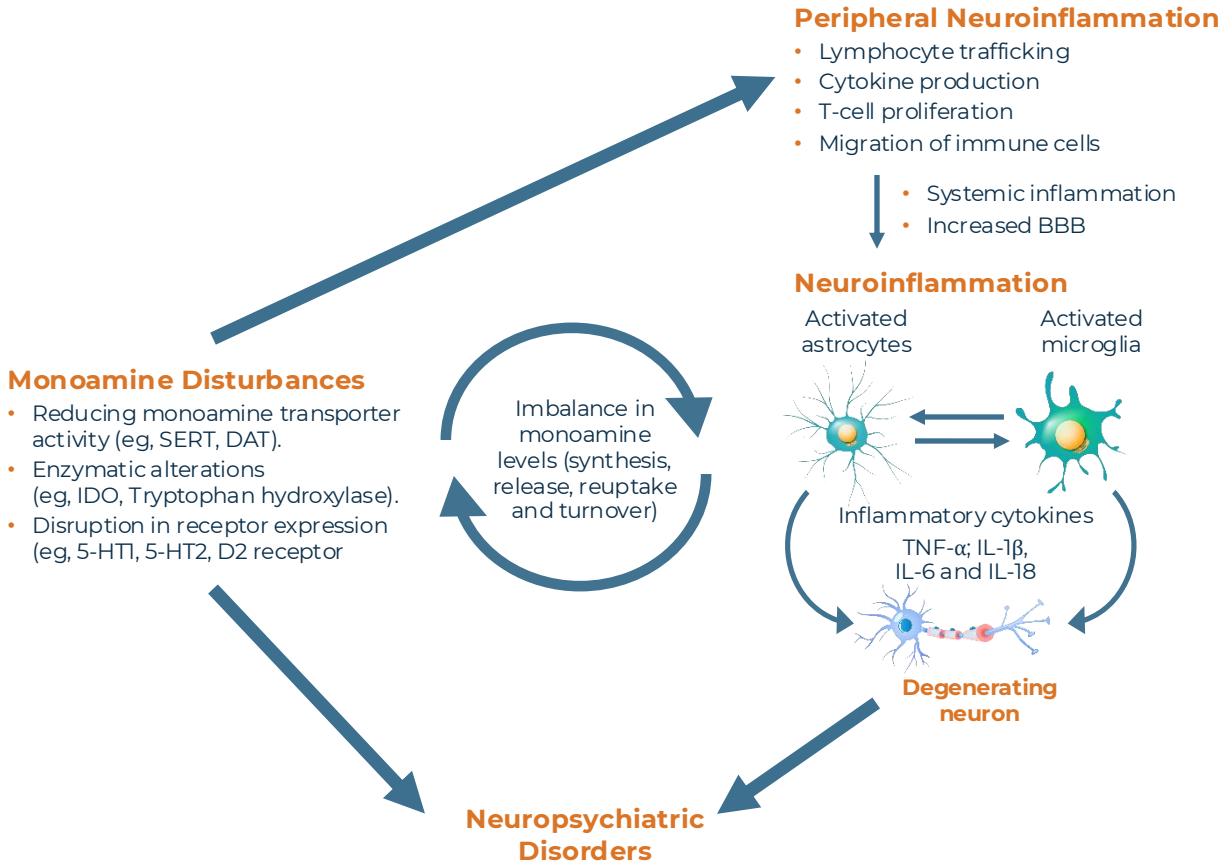
Neuroinflammation: A Key Player In Mental Health

- Neuroinflammation affects structural and functional changes in the brain that predispose individuals to mental illnesses[1]
- A bidirectional relationship exists between monoamine neurotransmitters (NE, DA, 5-HT) and neuroinflammation in neuropsychiatric disorders[2]
  - Pro-inflammatory cytokines directly interfere with monoamine synthesis, release, reuptake, and turnover
  - This imbalance contributes significantly to the pathophysiology of disorders such as MDD and AD, **suggesting combined therapeutic approaches to target both inflammatory and monoaminergic pathways**



5-HT, serotonin; AD, Alzheimer's disease; BBB, blood-brain barrier; DA, dopamine; DAT, DA transporter; IDO, indoleamine 2,3-dioxygenase; IL-18, interleukin-18; IL-1β, interleukin-beta; IL-6, interleukin-6; MDD, major depressive disorder; NE, norepinephrine; SERT, 5-HT transporter; TNF, tumor necrosis factor.

Image reference: Recreated infographic based on Saggu S, et al. *Front Immunol*. 2025;16:1543730, with permission through the Creative Commons Attribution License (CC BY).

References:

1. Calcia MA, et al. *Psychopharmacology (Berl)*. 2016;233(9):1637-50.
2. Saggu S, et al. *Front Immunol*. 2025;16:1543730.

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Early Life Stress Has Consequences On Mental Health

Early life stress broadly refers to stress occurring in childhood (prior to the age of 18)[1]

- Encompasses many kinds of adverse experiences a child might encounter
- Severe and chronic exposure to these types of situations has long-term negative consequences on a wide range of cognitive, emotional, and behavioral processes

