Resilience and Late Life Depression: Clinical Features, Biomarkers and Interventions

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1

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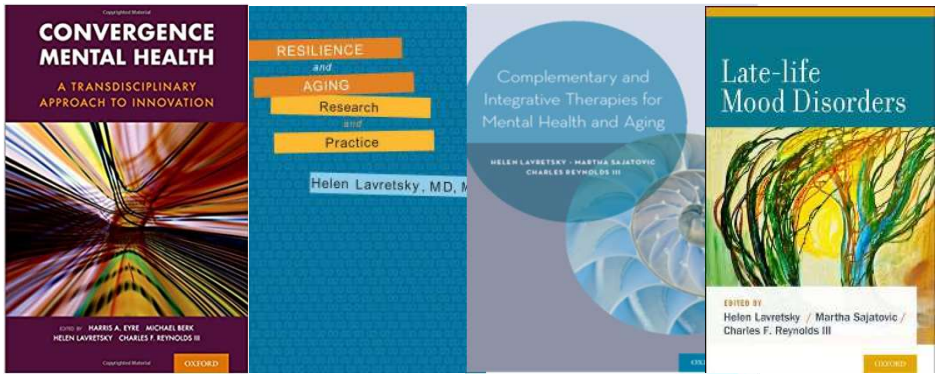

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Objectives

- Provide definitions of Resilience
- Describe biomarkers of psychological resilience
- Resilience as predictor of response to antidepressant treatment
- Mind-body therapies enhance resilience and improve depression outcomes

3

"Happiness is a Choice and a Birthright"
Gurmukh Khalsa

"Happiness is the consequence of personal effort. You fight for it, strive for it, insist upon it, and sometimes even travel around the world looking for it. You have to participate relentlessly in the manifestations of your own blessings. And once you have achieved a state of happiness, you must never become lax about maintaining it. You must make a mighty effort to keep swimming upward into that happiness forever, to stay afloat on top of it."

Elizabeth Gilbert "Eat, Pray, Love" (EPL)

4

Our greatest glory is not in never falling,
but in rising every time we fall.
Confucius

Resilience is a precious skill. People who have it tend to also have three underlying advantages: a believe that they can influence life events; a tendency to find meaningful purpose in life's turmoil; and a conviction that they can learn from both positive and negative experiences.
Amanda Ripley

Success is not final, failure is not fatal:
it is the courage to continue that counts.
Winston Churchill

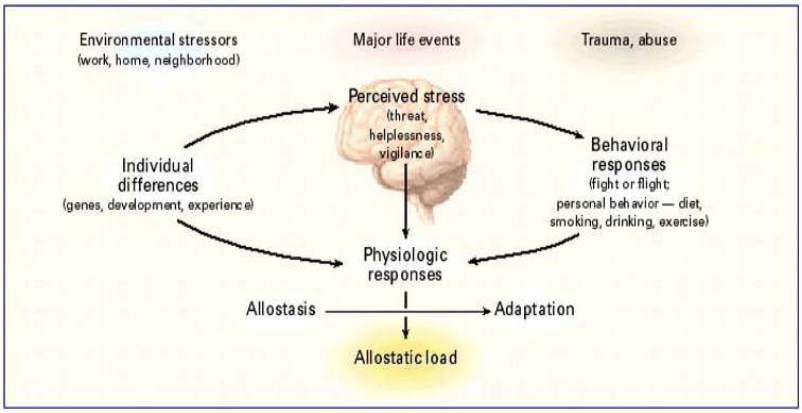
5

Resilience

- **Resilience** is a dynamic characteristic of the interaction between individuals and their environments- Ability to recover from adversity / trauma / stress / depression
- **Does it require a major traumatic experience to manifest?- What about surviving day-to-day?**
- This construct can be fostered in both younger and older individuals- leading to:
- **Effective and positive coping**
- **Turning adversity into an opportunity for growth**
- Consequentially leads to better outcomes for medical and mental disorders of aging

6

Model of Stress and Health: Relevance to Mood Disorders



7

Allostatic Load =price of adaptation to stress and aging

- ALLOSTASIS=maintaining stability through change (Sterling & Eiler 1988)
- Systolic BP (> = 148 mm Hg)
- Diastolic BP (> = 83 mm Hg)
- Waist-hip ratio (> = 0.94)
- Ratio total cholesterol/HDL (> = 5.9)
- Glycosylated hemoglobin (> = 7.1%)
- Urinary CORTISOL (> = 25.7 ug/g creatinine)
- Urinary NOREPINEPHRINE (> = 48 ug/g creatinine)
- Urinary EPINEPHRINE (> = 5 ug/g creatinine)
- High Density Lipoprotein cholesterol (< = 37 mg/dl)
- Dihydroepiandrosterone sulfate (DHEA-S) (< = 350 ng/ml)

Seeman TE et al PNAS 2001 McEwen 2004 (McArthur Study of Successful Aging)

8

Historical Perspectives on Resilience

- Resilience as a personality trait
- Depression as resilience deficiency

Recent Perspectives

- Resilience varies across the lifespan (Windle, 2011)
- Resilience varies substantially even among those who are clinically depressed (Min et al., 2013)

