PsychU®
Improving mental health care... together®

Wellness in Mental Health:

Examining Its Neurobiology and Clinical Application

May 2022 US.PSY.D.22.00004

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

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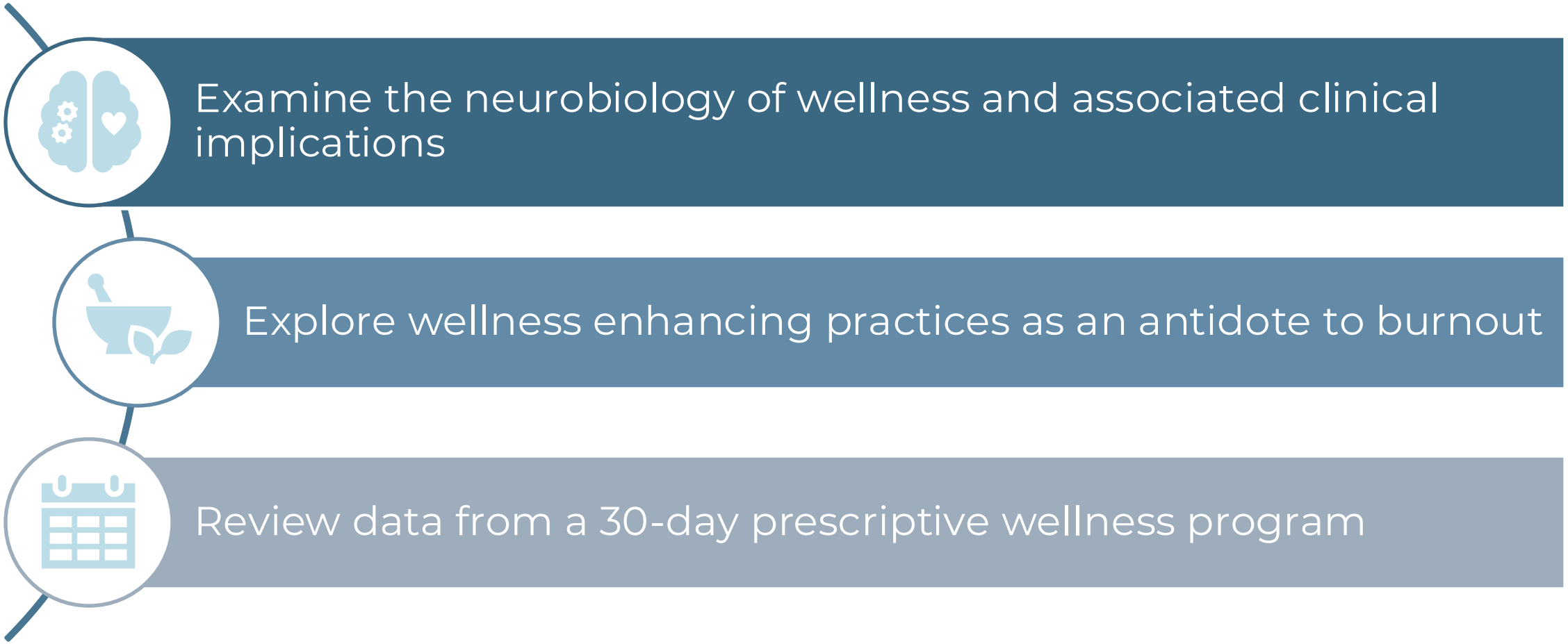
Key Objectives



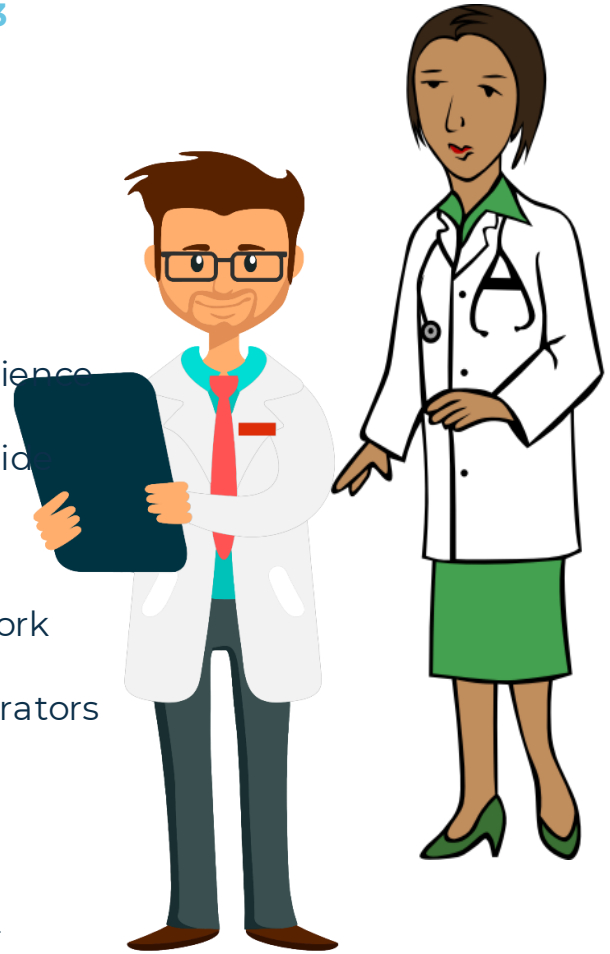
American Landscape of Burnout

THE PATIENT[1]

- ~10 million (1 in 25) American adults live with severe mental illness*
  - 2.4 million with schizophrenia
  - 6.1 million with bipolar disorder
  - 16 million with major depression
  - 42 million with anxiety disorders
- $193.2 billion in costs to the US in lost earnings due to SMI
- Worldwide nearly 800,000 people die of suicide each year

THE PROVIDER[2,3]

- Burnout is defined as:
  - loss of enthusiasm for work
  - feelings of cynicism
  - low sense of personal accomplishment
- 41% of providers in psychiatry experience burnout
  - 15% have had thoughts of suicide
- Factors contributing to burnout:
  - Stressful work environment
  - Spending to many hours at work
  - Too many bureaucratic tasks
  - Lack of respect from administrators and colleagues

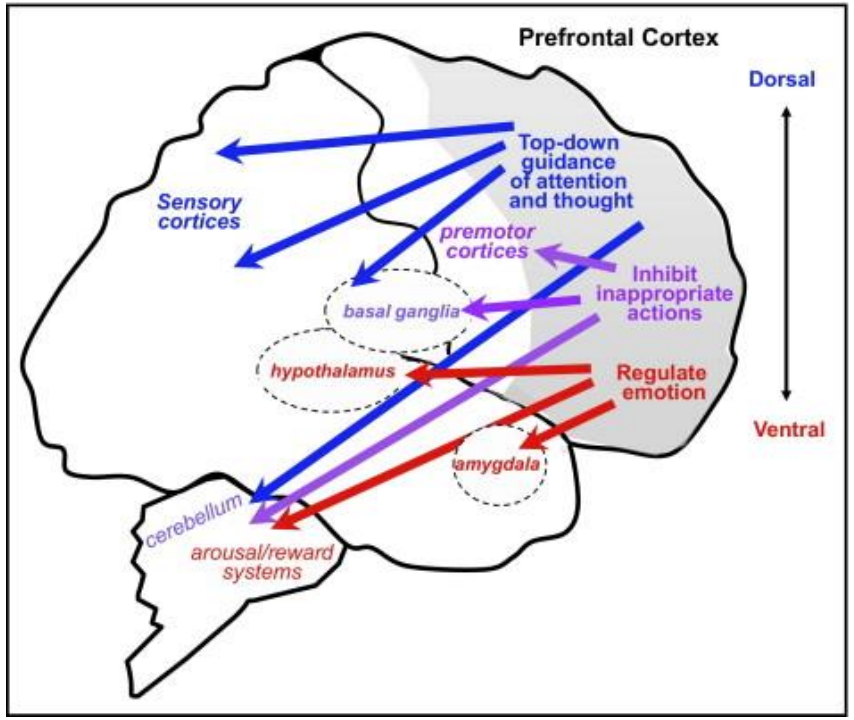


*Based on data from the 2016 National Survey on Drug Use and Health (NSDUH) performed by the Substance Abuse and Mental Health Services Administration (SAMHSA).
SMI, severe mental illness; US, United States.