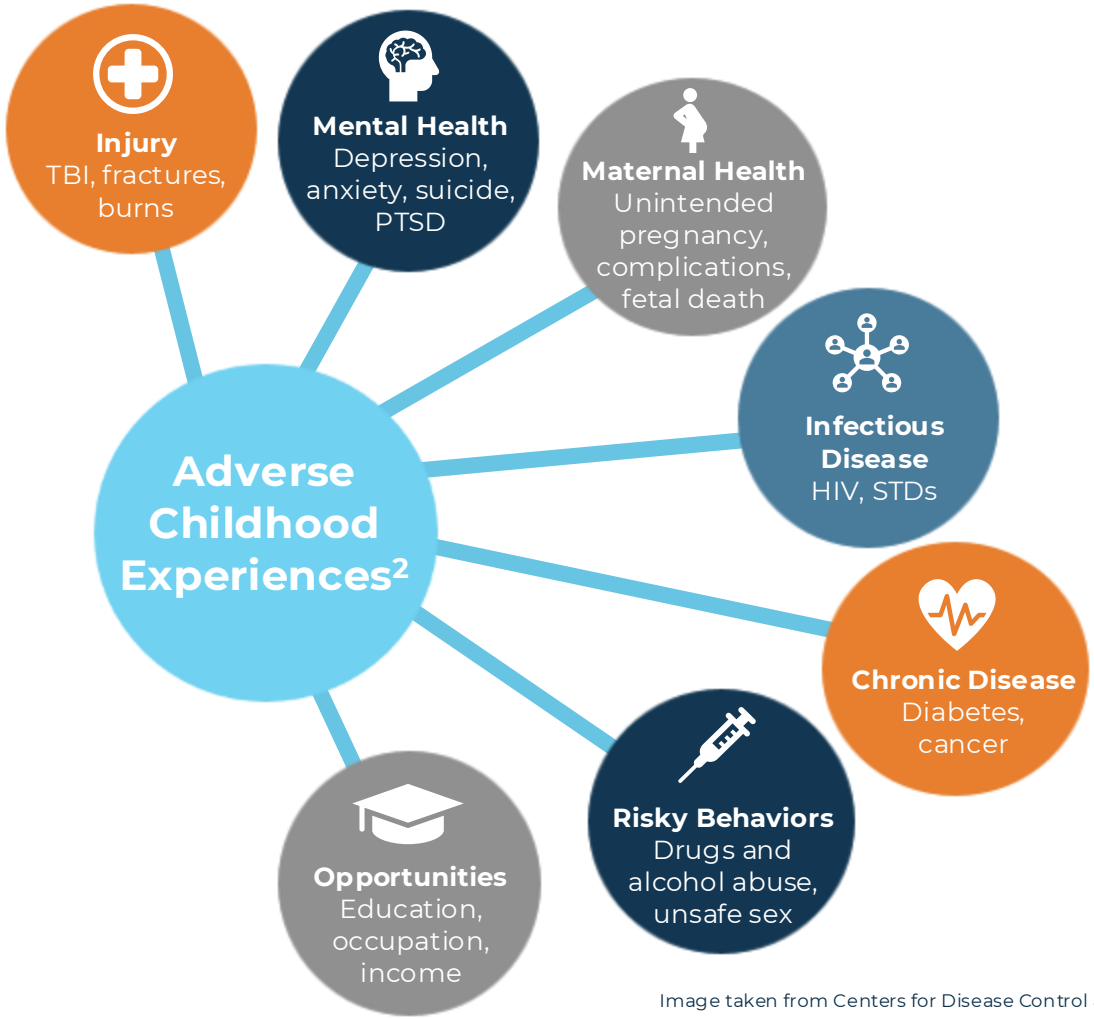

Image taken from Centers for Disease Control and Prevention

HIV, human immunodeficiency virus; PTSD, post-traumatic stress disorder; STD, sexually transmitted disease; TBI, traumatic brain injury.

References:

1. Smith KE, Pollak SD. *J Neurodev Disord*. 2020;12(1):34.
2. Centers for Disease Control and Prevention. About the CDC-Kaiser ACE study. www.cdc.gov. Published April 6, 2021. Accessed June 25, 2025. https://www.cdc.gov/violenceprevention/aces/about.html.

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Negative Impact Of Stress On Brain Function And Structure

Early life stress (ELS) leads to long-lasting alterations in brain structure and function, significantly increasing vulnerability to cognitive and neuropsychiatric disorders in adulthood[1]

Key brain regions affected[2,3]:

- **Prefrontal cortex:** ELS can lead to reduced gray matter volume and altered functional connectivity in the PFC, impairing executive functions such as decision-making, working memory, attention, and impulse control
- **Hippocampus:** Chronic stress during critical developmental windows can result in reduced hippocampal volume
- **Amygdala:** ELS often leads to amygdala hypertrophy and hyper-reactivity

The brain under stress:
structural remodeling[3]

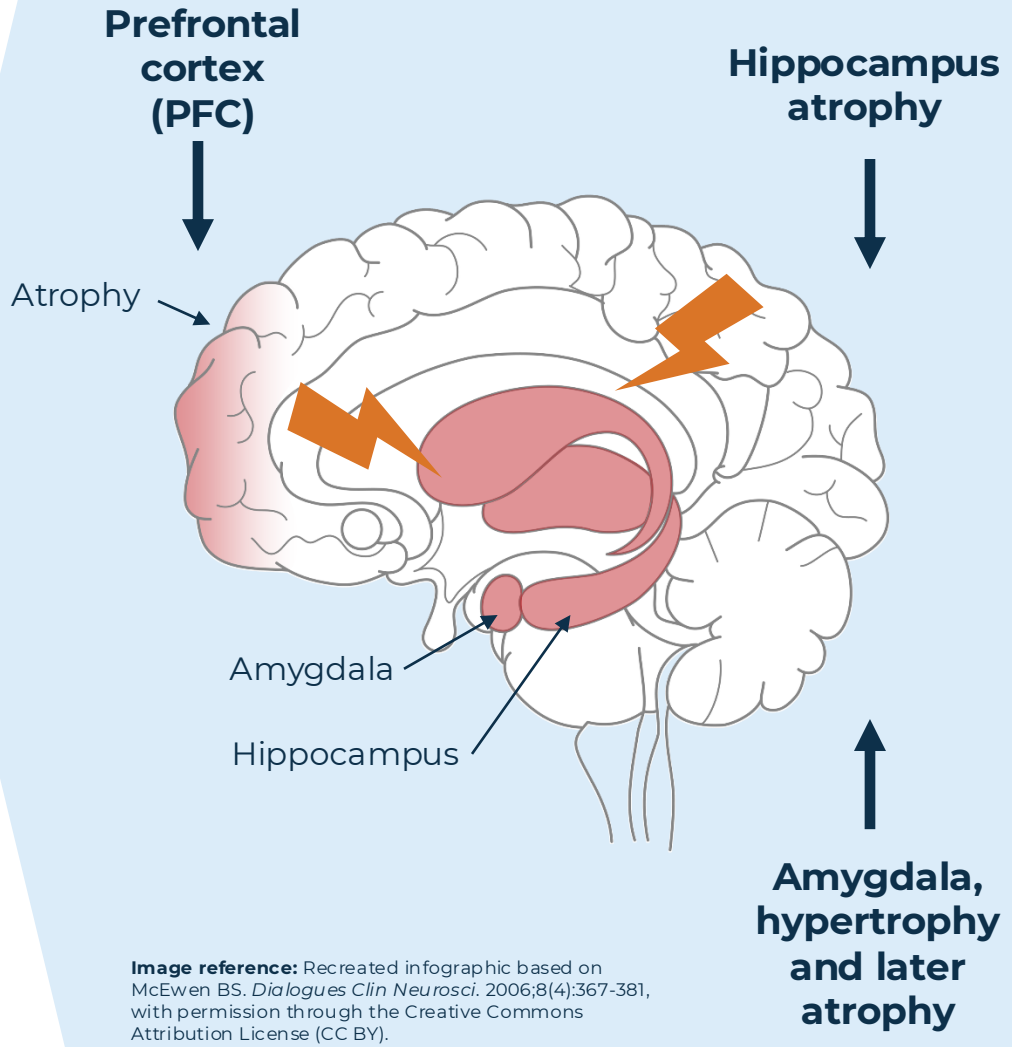

Image reference: Recreated infographic based on McEwen BS. *Dialogues Clin Neurosci*. 2006;8(4):367-381, with permission through the Creative Commons Attribution License (CC BY).