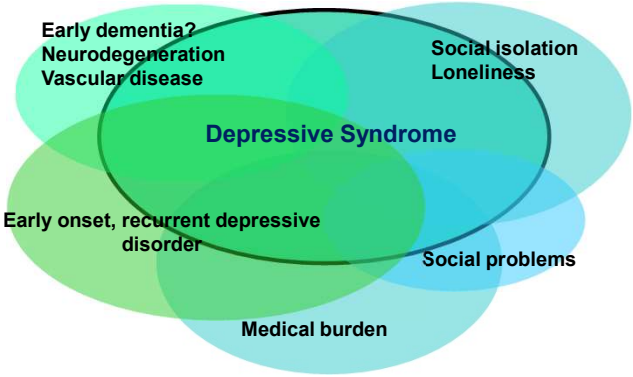
9

Psychological Factors Specific to Late Life

- **Stressors** such as chronic illness, cognitive decline, caregiving, financial stress, loss of independence, loneliness, and bereavement
- **Attitudes and stereotypes** surrounding aging
- **Social role and identity changes** such as retirement, widowhood, loss of independence
- **Emotion regulation** improves with age ("don't sweat the small stuff")
- **Depression is not simply the absence of Resilience**

10

A Multifactorial Nature of Geriatric Depression



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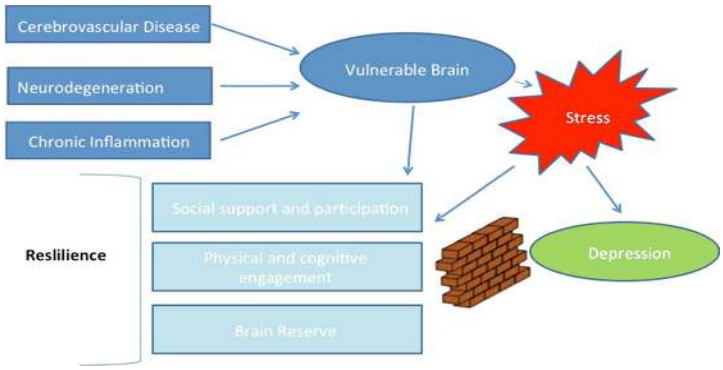
12

Vulnerability and Resilience Factors in Geriatric Depression



Weisenbach, Kumar 2014

13

Biomarkers of Resilience

- **Neuroimaging studies** demonstrate neural substrates including the prefrontal cortex, hippocampus, amygdala, anterior cingulate as forming a pathway for resilience.
- WMH and neurodegeneration- risk factors
- **HPA axis (cortisol, DHEA) and Inflammatory mediators** may constitute a link between lifestyle factors, infection, and the physiological changes of aging on the one hand and risk factors for age-associated diseases on the other and could serve as targets or biomarkers for resilience-building interventions.
- **BDNF, neuropeptide Y,** and neuroplasticity factors
- **Genetic factors:** APOE4-; COMT (VAL-VAL (highest activity of COMT) vs VAL – MET) – risk or resilience factors

14

Biopsychosocial correlates of late-life depression

Laird et al 2018

Psychosocial factors	Resilience correlates	LLD correlates
Temperament	Positive emotionality	Behavioral inhibition
Attachment	Secure attachment	Insecure attachment
Personality	Extroversion, conscientiousness, grit	Neuroticism
Beliefs	Self-esteem, self-efficacy, mastery, growth mindset, sense of purpose	Depression-related stigma, negative attitudes about aging
Coping	Active coping, accommodative coping, religious/spiritual practice	Passive coping
Social factors	Social support, formal volunteering	Trauma, chronic stress, more social role "absences", loneliness
Lifestyle factors	Physical exercise, healthy diet	Sedentary lifestyle, nutritional deficiencies, substance abuse

Biological factors	Resilience correlates	LLD correlates
Genetics	Val/Val allele, higher expression of mineralocorticoid receptors	Val/Met allele, APOE-4e, SLC6A4, female sex
Neurophysiological	Higher methylation of BDNF, higher neuropeptide Y, efficient monoamine transmission	Neurodegeneration, white matter hyperintensities/vascular deficiencies, shortened telomeres, lower heart rate variability, hippocampal atrophy
Steroid hormones	Higher dehydroepiandrosterone (DHEA), moderate availability of estrogens	Lower DHEA, low or very high availability of estrogens

15

Resilience in Late life Depression

1: Laird KT, Lavretsky H, Wu P, Krause B, Siddarth P. Neurocognitive Correlates of Resilience in Late-Life Depression. Am J Geriatr Psychiatry. 2019 Jan;27(1):12-17.

2: Laird KT, Lavretsky H, St Cyr N, Siddarth P. Resilience predicts remission in antidepressant treatment of geriatric depression. Int J Geriatr Psychiatry. 2018 Dec;33(12):1596-1603.

3: Vlasova RM, Siddarth P, Krause B, Leaver AM, Laird KT, St Cyr N, Narr KL, Lavretsky H. Resilience and White Matter Integrity in Geriatric Depression. Am J Geriatr Psychiatry. 2018 Aug;26(8):874-883.

4: Leaver AM, Yang H, Siddarth P, Vlasova RM, Krause B, St Cyr N, Narr KL, Lavretsky H. Resilience and amygdala function in older healthy and depressed adults. J Affect Disord. 2018 Sep;237:27-34. doi: 10.1016/j.jad.2018.04.109. Epub 2018 Apr 25. PubMed PMID: 29754022;

5: Laird KT, Lavretsky H, Paholpak P, Vlasova RM, Roman M, St Cyr N, Siddarth P. Clinical correlates of resilience factors in geriatric depression. Int Psychogeriatr. 2018 Jan 16:1-10.