1. NAMI. Mental Health Facts in America. Available at: https://www.nami.org/NAMI/media/NAMI-Media/Infographics/GeneralMHFacts.pdf. Accessed October 2, 2018.
2. Maslach, C., & Leiter, M. P. World Psychiatry, 2016; 15: 103-111.
3. Kane, L. Medscape National Physician Burnout & Suicide Report 2021. January 22, 2021. Available at: www.medscape.com/slideshow/2021-lifestyle-burnout-6013456#1. Accessed April 7, 2022.

Impact of Stress on the Prefrontal Cortex (PFC)

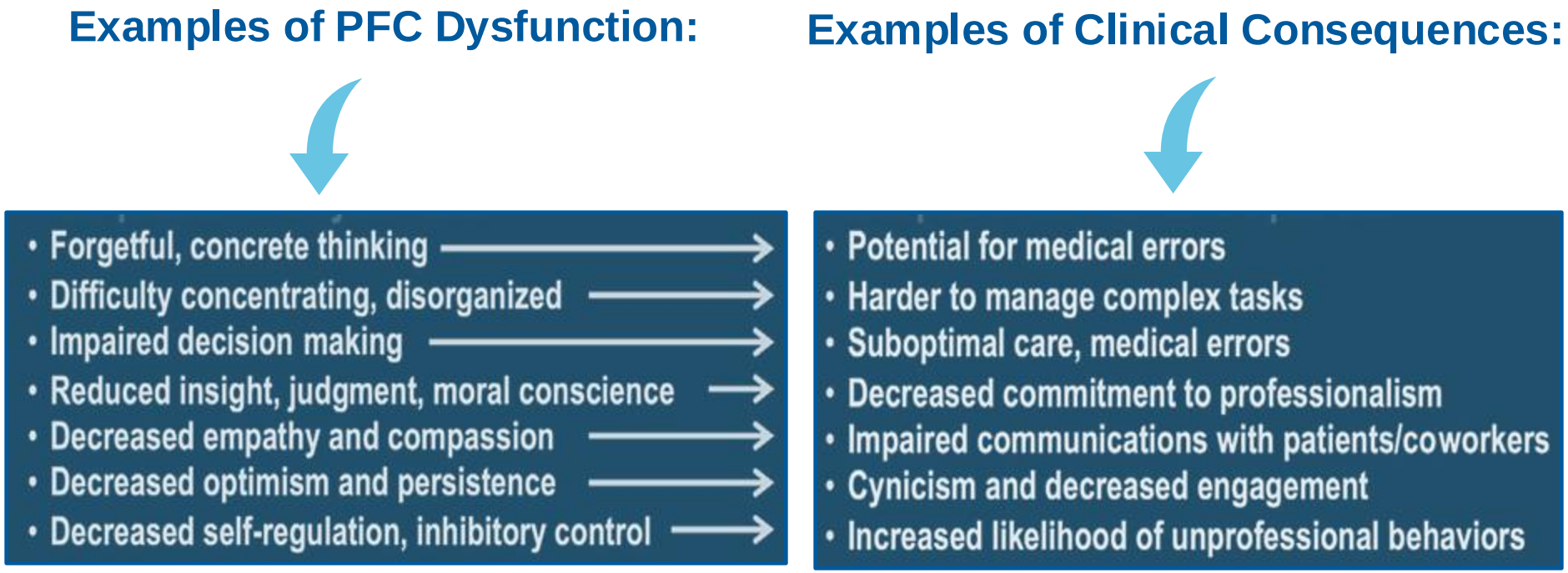
- PFC resides in the brain's frontal lobe
- Has extensive connections with cortical and subcortical brain areas
- Provides top-down control over thought, attention, action, and emotion when we feel rested, interested, and in control
- Under extreme stress or fatigue, PFC connections are weakened (gray)
- Loss of top-down control and impaired PFC cognitive functions
- Stress activates more primitive brain circuits (highlighted in red) that mediate unconscious responses and habits
- Chronic stress exposure causes atrophy of PFC connections, which weaken the thoughtful, evaluative responding needed for professional and personal fulfillment



PFC, prefrontal cortex.

1. Arnsten AFT, et al. *Mayo Clin Proc*. 2021;96(3):763-769.

Prefrontal Cortex (PFC) Dysfunction



PFC, prefrontal cortex.

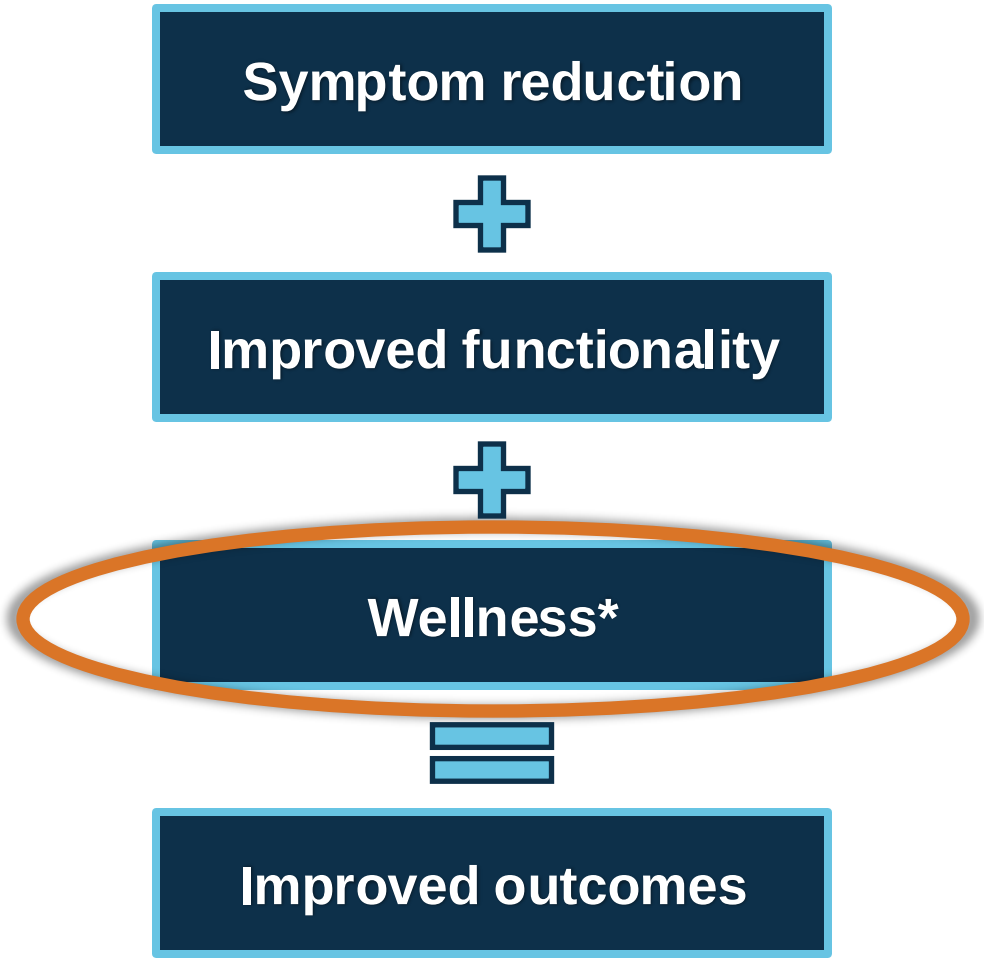
1. Arnsten AFT, et al. Mayo Clin Proc. 2021;96(3):763-769.