References:

1. Ozturk H. *Journal of Brain and Neurological Disorders*. 2023;5(1):1-4.
2. Lenart-Bugla M, et al. *Psychoneuroendocrinology*. 2022;145:105917.
3. McEwen BS. *Dialogues Clin Neurosci*. 2006;8(4):367-381.

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ELS As A Risk Factor For Mental Health Disorders

- Childhood adversity increases the risk of later mental health disorders[1]
- ELS is linked to a range of mental health disorders, and its impact is thought to be mediated through various neurobiological and psychological pathways[2-5]

ADHD

The severity of stress, in early and later childhood, and the number of stressful experiences may be associated with symptoms of ADHD.[2]

MDD

A review of 77 studies found that individuals who experienced any form of childhood maltreatment were ~2.5x more likely to develop depression in adulthood[3]

Bipolar Disorder

Individuals with bipolar disorder were 2.63x more likely to have experienced childhood adversity compared to those without the disorder. This association was particularly strong for emotional abuse[4]

Schizophrenia

A systematic review and meta-analysis found significant gene-environment correlation (r=0.02) between schizophrenia polygenic risk scores and childhood adversity, suggesting an individual's genetic risk for schizophrenia may influence their exposure to childhood adversity[5]

ADHD, attention-deficient hyperactivity disorder; ELS, early life stress; HPA, hypothalamus-pituitary-adrenal; MDD, major depressive disorder.

References:

1. McKay MT, et al. *J Psychiatr Res*. 2022;156:268-283.
2. Humphreys KL, et al. *J Abnorm Child Psychol*. 2019;47(3):421-432.
3. Watson CB, et al. *Acta Psychiatr Scand*. 2025;151(5):572–599.
4. Palmier-Claus JE, et al. *Br J Psychiatry*. 2016;209(6):454-459.
5. Woolway GE, et al. *Schizophr Bull*. 2022;48(5):967-980.

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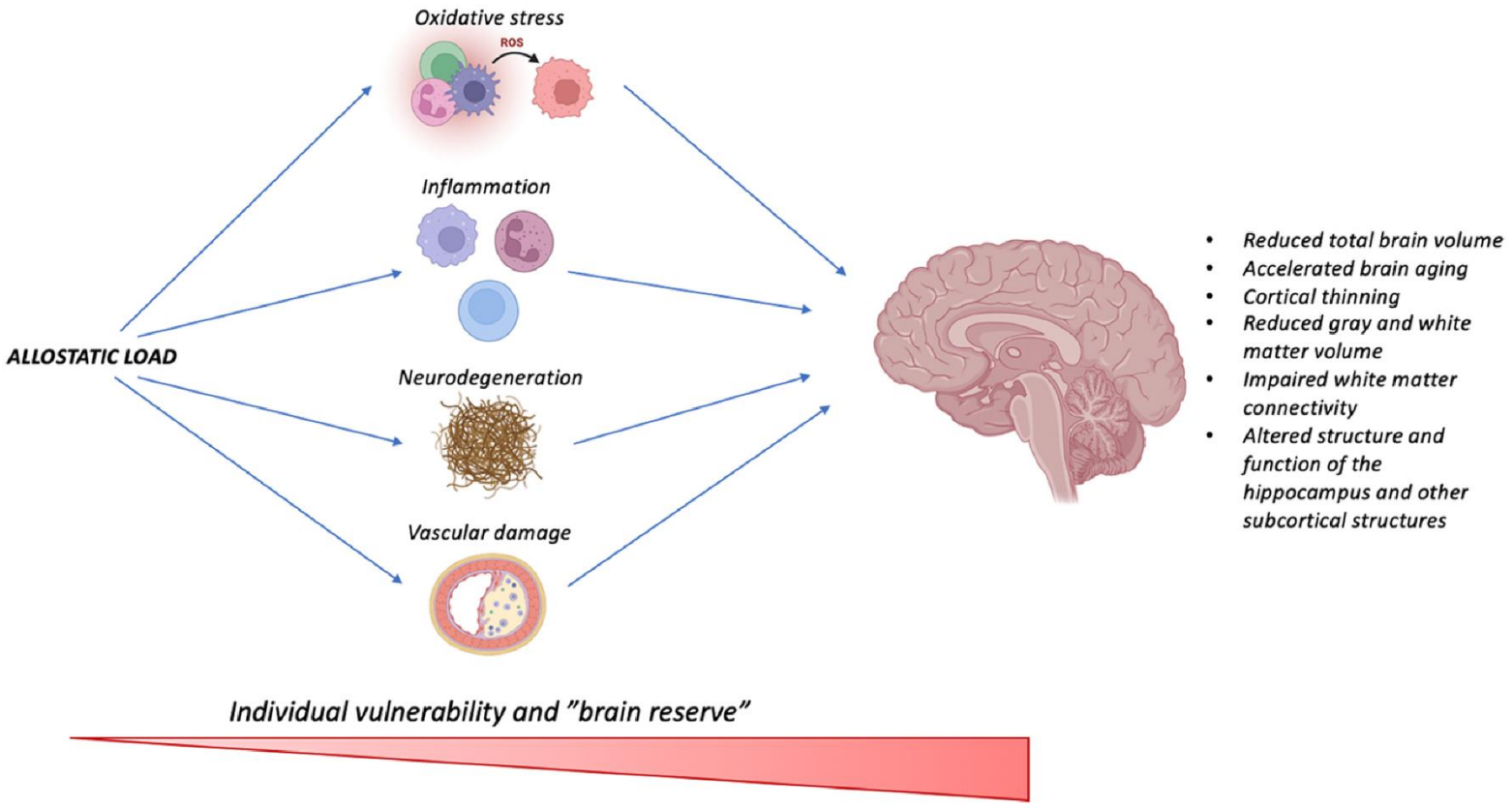
Allostatic Load Affects A Variety Of Brain Regions[1]

- Chronic stress, defined as allostatic load, might be associated with brain alterations in adulthood
- Higher allostatic load is found to be linked to changes in various brain regions, including the hippocampus, amygdala, and prefrontal cortex
- The effects of prolonged stress can manifest as reduced gray matter volume, altered white matter integrity, and changes in density across different brain areas



ROS, reactive oxygen species.