16

Objectives

- Conduct an exploratory factor analysis (EFA) to identify the facets of resilience in older adults with depression
- Explore the association of these factors with:
  - Demographic variables
  - Clinical variables
  - Neurobiology
  - Subsequent remission of depressive symptoms

17

Subjects

- 337 adults over 60 years with Major Depressive Disorder
- No dementia (MMSE>23)
- EFA used baseline data from three clinical trials (interventions included trials of Methylphenidate, Memantine, and Tai Chi for geriatric depression)

18

Variables

- 25-item Connor Davidson Resilience Scale (CD-RISC)
- Depression:
  - Geriatric Depression Scale (GDS)
  - Hamilton Depression Rating Scale (HAM-D)
- Hamilton Anxiety Rating Scale (HAM-A)
- Apathy Evaluation Scale (AES)
- Cumulative Illness Rating Scale (CIRS)
- Cerebrovascular risk
- Quality of life:
  - Enjoyment and Satisfaction Questionnaire (QLESQ)
  - SF-36

19

Sample Characteristics

	Mean (SD) / N(%)
Sex	
Female	202 (59.94%)
Male	135 (40.06%)
Race	
White	266 (78.93%)
Hispanic	27 (8.01%)
Black	26 (7.72%)
Asian	12 (3.56%)
Other	6 (1.78%)
Age	70.45 (7.04)
Education (Years)	15.80 (2.46)
MMSE	28.42 (1.47)
GDS	17.03 (6.95)
HAM-D	18.25 (3.17)

20

	Factor 1:	Factor 2:	Factor 3:	Factor 4:
	"Grit"	"Control Coping Self-Efficacy"	"Accommodative Coping Self-Efficacy"	"Spirituality"
Variance Explained	30.40%	29.73%	28.50%	11.36%
I work to attain my goals	0.64	0.30	0.23	0.04
I have a strong sense of purpose	0.55	0.41	0.12	0.22
When things look hopeless, I don't give up	0.52	0.20	0.23	0.14
I take pride in my achievements	0.49	0.22	0.20	0.11
I give my best effort no matter what	0.49	0.07	0.30	0.27
I am not easily discouraged by failure	0.48	0.43	0.38	0.11
I believe I can achieve my goals	0.41	0.35	0.35	0.24
I have close and secure relationships	0.29	0.02	0.24	0.15
I make unpopular or difficult decisions	0.13	0.66	0.17	0.06
I think of myself as a strong person	0.42	0.49	0.33	0.07
I like challenges	0.39	0.47	0.21	-0.10
I have to act on a hunch	0.09	0.46	0.18	0.19
I am in control of my life	0.43	0.45	0.28	0.13
I can handle unpleasant feelings	0.31	0.40	0.34	0.13
I prefer to take the lead in problem solving	0.25	0.62	0.32	-0.08
Under pressure, I can focus and think clearly	0.22	0.42	0.42	0.09
Past success gives me confidence for new challenges	0.36	0.17	0.50	0.18
I know where to turn for help	0.33	0.13	0.38	0.24
I am able to adapt to change	0.25	0.28	0.54	0.06
I tend to bounce back after illness or hardship	0.24	0.34	0.59	0.12
I see the humorous side of things	0.24	0.24	0.42	0.05
I believe coping with stress strengthens me	0.23	0.31	0.44	0.21
I can deal with whatever comes my way	0.16	0.26	0.57	0.13
I believe things happen for a reason	0.13	0.07	0.10	0.59
I believe that sometimes fate or God can help	0.11	0.03	0.11	0.58

21

Pearson Correlations Between Resilience, Demographic and Clinical Factors

Demographic Factors	CD-RISC Total	Factor 1: "Grit"	Factor 2: "Active Coping"	Factor 3: "Accommodative Coping"	Factor 4: "Spirituality"
AGE	0.13*	0.11*	0.07	0.12*	-0.01
Education	0.07	0.05	0.12*	0.10	-0.18**
Clinical Factors					
MMSE	-0.15**	-0.09	-0.12*	-0.03	-0.16**
Depression (GDS)	-0.63**	-0.50**	-0.36**	-0.45**	-0.11*
Depression (HAM-D)	-0.36**	-0.24**	-0.20**	-0.31**	-0.08
Apathy (AES)	0.45**	0.34**	0.27**	0.28**	0.12*
Anxiety (HAM-A)	-0.20**	-0.11*	-0.15**	-0.24**	0.09
Cerebrovascular Risk	0.16**	0.12*	0.07	0.09	0.11
Cumulative Illness (CIRS)	0.11*	0.11*	0.05	0.05	0.02

22

Pearson Correlations Between Resilience and QOL Factors

	CD-RISC Total	Factor 1: "Grit"	Factor 2: "Active Coping"	Factor 3: "Accommodative Coping"	Factor 4: "Spirituality"
QLESQ	0.60**	0.47**	0.31**	0.46**	0.14**
Role Emotional	0.35**	0.29**	0.18**	0.26**	0.13*
Vitality	0.48**	0.41**	0.29**	0.28**	0.12*
Mental Health	0.54**	0.42**	0.31**	0.42**	0.06
Social Functioning	0.37**	0.30**	0.21**	0.32**	-0.02
General Health	0.34**	0.19**	0.20**	0.31**	0.10
Physical Functioning	<0.01	0.07	0.01	-0.01	-0.09
Role Physical	0.06	0.10	0.03	0.06	-0.08
Bodily Pain	0.05	0.07	0.06	0.04	-0.10