Health Is Complex and Entails Many Factors

"[Health is] a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."

1. World Health Organization. https://www.who.int/mental_health/evidence/MH_Promotion_Book.pdf. Accessed July 24, 2017.

Are Traditional Treatment Goals Comprehensive?



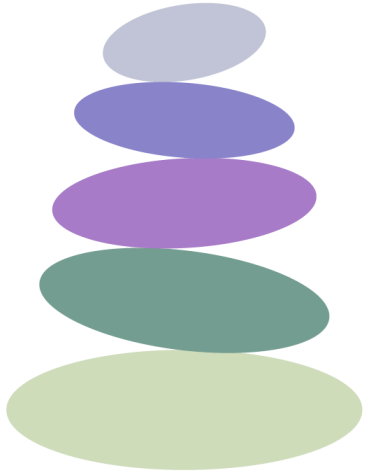
*Information based on Dr Jain's own experience in psychiatric settings.

1. Becker et al. Adm Policy Ment Health. 2011;38:440-458.

What Factors Define “Wellness”?

*Information based on Dr Jain’s own experience in psychiatric settings.

1. Kahn et al. J Med Internet Res. 2016;18:e255.
2. Foucher-Urcuyo et al. J Am Board Fam Med. 2017;30:350-361.
3. Booth et al. Compr Physiol. 2012;2:1143-1211.
4. Upchurch and Rainisch. J Altern Complement Med. 2014;20:32-39.



WILD5

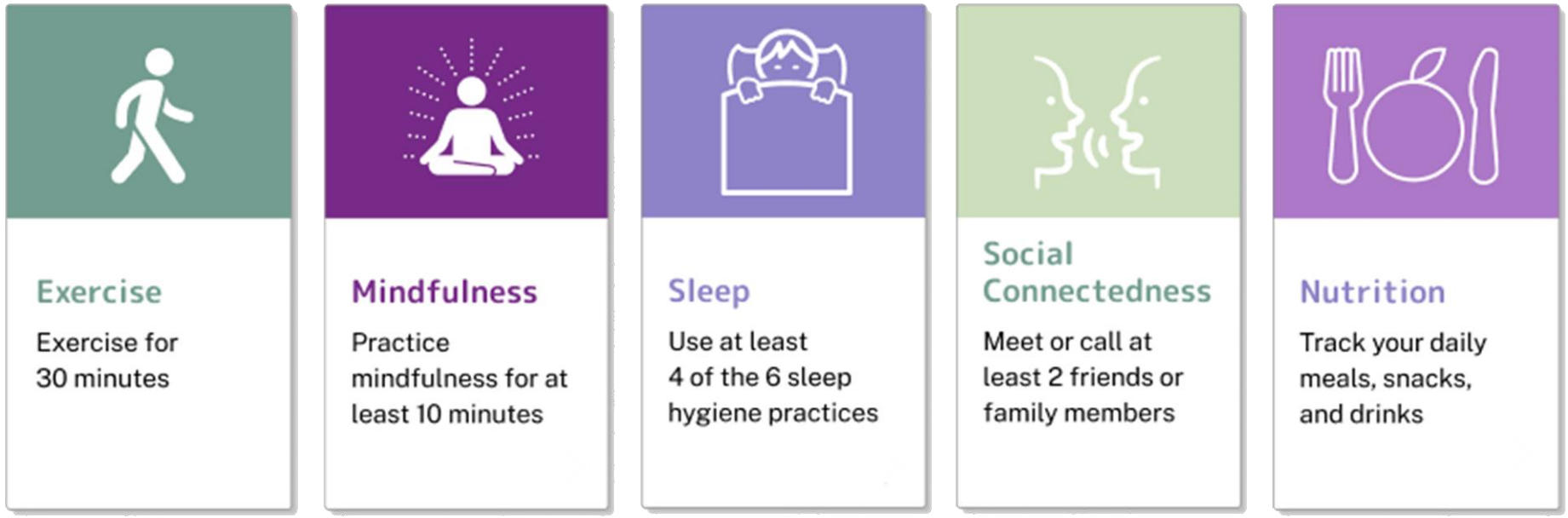
A Proven Path to Wellness

Wellness interventions were lacking in our practice. To meet our patients' needs, we designed a 30-day wellness program.

1. Rolin, D. Fox, I., et al. Journal of the American Psychiatric Nurses Association, 2020; 26(5): 493-502.

WILD 5: A Proven Path to Wellness

Wellness-Enhancing Practices



Daily for 30 Days

1. Rolin, D. Fox, I., et al. Journal of the American Psychiatric Nurses Association, 2020; 26(5): 493-502.

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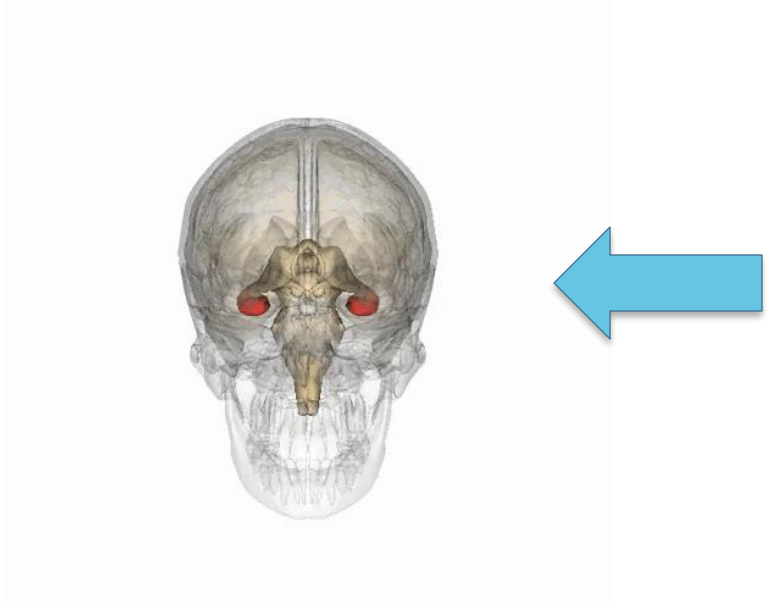
Wellness-Enhancing Practices

Daily for 30 Days

1. Rolin, D. Fox, I., et al. Journal of the American Psychiatric Nurses Association, 2020; 26(5): 493-502.

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 pre-post 6 months of 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 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

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

Hippocampal Response to Long-Term Program of Moderately Intense Exercise

- Sedentary adults (N =26) at-risk for mobility disability in a 24-month randomized intervention program of physical activity or health education
  - Volumes of total hippocampus were measured at baseline and at 24-month follow-up using 7 Tesla MRI

Participation in a 24-month PA program was associated with larger hippocampal volume

Larger hippocampal volume was associated with higher percent sessions attended for the PA group, but not for the HE group

Results were similar after adjustment for dementia-related factors (education, APOE, diabetes, cardiovascular diseases, and brain atrophy)

Among older and frail adults there is a positive effect on hippocampal volume post-intervention

PA, physical activity (walking at moderate intensity, lower extremity resistance exercises, balance exercises, stretching, and behavioral counseling); HE, health education (education seminars regarding health-related matters and upper extremity stretching); MRI = magnetic resonance imaging.

1. Rosano C, et al. Am J Geriatr Psychiatry. 2017;25(3):209-217.

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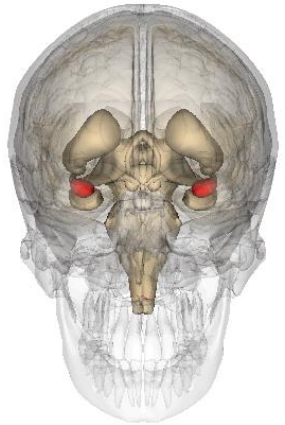
1. Rolin, D. Fox, I., et al. Journal of the American Psychiatric Nurses Association, 2020; 26(5): 493-502.