Reference:

1. Lenart-Bugla M, et al. *Psychoneuroendocrinology*. 2022;145:105917.

Image reference: Lenart-Bugla M, et al. *Psychoneuroendocrinology*. 2022;145:105917, with permission through the Creative Commons Attribution License (CC BY).

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Stress As A Risk Factor For Dementia

Stress, including events experienced earlier in life and chronic stress, is recognized as a risk factor for the development and progression of dementia[1]

Results from a systematic review suggest that stressful life events, such as loss of a parent and extreme stress responses, correlate with higher risk of dementia[1]

- **Stressful stimuli**—such as environmental disruptions, pain, or unmet needs—are major causes of agitation associated with dementia due to Alzheimer's disease[2,3]

References:

1. Luo J, Beam CR, Gatz M. *Prev Sci*. 2023;24(5):936-949.
2. Carrarini C, et al. *Front Neurol*. 2021;12:644317.
3. Scales K, Zimmerman S, Miller SJ. *Gerontologist*. 2018;58(suppl_1):S88-S102.

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Wellness Approaches To Reducing Stress And Enhancing Brain Health

Adopting proactive wellness strategies is crucial for both mental and cognitive well-being[1]

These approaches aim to build resilience, optimize brain function, and reduce the risk of stress-related health issues, including long-term cognitive decline[2,3]

- Exercise
- Nutrition
- Mindfulness meditation
- Socialization
- Sleep

References:

1. Worthen M, Cash E. Stress management. In: *StatPearls*. Treasure Island, FL; 2025.
2. Kip E, Parr-Brownlie LC. *Front Neurosci*. 2023;17:1092537.
3. Holt-Lunstad J. *World Psychiatry*. 2024;23(3):312-332.

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Exercise

Effects Of Aerobic Exercise On Inflammation[1]

- A meta-analysis of 15 studies with 1,160 participants found evidence that aerobic exercise could significantly lower circulating inflammatory factor, TNFα, in healthy adults
  - However, aerobic exercise had no significant effects on CRP levels
- A subgroup analysis showed aerobic exercise with a duration>12 weeks at moderate intensity could significantly reduce levels of another inflammatory factor, IL-6
  - The degree of exercise-induced IL-6 response depends on the intensity of the exercise, while the mode of exercise has little influence
- There is increasing evidence suggesting endurance training and combined training of endurance, strength, balance, and flexibility can reduce plasma TNFα levels in healthy elderly people

CRP, C-reactive protein; IL-6, interleukin-6; TNFα, tumor necrosis factor-alpha.

Reference:

1. Wang YH, et al. *Eur Rev Med Pharmacol Sci*. 2022;26(12):4163-4175.

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Aerobic Exercise Has An Effect On Molecular Pathways And Neural Mechanisms In Depression[1]

- A review explored the molecular, neural, and physiological mechanisms by which exercise exerts its antidepressant effects and discussed various exercise interventions for managing depression
- Exercise influences peripheral tryptophan metabolism, central inflammation, and brain-derived neurotrophic factors
  - Exercise impacts these factors partly through the peroxisome proliferator-activated receptor activating factor 1α (PGC-1α) in skeletal muscles
- Uncarboxylated osteocalcin, upregulated by exercise, plays a role in bone-brain communication related to mental well-being

- Additional findings on exercise benefits include:
  - Correction of atypical expression of brain-gut peptides and modulation of cytokine production and neurotransmitter release
  - Regulation of inflammatory pathways and microRNA expression
- Aerobic exercise 3-5 times per week with medium to high intensity contributes to antidepressant effects

Reference:

1. Ren J, Xiao H. *Life (Basel)*. 2023;13(7):1505.

Yoga Program Increases Bilateral Hippocampus Gray Matter Volume

- Sample (N=7) from a larger RCT comparing cognitive and other effects of yoga and wait-listing in the elderly (69-81 years)
  - MRI done before and 6 months after yoga taught 5 days a week (~1 hour) for 3 months
  - After 3 months of training, the participants received a manual describing these practices and were encouraged to continue the practices daily with “booster” training sessions at monthly intervals or any other day if requested

- Effect on hippocampus volume paired sample t-test of grey matter images with apriori region of interest of hippocampus revealed a significant increase in bilateral hippocampus volume (posterior region)
  - Left hippocampus: X=-33, Y=-30, Z=-11; T=2.9; uncorrected P=0.001
  - Right hippocampus: X=32, Y=-22, Z=-18; T=2.3; uncorrected P=0.03
  - No change in volume was observed in the control brain region (superior occipital gyrus)

MRI, magnetic resonance imaging; RCT, randomized controlled trial.

Reference:

1. Hariprasad VR, et al. *Indian J Psychiatry*. 2013;55(Suppl 3):S394-S396.

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Nutrition

Nutrition And Inflammation Reduction

- Diet quality can significantly impact inflammation, which is a key link between chronic stress and various health issues, including those affecting the brain[1]
- Diets rich in antioxidants and dietary fibers may improve mental health and offer neuroprotection[2]
- Emerging research also suggests saffron may have antidepressant potential via neurotransmitter modulation and strong antioxidant properties[4]
- Promoting an anti-inflammatory, nutrient-dense dietary pattern shows promise as an adjunct intervention for management of mental disorders[1-4]

Evidence-based dietary patterns can include[3]:

- **Mediterranean-DASH Intervention For Neurodegenerative Delay (MIND) Diet:** targets neuroprotection with brain-healthy food groups (eg, green leafy vegetables, nuts, whole grains, fish)
- **EAT-Lancet Diet:** emphasizes a rich variety of fruits and vegetables, whole grains, unsaturated oils, nuts, and legumes

References:

1. van Zonneveld SM, et al. *Nutrients*. 2024;16(16):2646.
2. Kamrani F, et al. *BMC Psychiatry*. 2024;24(1):709.
3. Chauhan S, et al. *Yale J Biol Med*. 2024;97(3):365-381.