23

Modeling of Total Resilience

- The final general linear model for total CD-RISC identified the following variables significantly and independently explaining variability in resilience
  - Depression (GDS) $F(1,318) = 14.11$, $\beta = -0.59$, $p = 0.0002$
  - Apathy $F(1,318) = 4.87$, $\beta = 0.13$, $p = 0.03$
  - Medical comorbidity ($F(1,318) = 10.55$, $\beta = 0.59$, $p = 0.001$
  - Several QOL measures:
    - QLESQ $F(1,318) = 13.92$, $\beta = 0.41$, $p = 0.0002$
    - SF-36 mental health $F(1,318) = 4.35$, $\beta = 0.10$, $p = 0.04$
    - SF-36 general health $F(1,318) = 8.48$, $\beta = 0.13$, $p = 0.004$

24

Exploring the neurobiological mechanisms of resilience: White Matter Integrity
Vlasova et al AJGP 2018

- White matter abnormalities are amongst the most commonly identified imaging abnormalities in geriatric depression (Houenou et al., 2016)
- We aimed to determine whether resilience is associated with greater white matter integrity among older adults with MDD

25

Regions of interest (ROIs)

- Chosen based on their links with cognitive control and emotion regulation:
  - Cingulum bundle (CB)
  - Genu of corpus callosum (GCC)
  - Anterior limb of the internal capsule (ALIC)
- The corticospinal tract (CST) was included as a control region

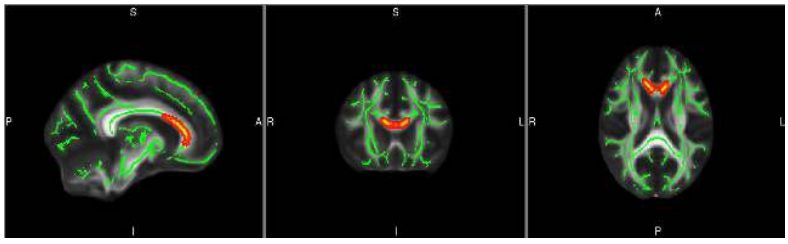
26

Correlations of Fractional Anisotropy with Resilience

	ROIs: F(p-value); df = 1,64			Control
Factors	CB	GCC	ALIC	CST
Grit	4.47 (0.04)*	7.54 (0.008)*	1.14 (0.29)	0.56 (0.46)
Active Coping Self-efficacy	0.44 (0.51)	0.27 (0.60)	0.50 (0.48)	0.63 (0.43)
Accommodative Coping Self-efficacy	1.24 (0.27)	0.21 (0.65)	0.10 (0.75)	0.70 (0.41)
Spirituality	0.99 (0.32)	0.01 (0.97)	1.14 (0.29)	0.02 (0.88)
Total CD-RISC	2.22 (0.14)	0.87 (0.35)	0.01 (0.94)	0.16 (0.69)

27

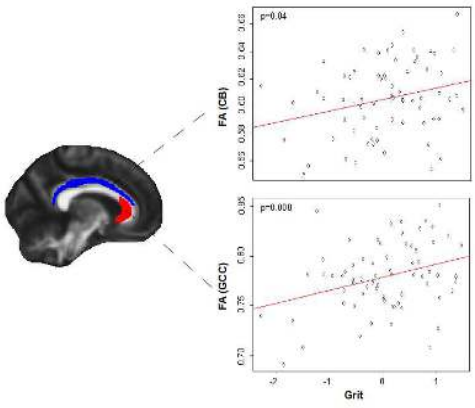
Results of TBSS analysis



- Regions of significant positive association between Grit and FA are highlighted in red ($p < 0.05$, TFCE-corrected)
- Significant voxels are overlaid on the group mean white matter skeleton (green) and the FA MNI template (Montreal Neurological Institute)

28

Scatterplots with GLM fits demonstrating associations between Grit and FA in ROIs



- CB tract shown in blue; GCC tract shown in red
- Values for left and right CB were averaged for scatterplot
- Effects of age and gender were controlled for
- Consistent with other studies of emotion regulation and cognitive control in depression

29

Conclusion

- The association between "Grit" with FA in the GCC and CB is consistent with prior evidence of the involvement of these regions in emotion regulation and cognitive control
- These findings provide further support for the conceptualization of resilience as a complex system comprised of multiple factors, each of which may have distinct relations to pathway-specific brain white matter integrity.