Mindfulness Associated with Smaller Amygdala Volume

- Self-report 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**

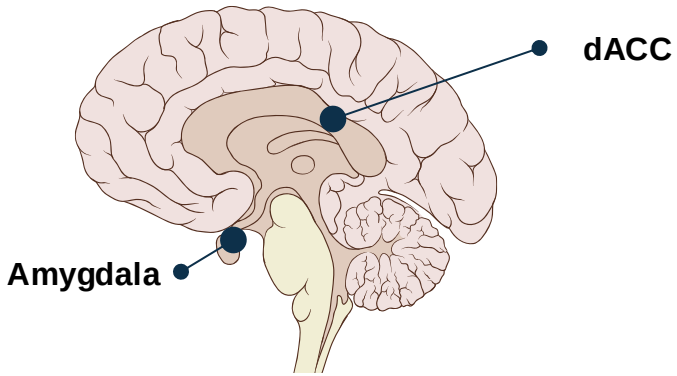
MAAS, Mindful Attention Awareness Scale; MM, mindfulness meditation

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

Mindfulness May Reduce Stress

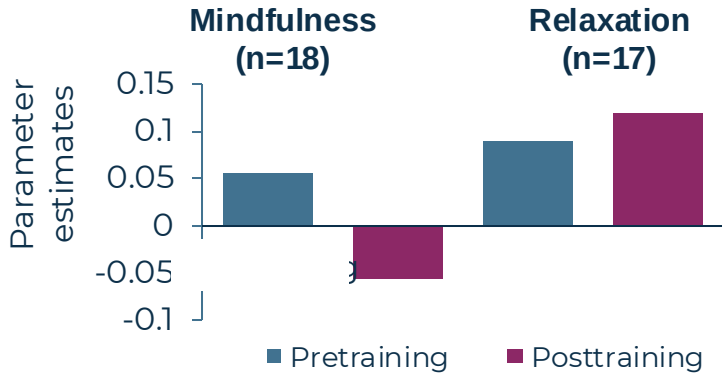
Study 1 (N=130)

Greater amygdala-ACC connectivity was observed in those with perceived stress vs unstressed adults (*P*<0.001)



Study 2

Mindfulness meditation training significantly decreased amygdala-ACC connectivity in unemployed job-seeking adults



Results from the first study showed that stress increased amygdala-ACC connectivity. In the second study, mindfulness meditation training, but not relaxation training, decreased this connectivity and improved perceived stress

ACC, anterior cingulate cortex; MRI, magnetic resonance imaging.
*P<0.05, postretreat mindfulness compared with preretreat mindfulness parameter estimates.

1. Taren et al. Soc Cogn Affect Neurosci. 2015;10:1758-1768.

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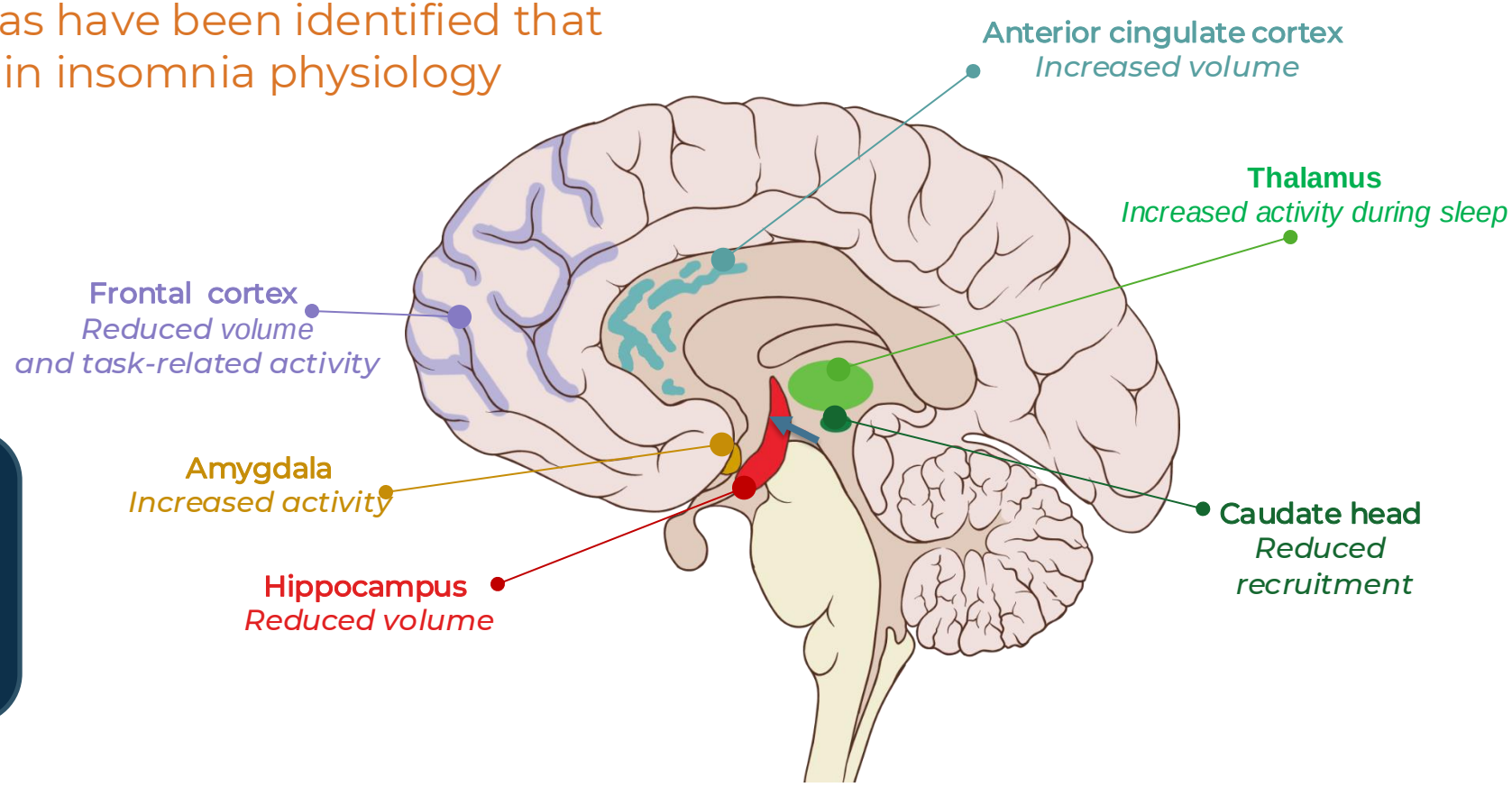
1. Rolin, D. Fox, I., et al. Journal of the American Psychiatric Nurses Association, 2020; 26(5): 493-502.