ELD And MIND Diet Impacts On Mental Well-Being[1]

Research involving 4,579 participants used dietary questionnaires and the DASS-21 scale to assess mental health to determine the association between adherence to the ELD and MIND diets and the risk of depression, anxiety, and stress

ELD

- Higher adherence to ELD was associated with a 35% reduced risk of depression
- However, the study found no significant association between ELD adherence and anxiety or stress

MIND

- Higher adherence to the MIND diet was significantly associated with a reduced risk of depression (39%), anxiety (45%), and stress (38%)
- Participants in the highest quartile of MIND diet adherence showed notably lower odds for all three outcomes

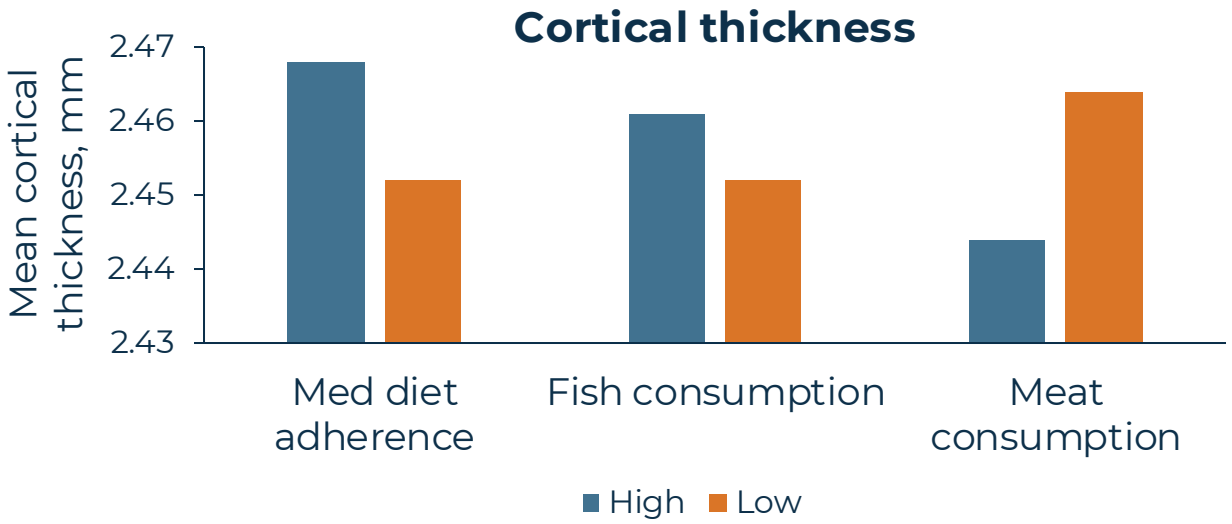
DASS-21, Depression, Anxiety, and Stress Scale-21; ELD, EAT-Lancet reference diet; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay.

Reference:

1. Kamrani F, et al. *BMC Psychiatry*. 2024;24(709):1-11.

Association Of Med Diet, Fish, And Meat With Cortical Thickness[1]

In elderly adults without dementia (N=674), high adherence to a Med diet, higher fish intake, and lower meat intake were associated with more cortical thickness, as measured by MRI



Several food groups and dietary components may play a role in the risk of mental disorders and symptom management[2]

- Through anti-inflammatory and neuroprotective properties, foods such as fruits and berries, green leafy vegetables, and nuts provide nutrition to sustain brain plasticity

In this study of elderly adults, those eating a Med diet, more fish, and less meat had less brain atrophy, which has been related to cognitive decline

Med diet, Mediterranean diet; MRI, magnetic resonance imaging.

Reference:

1. Gu Y, et al. *Neurology*. 2015;85:1744-1751.
2. van Zonneveld SM, et al. *Nutrients*. 2024;16(16):2646.

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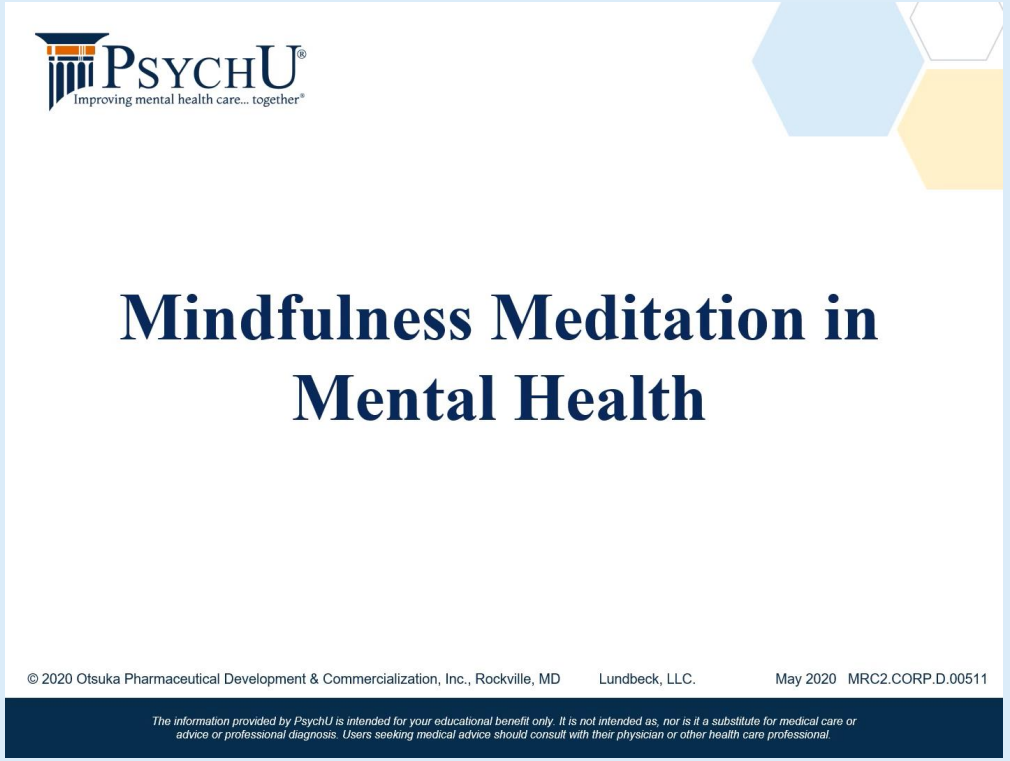
Mindfulness Meditation

What Is Mindfulness Meditation?

Mindfulness meditation is a family of meditation practices that shares an emphasis on reducing distraction and enhancing awareness of present moment experience, while adopting an attitude of openness or acceptance[1,2]

- Most rely on principles from mindfulness-based stress reduction (MBSR)[2]
- Other mindfulness interventions:[1]
  - Mindfulness-based cognitive therapy (MBCT)
  - Mindfulness-based relapse prevention (MBRP)
  - Brief mindfulness meditation training interventions



References:

1. Creswell JD. *Annu Rev Psychol.* 2017;68:491-516.
2. Wielgosz J, et al. *Annu Rev Clin Psychol.* 2019;15:285-316.

The Role Of Mindfulness In Modulating Inflammation

Mindfulness-based interventions hold promise for influencing inflammatory processes, particularly in the context of stress and psychiatric disorders[1,2]

- A 30-day smartphone mindfulness program reduced pro-inflammatory NF-κB gene expression in stressed adults, suggesting a positive impact on immune cell gene expression

The effects on inflammatory biomarkers are modest in psychiatric populations, but these app-based mindfulness programs offer an accessible approach to managing stress[2]

NF-$_{\kappa}$B, nuclear factor enhancer of the kappa light chains of activated B cells.