30

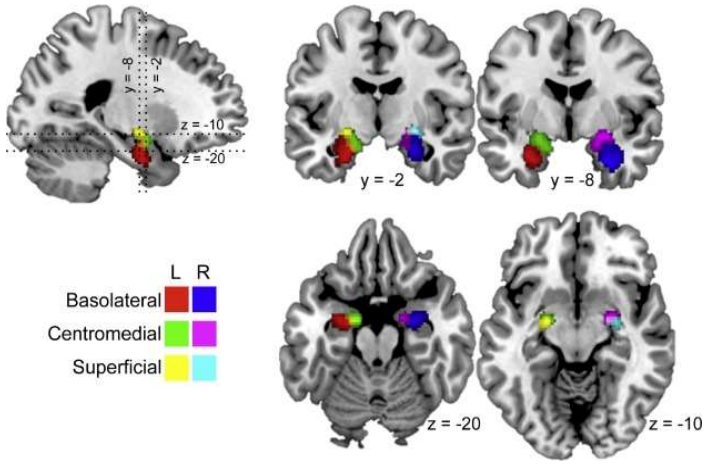
Resilience and emotion regulation networks

Leaver et al, 2018

- Amygdala nuclei and related brain circuits have been linked to negative affect, and depressed patients have been demonstrated to have abnormal amygdala function.
- We examined psychological resilience measures correlations with amygdala function measured with resting-state arterial spin-labelled (ASL) and blood-oxygenation-level-dependent (BOLD) functional magnetic resonance imaging (fMRI) in the basolateral, centro-medial, and superficial nuclei groups of the amygdala

31

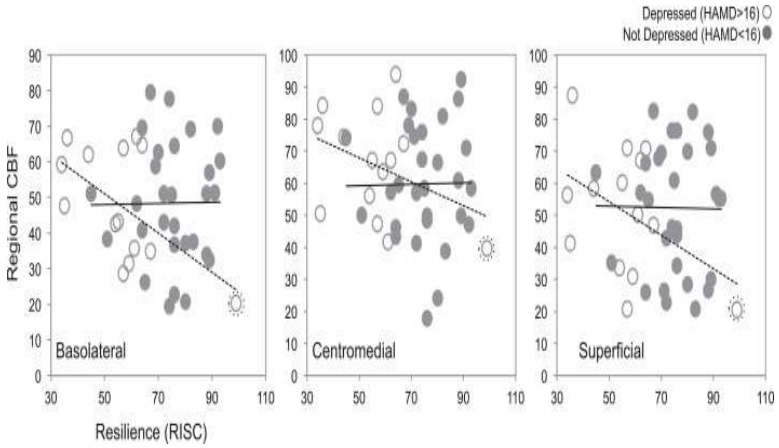
Amygdala subnuclei. The Jülich histological atlas was used to locate groups of amygdala subnuclei. The basolateral, centromedial, and superficial groups are displayed for each hemisphere, with color key given at lower left.



32

Resilience Scores Correlate with Amygdala Function Measured with ASL fMRI.

Mean cerebral blood flow (CBF, y axis) for the basolateral (left), centromedial (middle), and superficial (right) nuclei plots resilience scores (x axis), averaged across hemisphere. Depressed and non-depressed groups are shown in open and closed circles respectively.



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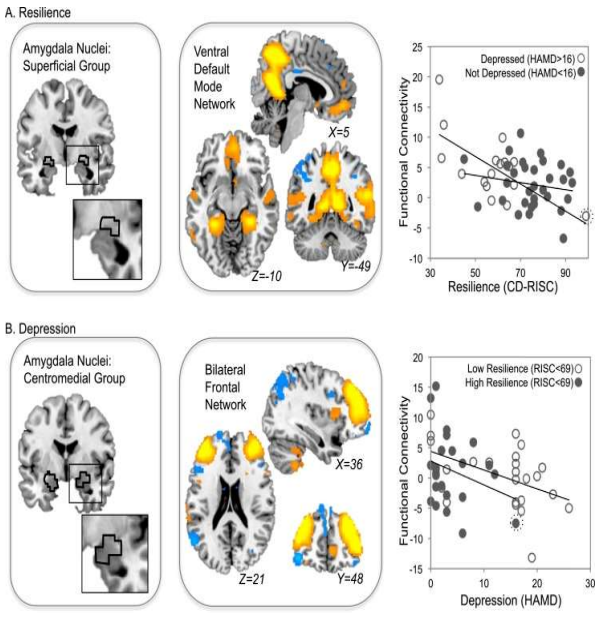


Resilience and Depression Measures Correlate with Amygdala Connectivity with BOLD fMRI.

A. Resilience correlated with connectivity between the Superficial Group of amygdala nuclei (left) and the Ventral Default Mode Network.

Functional connectivity scores (superficial amygdala nuclei vs. ventral DMN) are plotted against resilience scores (CD-RISC)

B. Depression scores (HAMD) were negatively correlated with connectivity between the centromedial group of amygdala nuclei (left) and a Bilateral Frontal Network (middle).

Functional connectivity between CM amygdala and Bilateral Frontal Network

34

CONCLUSION

-High levels of psychological resilience correlated with lower basal levels of amygdala activity measured with ASL fMRI.

-High resilience also correlated with decreased connectivity between amygdala nuclei and the ventral default-mode network independent of depression status.

-Instead, lower depression symptoms were associated with higher connectivity between the amygdalae and dorsal frontal networks.

-Resilience in older adults is more closely related to function in ventral amygdala/DMN networks, while Depression is related to reduced connectivity between the amygdala and dorsal frontal regions.