Neuroimaging Shows Various Brain Areas Are Involved in Insomnia Pathophysiology

Several brain areas have been identified that may be involved in insomnia physiology

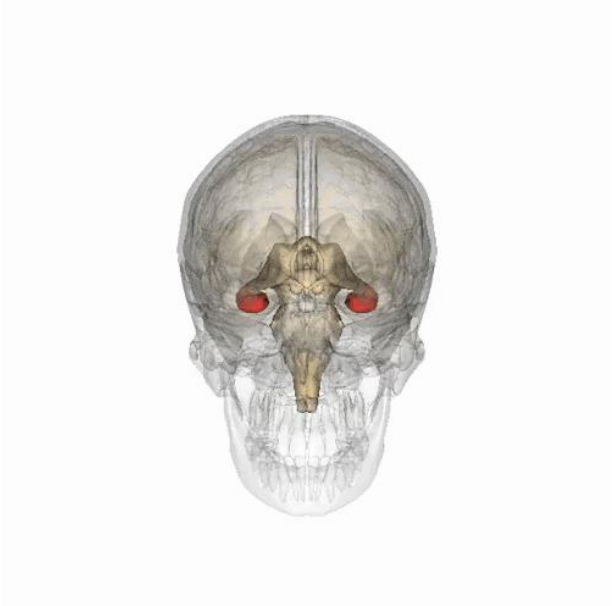


From neuroimaging studies, overactivity of the arousal, emotion-regulating, and cognitive systems may be involved in the pathophysiology of insomnia

1. Riemann et al. Lancet Neurol. 2015;14:547-558.

Sleep Deprivation Contributes to Reduction in Hippocampal Volume

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



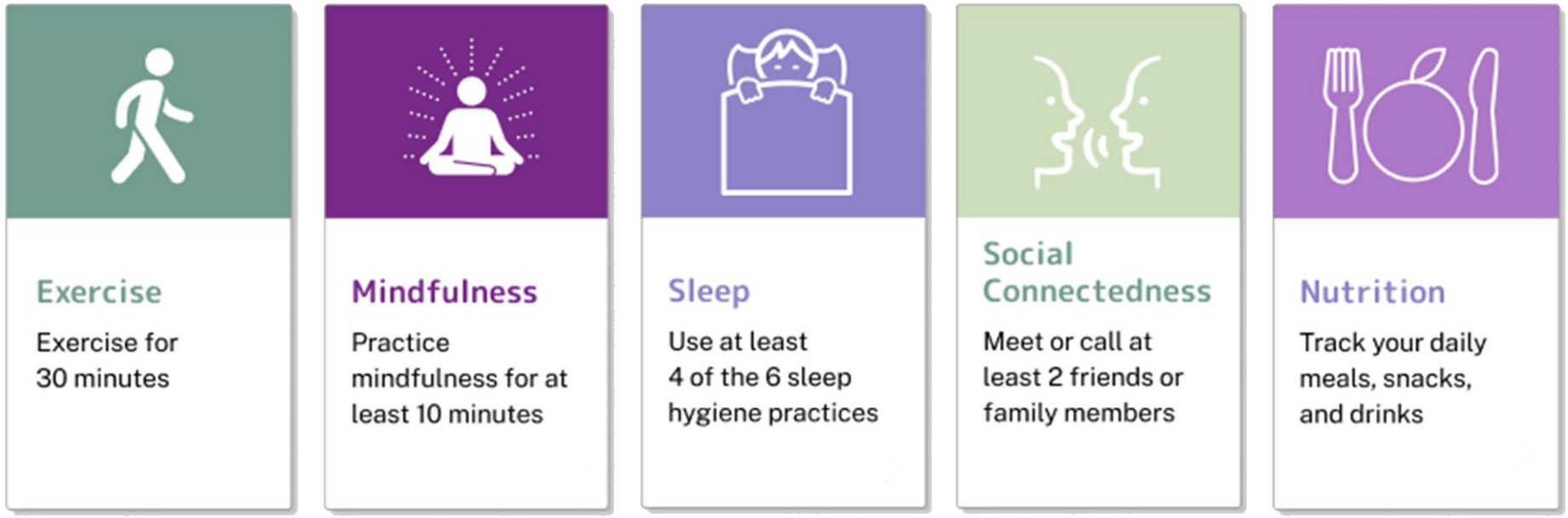
- Left or right hippocampal volume was negatively correlated with:
  - Longer insomnia duration (left: r=-.87, p<.001; right: r=-.87, p<.001)
  - Higher arousal index in nighttime polysomnography (left: r=-0.44, p=.045; right: r=-.41, p=.026)

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

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

WILD 5: A Proven Path to Wellness

Wellness-Enhancing Practices

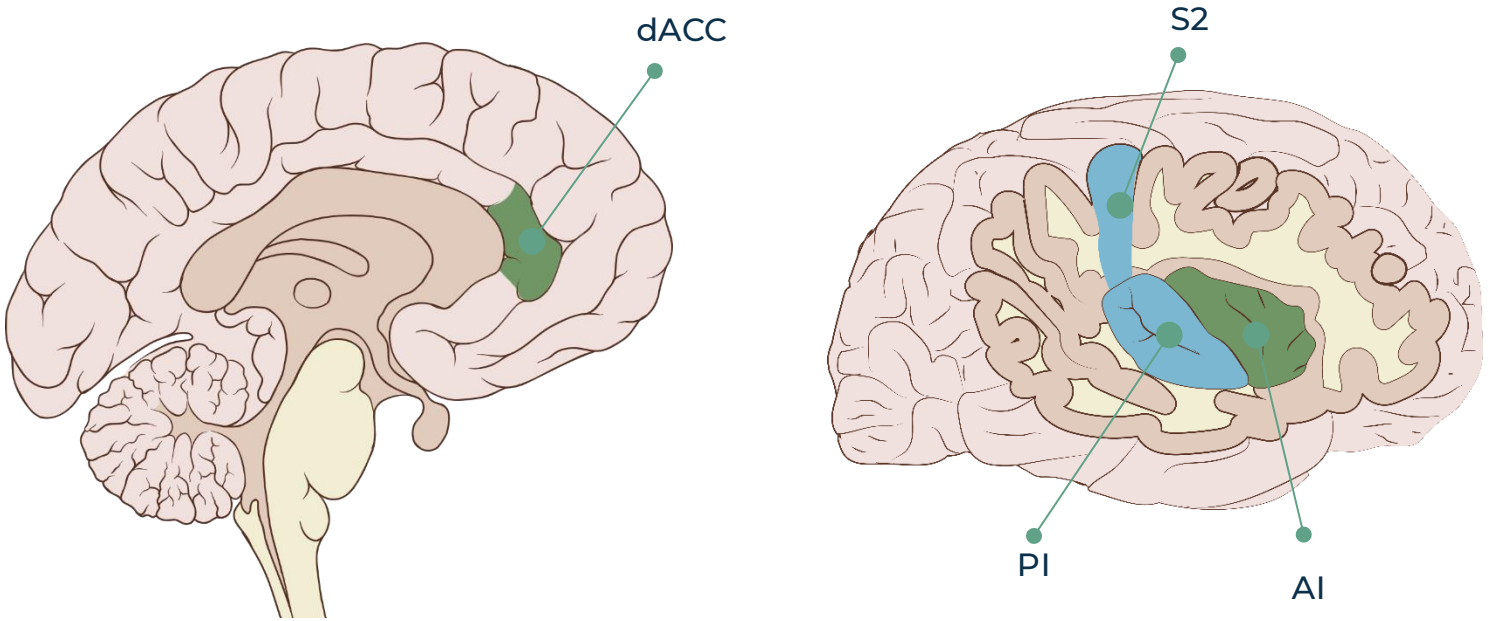


Daily for 30 Days

1. Rolin, D. Fox, I., et al. Journal of the American Psychiatric Nurses Association, 2020; 26(5): 493-502.

Physical and Social Pain May Share Similar Neural Circuitry

Affective regions (dACC, AI) and sensory regions (PI, S2) show neural activity in response to physical and social pain tasks