References:

1. Dutcher JM, et al. *Brain Behav Immun*. 2022;103:171-177.
2. Sanada K, et al. *Int J Mol Sci*. 2020;21(7):2484.

Mindfulness-Based Interventions Have Potential For Improving Mental Health And Inflammation[1]

A meta-analysis of 10 trials with 998 participants were reviewed to determine the effects of mindfulness-based interventions (MBIs) on biomarkers in psychiatric disorders

Significant findings include improvements in:

- ERP amplitudes in patients with ADHD
- Salivary levels of IL-6 and TNF-α in participants with depressive symptoms
- Blood levels of ACTH, IL-6, and TNF-α in patients with GAD

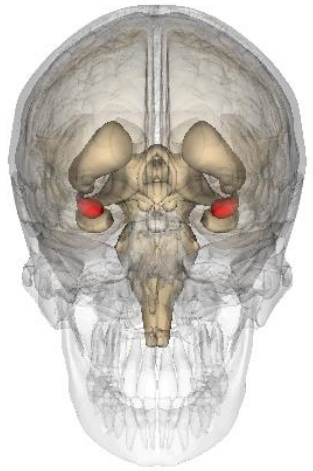
ACTH, adrenocorticotropic hormone; ADHD, attention-deficit hyperactivity disorder; CRP, C-reactive protein; ERP, event-related potential; GAD, generalized anxiety disorder; IL-6, interleukin-6; PTSD, post-traumatic stress disorder; TNF-α, tumor necrosis factor-α.

Reference:

1. Sanada K, et al. *Int J Mol Sci*. 2020;21(7):2484.

Mindfulness Associated With Smaller Amygdala Volume[1]

Self-reported measure of dispositional mindfulness (MAAS) and structural MRI images were obtained from 155 healthy community adults



- Higher dispositional mindfulness is associated with **decreased gray matter volume** in the right amygdala
- Smaller amygdala volumes may reflect a potential neurobiological mechanism for:
  - **Reduced stress reactivity in more mindful individuals**
  - **Lower negative affect in daily life**

MAAS, Mindful Attention Awareness Scale; MM, mindfulness meditation

Reference:

1. Taren AA, et al. *PLoS One*. 2013;8(5):e64574.

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Socialization

The Multifaceted Impact Of Socialization On Brain Health

Social connection is increasingly recognized as a factor linked to both mental and physical health[1,2]

Mental health: Social connections play an important role in preventing mental health problems, maintaining good mental health, and helping in the recovery of mental health conditions

Stress levels: Social support can act a buffer against stress and can foster resilience and well-being

Cognitive health: Having stronger social interactions is associated with better cognitive function

References:

1. Holt-Lunstad J. *World Psychiatry*. 2024;23(3):312-332.
2. Delgado MR, et al. *Neuron*. 2023;111(24):3911-3925.

Social Connection Plays A Vital Role In Mental Health[1]

- A strong, consistent link exists between **social isolation** and **loneliness with depression** from youth to older adulthood
- Conversely, higher social connectedness is a protective factor, actively guarding against depressive symptoms and disorders. **Even living alone or lacking emotional support independently raises depression risk**
- Research, including longitudinal and genetic studies, reveals that associations appear to have a bidirectional relationship; **social isolation and loneliness could increase the risk for poorer mental health, and poorer mental health could increase the risk for isolation and loneliness**
- The link between social connection and mental well-being extends beyond general population studies, **affecting groups like health care workers who experience burnout and stress**

Reference:

1. Holt-Lunstad J. *World Psychiatry*. 2024;23(3):312-332.

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Social Connection Also Plays A Role In Cognitive Health[1]

Stronger social connections are consistently linked to better cognitive function and a lower risk of dementia, including:

- Social networks: number of contacts, marital status, living arrangements
- Social engagement: attending social groups, visiting loved ones, volunteering

A large meta-analysis of **over 2.3 million participants** show that living alone, smaller social networks, lower frequency of social contact, and **poor social support were risk factors for dementia**

While some extensive meta-analyses did not find a direct link between loneliness and dementia risk, **others have reported an association between greater loneliness and incident dementia**

Reference:

1. Holt-Lunstad J. *World Psychiatry*. 2024;23(3):312-332.

Sleep

Sleep, Inflammation, And Mental Health Are Interconnected

Poor sleep can foster a state of allostatic overload and impair brain neuroplasticity and activate stress-immune pathways, **ultimately contributing to mental health disorders through increased inflammation**[1]

Sleep also supports immune function by ensuring proper production of immune cells and reducing the body's inflammatory burden[2]

Targeted interventions to improve sleep quality consistently demonstrate significant clinical improvement in psychiatric symptomology[3]

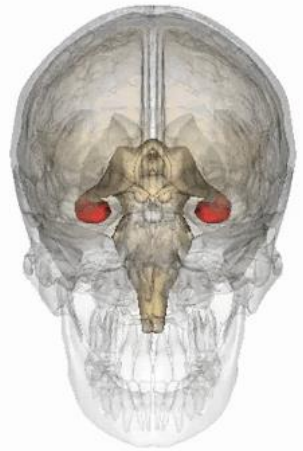
- These include reductions in depression, anxiety, perceived stress, and maladaptive rumination

References:

1. McEwen BS, et al. *Sleep Med Clinl.* 2022;17(2):253-262.
2. NHLBI News. NIH-funded study shows sound sleep supports immune function. Published September 21, 2022. Accessed June 17, 2025. https://www.nhlbi.nih.gov/news/2022/nih-funded-study-shows-sound-sleep-supports-immune-function.
3. Scott AJ, et al. *Sleep Med Rev.* 2021;60:101556.

Sleep Deprivation Contributes To Reduction In Hippocampal Volume[1]

Differences in hippocampal volume compared between chronic primary insomniacs (n=20) and good sleepers (n=20)



Left or right hippocampal volume was negatively correlated with:

- Longer insomnia duration (left: r=-.87, p<.001; right: r=-.87, p<.001)
- Higher arousal index in nighttime polysomnography (left: r=-0.44, p=.045; right: r=-.41, p=.026)

Long duration of insomnia (7.6 years) and poor sleep quality contributed to bilateral reduction in HV

HV, hippocampal volume.