35

Predicting Treatment Response and Remission
Laird et al

Sample:

- 143 older adults with MDD
- Normal cognitive functioning (MMSE>25)
- Enrolled in a 16-week placebo-controlled RCT evaluating the efficacy of methylphenidate, citalopram, or their combination
- Free of psychotropic medications before beginning trial

36

Outcomes

- Remission = HAM-D ≤ 6
- Treatment Response = 50% or greater reduction from baseline HAM-D score
- At 16-weeks, 44% of participants had remitted and 54% had responded

37

Univariate Analysis of Patient Characteristics Predicting Remission

Patient characteristic	OR	95% CI	P-value
Female sex	1.52	0.78-2.97	0.22
White race	0.79	0.37-1.69	0.54
Age	0.99	0.94-1.03	0.52
Years education	1.01	0.90-1.14	0.87
MMSE	1.06	0.82-1.37	0.64
GDS	0.96	0.90-1.01	0.12
HAM-D	0.90	0.80-1.01	0.08
AES	1.02	0.99-1.06	0.18
Late life onset (≥50)	0.65	0.33-1.26	0.20
More than 2 episodes	1.20	0.62-2.32	0.59
CD-RISC	1.04	1.00-1.07	0.05
Cerebrovascular risk	0.96	0.90-1.02	0.21
CIRS	0.94	0.86-1.03	0.18

38

Final multivariable regression model of remission

- Only greater baseline resilience (Wald $\chi^2 = 3.8$, $p = 0.05$) significantly predicted remission
- A 20-point increase in baseline resilience score was associated with a nearly 2 times greater chance of remission (OR = 1.98)
- Examining the individual resilience factors, only accommodative coping self-efficacy (Wald $\chi^2 = 3.7$, p = 0.05, OR = 1.41) was significantly associated with remission

39

Moderation Analysis

- Treatment group did not moderate the effect of resilience on treatment response or remission, suggesting that individuals with higher baseline resilience were more likely to improve regardless of the treatment arm, to which they were randomized

40

Discussion

- These findings support for the conceptualization of resilience as a complex system comprised of multiple factors
  - Grit
  - Active Coping Self-efficacy
  - Accommodative Coping Self-efficacy
  - Spirituality
- Each factor may have distinct relations to:
  - Demographic variables (e.g., older age -> more accommodation)
  - Pathway-specific brain white matter integrity
  - Likelihood of treatment response and remission (accommodative coping -> greater chance of remission)

41

Implications

- *Accommodative coping self-efficacy* refers to an individual's confidence in his/her ability to adapt or "accommodate" to a source of stress
- Associated with more favorable mental health outcomes in the face of uncontrollable stress
- Consistent with ours and others' findings that older adults appear to engage in more accommodative coping
- Depressed older adults low in accommodative coping self-efficacy may benefit from interventions designed to increase acceptance of challenges

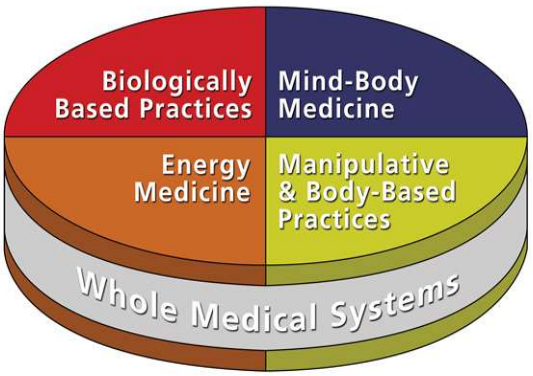
42

Resilience-Building interventions

- **Resilience enhancing interventions** include wellbeing therapy, learned optimism training, hardiness training, all of which focus on positive aspects of difficult experiences thereby promoting more positive perceptions of challenges.
- **Lifestyle factors** such as diet, sleep, exercise, spirituality can enhance resilience by creating physical and mental wellbeing.
- **Complementary and Integrative medicine (CIM)** is a holistic and integrative approach to wellness which encompasses varied approaches to wellness and stress reduction (e.g., yoga, meditation, humor therapy, aromatherapy and massage)

43

The Complementary and Integrative Domains & Whole Medical Systems



44

Mind-Body Medicine

Yoga
Guided imagery
Meditation
Hypnotherapy
Spirituality
Tai Chi
Art, dance, music therapies

45

A Challenge for Aging Research

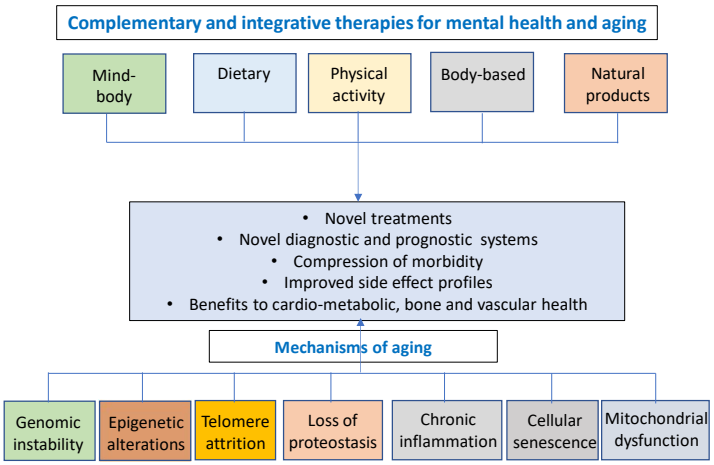
- **Enhance physical & mental health**
- **Reduce stress- related symptoms (insomnia, pain, depression, anxiety, etc)**
- **Impact on health**
- **Prevent disease**