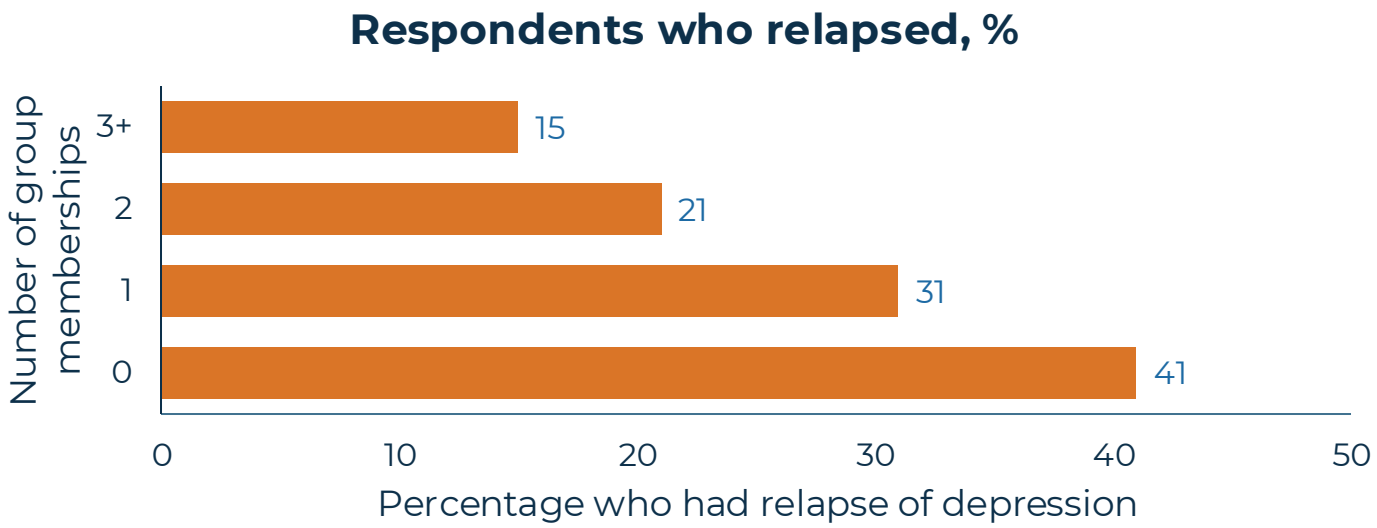


Brain regions associated with social pain have been shown to overlap with regions that process physical pain

1. AI, anterior insula; dACC, dorsal anterior cingulate cortex; PI, posterior insula; S2, secondary somatosensory cortex.
2. Eisenberger. Annu Rev Psychol. 2015;66:601-629.

Social Group Membership May Be Protective Against Relapse in Depression

In a study analyzing 4 years of population data of respondents with a history of depression (N=339), the number of groups a person belongs to was a strong predictor of subsequent depression

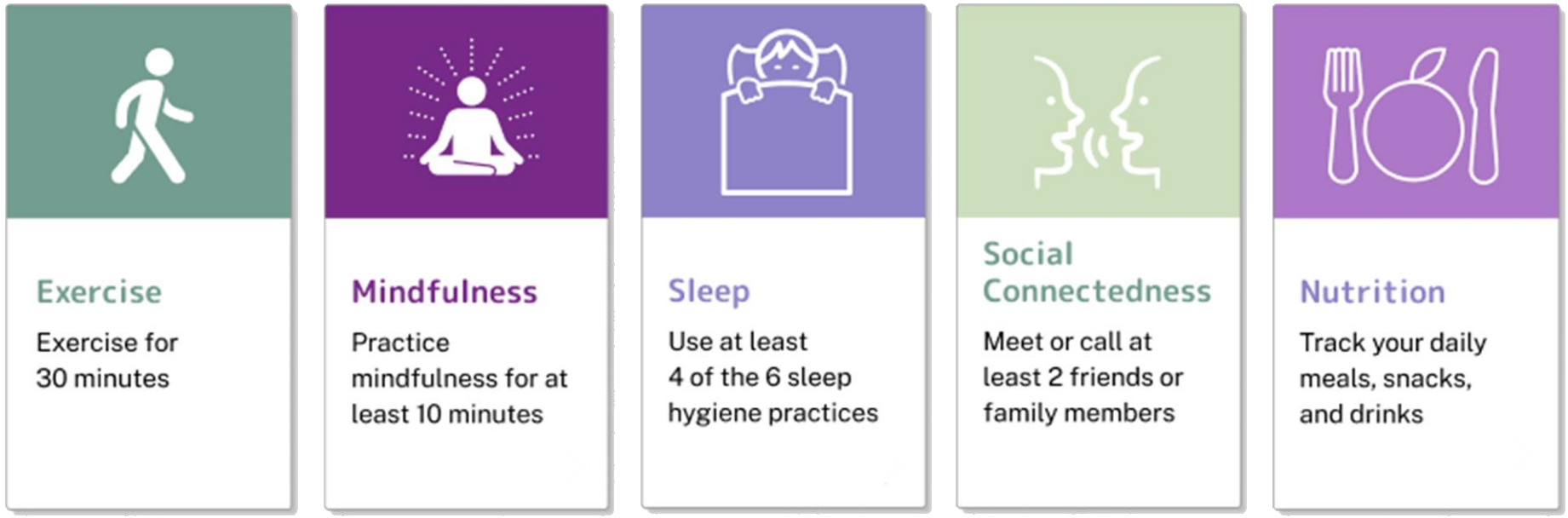


In patients with a history of depression, belonging to more social groups predicted a lower rate of relapse