Reference:

1. Noh HJ, et al. *J Clin Neurol.* 2012;8(2):130-138.

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Wellness Practices

Primary Prevention For Cognitive Decline[1]

Lifestyle modifications can optimize brain health and reduce risk of cognitive decline:

- Manage vascular and metabolic health
- Adopt a healthy diet
- Prioritize physical activity
- Foster social engagement
- Optimize sleep
- Engage in cognitive stimulation

Wellness practices are the first steps towards addressing brain health and preventing cognitive decline

Reference:

1. Sabbagh MN, et al. *Alzheimers Dement*. 2022;18(8):1569-1579.

Lifestyle Modifications For MCI/Early Alzheimer's Disease[1]

Comprehensive lifestyle changes are found to have notable gains in cognitive function and daily living activities

In a randomized controlled trial (n=51), participants experienced less cognitive decline compared to those receiving usual care after 20 weeks

Each participant received a book describing a multi-component lifestyle intervention which consisted of:

Whole foods plant-based diet, regular exercise for at least 30 minutes/day of aerobic exercises and mild strength training, daily stress management for one hour per day, group support, and supplements

After 20 weeks, the comprehensive lifestyle intervention yielded significant benefits

- The intervention group showed significant improvements in cognitive function and overall clinical status, including less disease progression, as measured by CGIC, CDR-SB, CDR Global, and ADAS-Cog test
- A favorable increase in the plasma Aβ42/40 ratio, a marker relevant to Alzheimer's disease pathology, which also correlated with improved cognition

ADAS-Cog, AD Assessment Scale–Cognitive Subscale; CGIC, Clinical Global Impression of Change; CDR Global, Clinical Dementia Rating Global; CDR-SB, Clinical Dementia Rating Sum of Boxes; MCI, mild cognitive impairment.

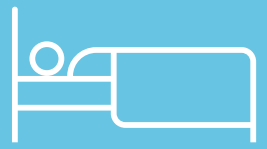
Reference:

1. Ornish D, et al. *Alzheimers Res Ther*. 2024;16(1):122.

WILD 5: A Proven Path To Wellness[1]

WILD 5 Wellness is a multi-domain intervention targeting five key areas, designed for patients as an adjunct to treatment, but applicable to general wellness

Wellness-Enhancing Practices: Daily For 30 Days



Use at least 4 of the 6 sleep hygiene practices:

1. Maintaining a 7-day-a-week regular bedtime
2. Enjoying a warm bath or shower before bed
3. Avoiding electronic gadgets 90 minutes before bedtime
4. Eliminating daytime napping
5. Removing ambient light in nighttime sleep environment
6. Skipping caffeinated beverages 10 hours before bedtime

Reference:

1. Rolin D, et al. *J Am Psychiatr Nurses Assoc*. 2020;26(5):493-502.

Clinical Outcomes Of The 30-Day WILD 5 Wellness Program[1,2]

Depression (measured by PHQ-9)

Mental health (n=82): 43% improvement
Pre-mean: 11.4
Post-mean: 6.4
p<0.0001

Pain (n=51): 43% improvement
Pre-mean: 11.9
Post-mean: 6.7
p<0.0001

Anxiety (measured by GAD-7)

Mental health (n=82): 40% improvement
Pre-mean: 9.9
Post-mean: 5.9
p<0.0001

Pain (n=51): 39% improvement
Pre-mean: 10.3
Post-mean: 6.2
p<0.0001

Sleep (measured by PSQI)

Mental health (n=82): 29% improvement
Pre-mean: 10.3
Post-mean: 7.3
p<0.0001

Pain (n=51): 29% improvement
Pre-mean: 11.8
Post-mean: 8.3
p<0.0001

GAD-7, General Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire; PSQI, Pittsburgh Sleep Quality Index.

References:

1. Jain S, et al. Poster presented at: 29th Annual US Psychiatric Congress Annual Meeting; October 21-24, 2016; San Antonio, TX.
2. Jain S, et al. Poster presented at: 29th Annual US Psychiatric Congress Annual Meeting; October 21-24, 2016; San Antonio, TX.

Wellness Programs And Mental Health Outcomes[1]

A systematic review of 96 randomized clinical trial studies confirmed that lifestyle interventions **reduce symptoms of anxiety, depression, and stress**

Programs often integrate physical activity, dietary changes, and sleep hygiene, showing combined benefits for mental well-being

These wellness programs offer a promising, often more accessible and cost-effective, complement to traditional treatments for common mental health issues

Reference:

1. Amiri S, et al. *Healthcare (Basel)*. 2024;12(22):2263.

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Medication And Healthy Lifestyle Interventions

Stress reduction in individuals with mental health disorders is most effective when combining **medication** with **healthy lifestyle interventions**[1]

- **Medication:** reduces symptoms of anxiety, depression, psychosis; improves neurochemical balance[2,3]
- **Lifestyle:** decreases stress, anxiety, and depression (Hedges' g ~ -.34, -.24, -.21, respectively); improves physical health[4]
- **Combined approach:** increases treatment adherence, enhances symptom relief, boosts well-being, and improves health markers[1]

References:

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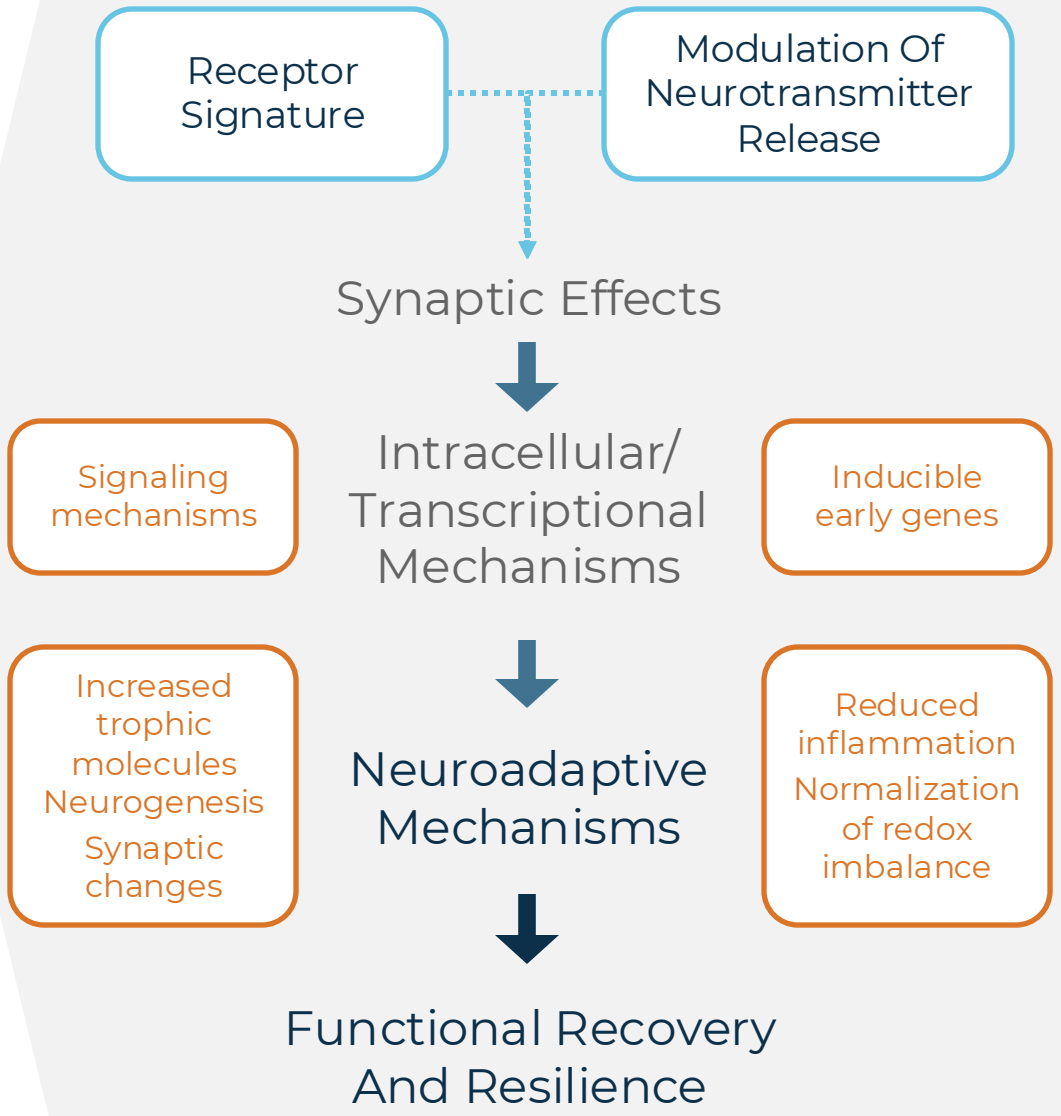
Atypical Antipsychotics Have An Effect On The Monoamine System And Beyond

- Atypical antipsychotics exert their effects through complex modulation of serotonin, dopamine, and norepinephrine receptors[1,2]
- Modulation of these monoamine systems, particularly serotonin 5-HT_{1A} receptor agonism and 5-HT_{2A} receptor antagonism, is implicated in their ability to increase BDNF levels and downstream signaling pathways that lead to neurogenesis and neuroprotection[1,2]
- Recent systematic reviews highlight the neuroprotective profile of atypical antipsychotics stemming from their engagement with a wider array of targets beyond monoamine receptors, potentially on multiple molecular signaling pathways[2]



BDNF, brain-derived neurotrophic factor.

References:

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Anti-Inflammatory And Neuroprotective Effects Of Atypical Antipsychotics

Mechanism	Description	Example Disorders	Supporting Evidence
Microglial Modulation[1]	Inhibit activation of brain immune cells (microglia), reducing pro-inflammatory cytokines	Schizophrenia	Review summary describing microglial inflammatory mechanisms and how atypical antipsychotics ↓ IL-6 and TNF-α after treatment
Cytokine Regulation[2-5]	Lower systemic and CNS levels of IL-6, TNF-α; increase IL-10	Depression, schizophrenia	Systematic review and meta-analyses on SSRIs and atypical antipsychotics; serum cytokine studies
Oxidative Stress Reduction[6]	Increase antioxidant enzymes (eg, SOD, glutathione), reduce reactive oxygen species	Schizophrenia	Meta-analysis of levels of oxidative stress-related markers between medicated and unmedicated patients
Mitochondrial Protection[7,8]	Stabilize mitochondrial membrane potential, reduce apoptosis	Bipolar disorder, neurodegeneration	Reviews of animal models on schizophrenia and neurodegenerative disorders and studies on impact of psychoactive drugs
Neurotrophic Effects[7,9]	Elevate BDNF levels to support neurogenesis and synaptic repair	MDD, cognitive symptoms	Systematic review and meta-analysis on BDNF concentrations

BDNF, brain-derived neurotrophic factor; CNS, central nervous system; IL-6, interleukin-6; IL-10, interleukin-10; MDD, major depressive disorder; SOD, superoxide dismutase; SSRI, selective serotonin reuptake inhibitor; TNF-α, tumor necrosis factor-α.

References:

1. Faustmann TJ, et al. *Front Psychiatry*. 2025;16:1522128.
2. Patlola SR, et al. *J Psychiatr Res*. 2023;160:126-136.
3. Alvarez-Herrera S, et al. *Front Endocrinol (Lausanne)*. 2020;11:195.
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5. Boiko AS, et al. *Pharmaceuticals (Basel)*. 2021;14(5):446.
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7. He J, Kong J, Tan QR, et al. *Cell Adh Migr*. 2009;3(1):129-137.
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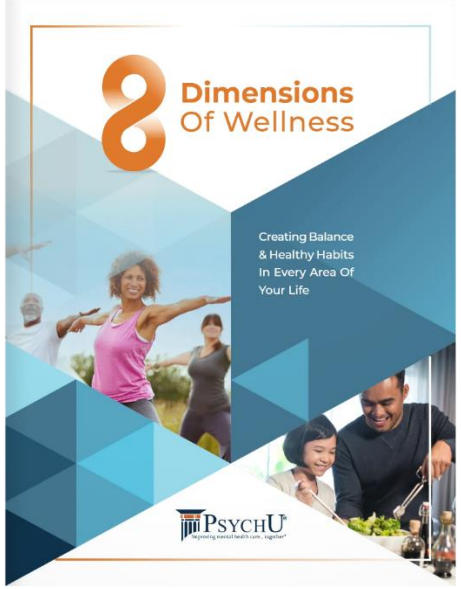

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Summary

- Stress exerts a profound and detrimental influence on nearly every system in the body
- Sustained stress impacts brain structure and function, contributing to cognitive impairment, emotional dysregulation, and increased vulnerability to neurological and psychiatric conditions
- Integrating evidence-based wellness practices—including regular exercise, balanced nutrition, mindfulness meditation, meaningful social engagement, and optimized sleep hygiene—offers accessible strategies for mitigating the effects of stress
- Stress reduction in individuals with mental health disorders is most effective when pharmacologic treatment is combined with healthy lifestyle interventions

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The Mind-Body Connection:
Understanding The Neurobiological Impact Of Stress And Enhancing Brain Health Through Wellness Strategies

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