46

2017 National Health Interview Survey (NHIS)

- Yoga was the most commonly used complementary health approach among U.S. adults in 2012 (9.5%) and 2017 (14.3%).
- The use of meditation increased more than threefold from 4.1% in 2012 to 14.2% in 2017. In 2012, chiropractic care was as popular as yoga, followed by meditation; however, the popularity of meditation surpassed that of chiropractic care to become the second most used approach among those surveyed in 2017.
- The use of chiropractors increased from 9.1% in 2012 to 10.3% in 2017.
- In 2017, women were more than twice as likely to use yoga compared with men (19.8% versus 8.6%). Women were also more likely than men to use meditation (16.3% versus 11.8%) and see a chiropractor (11.1% versus 9.4%).
- Non-Hispanic white adults were more likely to use yoga, meditation, and chiropractors compared with Hispanic and non-Hispanic black adults.
- The use of yoga was highest among adults aged 18 to 44 compared to older adults, while the use of meditation and chiropractic care was higher among adults aged 45 to 64 years compared with younger and older age groups.

47



48

49

Mind-Body Exercise

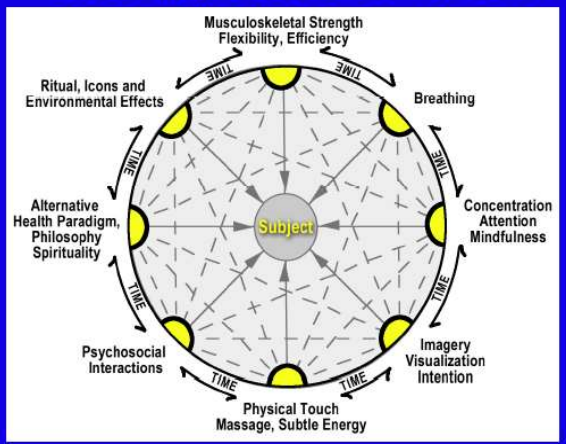
- **Mindful physical exercise** (e.g., yoga and Tai Chi) is increasingly utilized for improving psychological well-being, hypertension, cardiovascular disease, insulin resistance, depression, and anxiety
- Physical exercise executed with a profound inwardly directed contemplative focus or awareness
- **Key elements:**
- A non-competitive, non-judgmental meditative component,
- Mental focus on muscular movement and movement awareness combined with a low to moderate level of muscular activity,
- Centered breathing (conscious breath)
- A focus on anatomic alignment (i.e., spine, trunk, and pelvis) and proper physical form,
- Energy centric awareness of individual flow of intrinsic body energy

(life force, prana, sekhem, Qi, or Kundalini).

"Abbott, Lavretsky; Psychiatric Clinics 2013"

50

What at the key components or "active ingredients' of Tai Chi ?



From Wayne and Kaptchuk, JACM 2008

51

Putative mechanisms

- Promotes relaxation and decreases sympathetic output
- Reduces clinical somatic symptoms, and benefits anxiety, depression, blood pressure, and recovery from immune-mediated diseases
- Reduces levels of inflammatory markers (CRP), improves immune function and vaccine-response.
- Reduces stress hormones of the HPA axis
- Increases in peak oxygen uptake
- Increases blood levels of endorphins and baroreflex sensitivity, and
- Electroencephalopathy (EEG) studies have found increased frontal EEG alpha, beta, and theta wave activity, suggesting increased relaxation and attentiveness
- Growing number of neuroimaging studies identify areas of neuroplastic changes (increased grey matter volume in older adults (Tao et al 2017); increased connectivity in cognitive control network (Tao et al 2017))

52

Randomized Controlled Trials of Tai Chi and Qi Gong for Mental Disorders and Aging		
	Positive Findings	Negative Findings
Depression	13 studies with significant positive findings, Only two with clinically diagnosed depression populations.	One study did not find effect on depressive symptoms.
Stress	4 studies with significant positive findings subjective stress measures, body temperature, and salivary cortisol levels.	One study did not find effect on subjective stress measures.
Anxiety	8 studies with significant positive effects	One study had negative findings on anxiety
Mood and psychological wellbeing	7 studies with significant positive effects.	One study did not find positive effect on mood.
Self-Esteem	1 study with significant positive	Two without positive effect.
Parkinson's Disease	3 studies with significant positive effects.	
Sleep Disturbance	3 studies with significant positive effects.	None reported
Substance Abuse	1 study with significant positive effects	None reported
Cognition	2 studies with significant positive effects.	None reported

Abbott, Lavretsky, 2013, 2017

53

Complementary Use of Tai Chi Improves Resilience, Quality of life, and Cognitive Function in Depressed Older Adults.