1. Cruwys et al. *Soc Sci Med*. 2013;98:179-186.

WILD 5: A Proven Path to Wellness

Wellness-Enhancing Practices

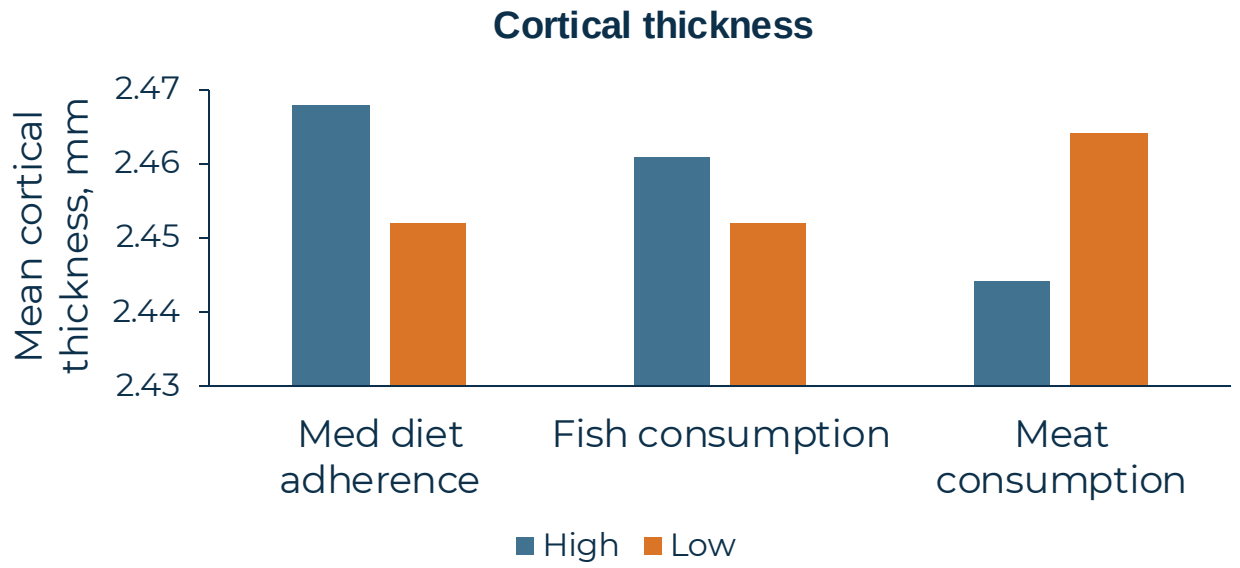


Daily for 30 Days

1. Rolin, D. Fox, I., et al. Journal of the American Psychiatric Nurses Association, 2020; 26(5): 493-502.

Association of Mediterranean Diet, Fish, and Meat With Cortical Thickness

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



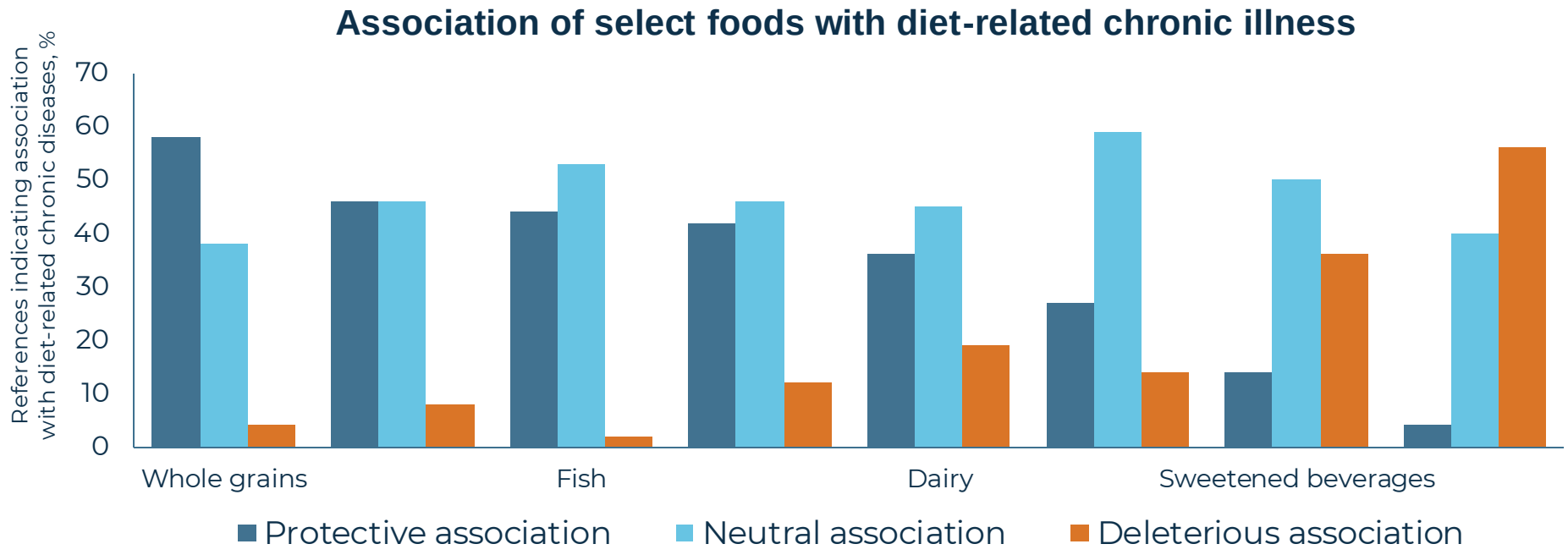
In this study of elderly adults, those eating a Med diet, more fish, and less meat had less brain atrophy

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

1. Gu et al. *Neurology*. 2015;85:1744-1755.

Select Foods Are Associated With Diet-Related Chronic Illness

An assessment of 304 pooled/meta-analyses and systematic reviews showed the association of select foods with diet-related chronic disorders, such as CVD, cancer, obesity, and mental illness



Plant-based food groups are more protective against diet-related chronic diseases than animal-based food groups

CVD, cardiovascular disease.

1. Fardet and Boirie. *Nutr Rev*. 2014;72:741-762.

Results from The 30-Day WILD 5 Wellness Program

30-Day WILD 5 Wellness Program: Study Designs

Study 1: Patients (N=82) were recruited from private practices in Texas, California, Oregon, and Canada[1,2]

Mental health (N=82)
All patients had a major psychiatric disorder[1]

Pain (N=51)
All patients had chronic pain[2]

Both studies included wellness interventions[1,2]

1. ≥30 minutes daily exercise
2. ≥8 minutes daily mindfulness meditation
3. Sleep hygiene interventions
4. Social connectedness enhancement
5. Nutrition optimization

Patients were assessed at baseline and at the end of the 30-day interventions on scales assessing[1,2]

- Depression
- Anxiety
- Sleep quality
- Diet
- Mindfulness
- Social connectedness
- Emotional eating patterns

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

Clinical outcomes[1,2]

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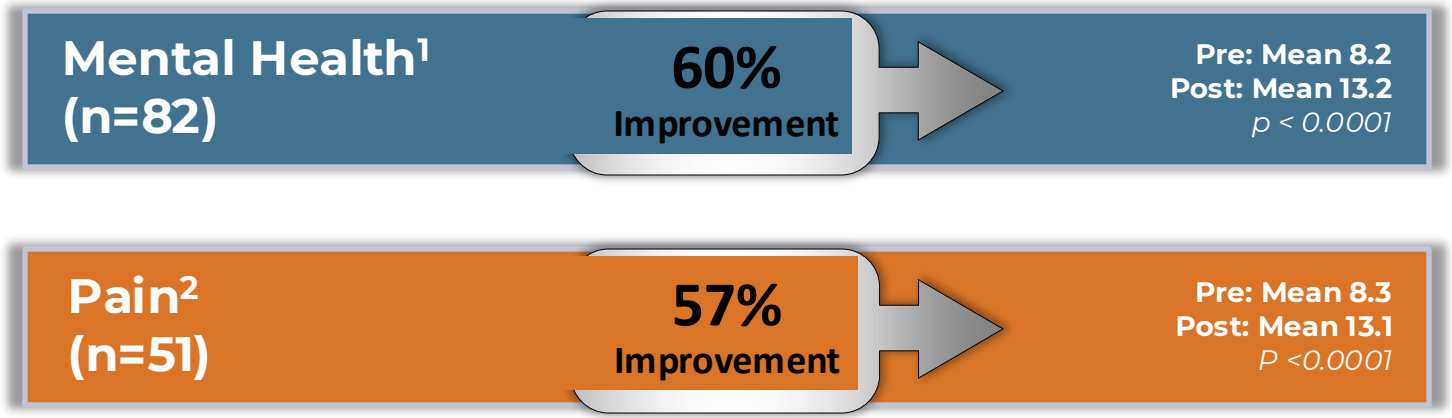
2. Jain S, Daniels N, Gonzales A, et al. Poster presented at: 29th Annual US Psychiatric Congress; October 21-24, 2016; San Antonio, TX.

Wellness Outcomes: WHO-5



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Neurobiology of Positive Emotions
(such as Happiness, Enthusiasm, Resilience, and Optimism)

Positive Emotions, such as:
Happiness
Enthusiasm
Resilience
Optimism

Regions Involved in Positive Emotions:
Ventral Striatum
Amygdala
Orbital PFC

Neurotransmitters Involved In Positive Emotional Processing:
Dopamine ,GABA, Opiate Receptors, Endogenous Opiates, Endogenous Endocannabinoids

GABA = gamma-aminobutyric acid; PFC = prefrontal cortex

1. Burgdorf J, et al. *Neurosci Biobehav Rev*. 2006;30(2):173-187.

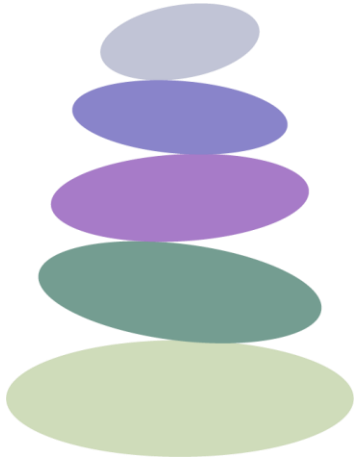
The HERO Wellness Scale

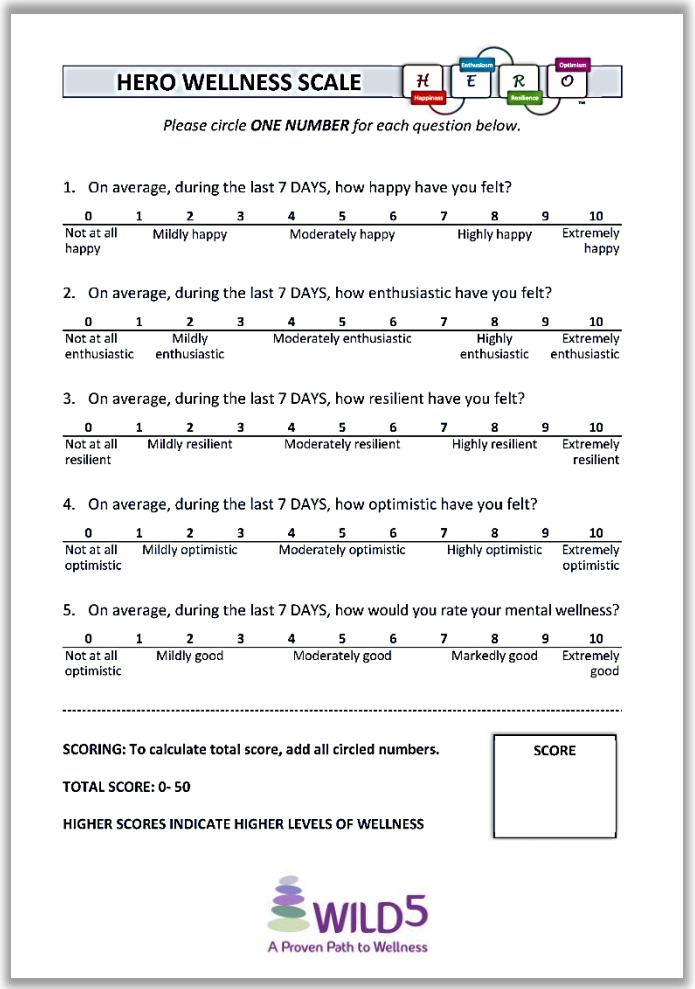
A Validated Wellness Scale

Scores range from 0–50.

Higher scores indicate higher levels of wellness.

The **HERO Wellness Scale allows the patient to become an active member in their treatment by tracking their own wellness.**





HERO WELLNESS SCALE

*Please circle **ONE NUMBER** for each question below.*

1. On average, during the last 7 DAYS, how happy have you felt?

0	1	2	3	4	5	6	7	8	9	10
Not at all happy		Mildly happy			Moderately happy			Highly happy		Extremely happy

2. On average, during the last 7 DAYS, how enthusiastic have you felt?

0	1	2	3	4	5	6	7	8	9	10
Not at all enthusiastic		Mildly enthusiastic			Moderately enthusiastic			Highly enthusiastic		Extremely enthusiastic

3. On average, during the last 7 DAYS, how resilient have you felt?

0	1	2	3	4	5	6	7	8	9	10
Not at all resilient		Mildly resilient			Moderately resilient			Highly resilient		Extremely resilient

4. On average, during the last 7 DAYS, how optimistic have you felt?

0	1	2	3	4	5	6	7	8	9	10
Not at all optimistic		Mildly optimistic			Moderately optimistic			Highly optimistic		Extremely optimistic

5. On average, during the last 7 DAYS, how would you rate your mental wellness?

0	1	2	3	4	5	6	7	8	9	10
Not at all optimistic		Mildly good			Moderately good			Markedly good		Extremely good

SCORING: To calculate total score, add all circled numbers.

TOTAL SCORE: 0- 50

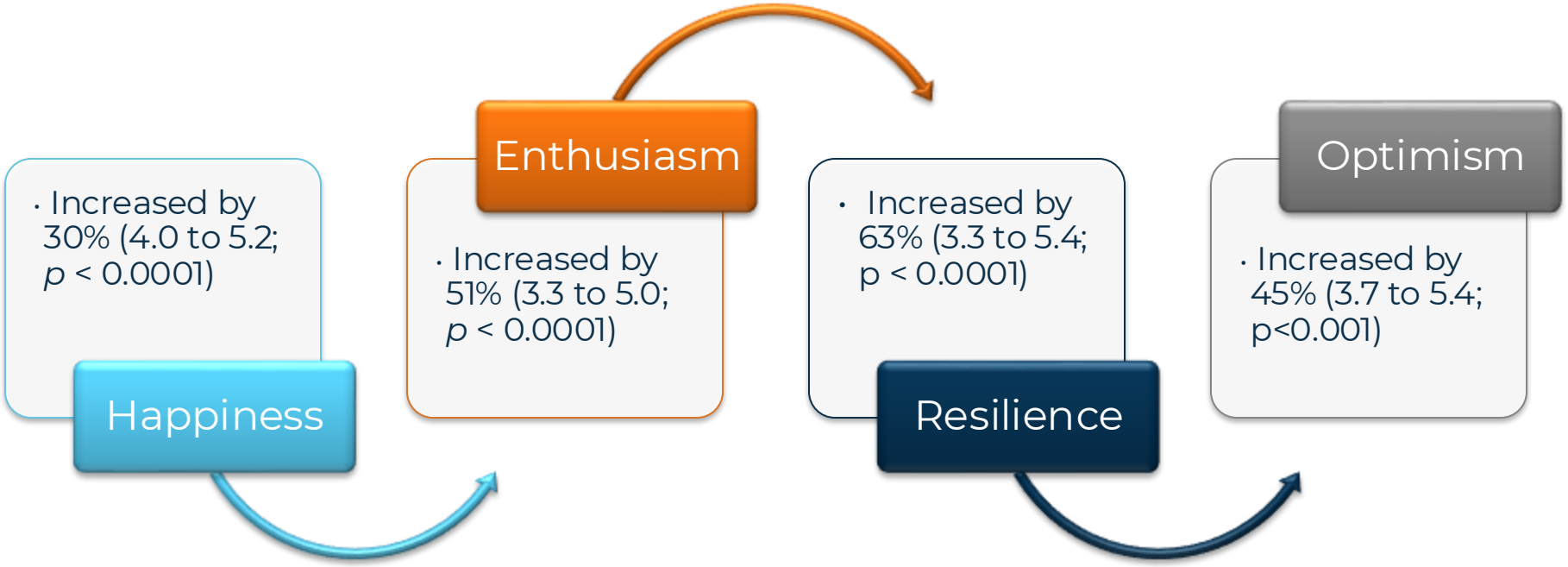
HIGHER SCORES INDICATE HIGHER LEVELS OF WELLNESS

SCORE

WILD5
A Proven Path to Wellness

1. Yakin, S., Jain, R. et al. Annals of Clinical Psychiatry: Official Journal of the American Academy of Clinical Psychiatrist, 2020; 32(1): 33-40.

WILD 5 Wellness Program: Wellness Markers HERO Wellness Scale[1,2]



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Additional Evidenced-Based Wellness Programs

- Positive Psychotherapy (PPT)[1]
  - 15-week program that aims to alleviate symptomatic stress by way of enhancing well-being

- Well-Being Therapy (WBT)[2]
  - 8-week strategy that is based on monitoring psychological well-being, whereby the patient progressively learns how to make it grow

1. Seligman, M. et al. American Psychologist, 2006; 61(8): 774.
2. Fava, G. A. Well-Being Therapy, 2016, 1-148.

Conclusions

Wellness and burnout have a neurobiological footprint

- Lower levels of wellness have a negative neurobiological imprint
- Higher levels of stress weakened prefrontal cortex connections

The combination of exercise, mindfulness, sleep, social connectedness, and nutrition provides an intervention that may improve wellness, reduce burnout/stress, and increase positive emotions

Closing

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May 2022 US.PSY.D.22.00004