Lavretsky et al Am J Geriatr Psychiatry. 2011

54

METHODS

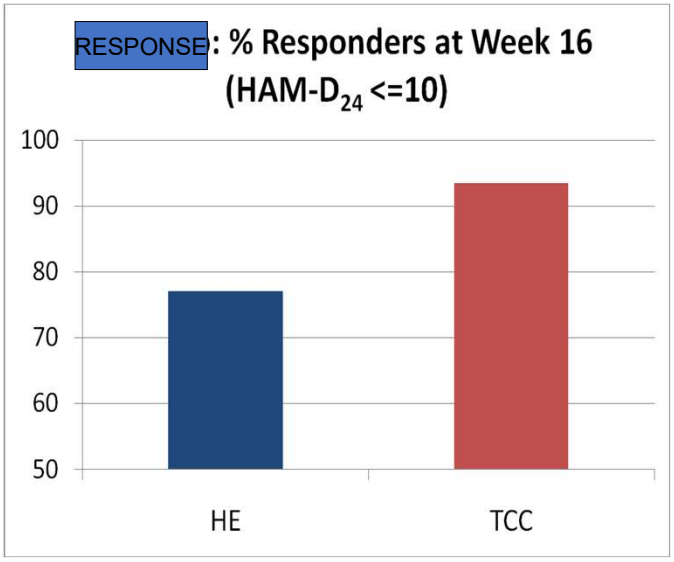
- 112 older adults with major depression age 60 years and older were recruited and treated with 10 mg of escitalopram for the first 6 weeks.
- 73 partial responders (Ham-D > 6 and more than 30% improvement) to escitalopram continued to receive 10 mg of escitalopram per day and were randomly assigned to 10 weeks of either complementary intervention :
- 1.Tai Chi Chih for 2 hours per week; or 2. Health Education Program for 2 hours per week.

55

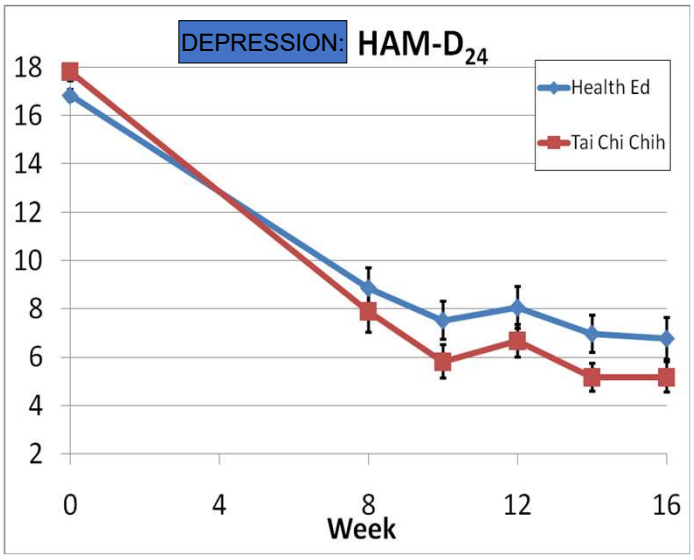
Results

- Both Tai Chi (TC) and Health education (HE) participants demonstrated improvement in the severity of depression, but TC subjects > HE
- Tai Chi group demonstrated significantly greater improvement compared to HE group in:
- Resilience
- Energy and psychomotor retardation
- Physical functioning
- Cognitive measures of executive cognitive function, attention, and memory

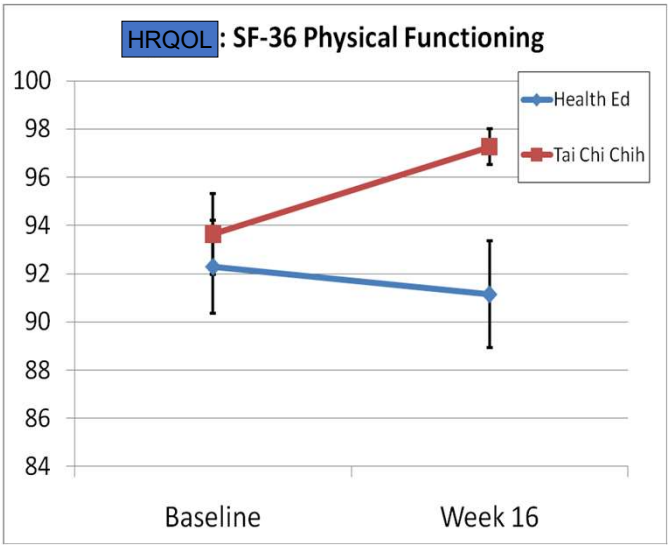
56


RESPONSE: % Responders at Week 16
(HAM-D24 <=10)
100
90
80
70
60
50
HE
TCC

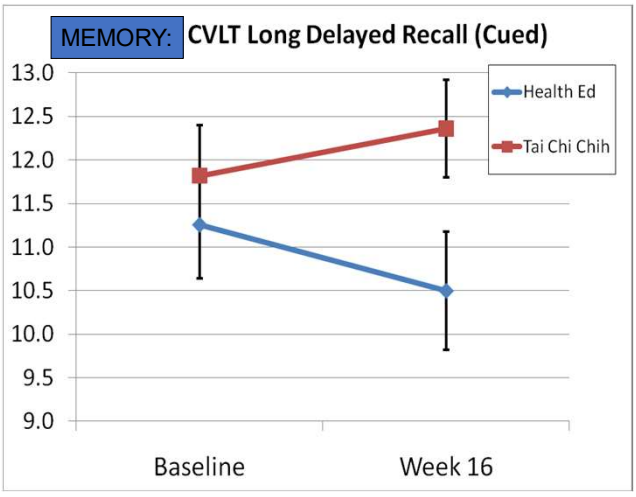
57


DEPRESSION: HAM-D24
Health Ed
Tai Chi Chih
18
16
14
12
10
8
6
4
2
0
4
8
12
16
Week

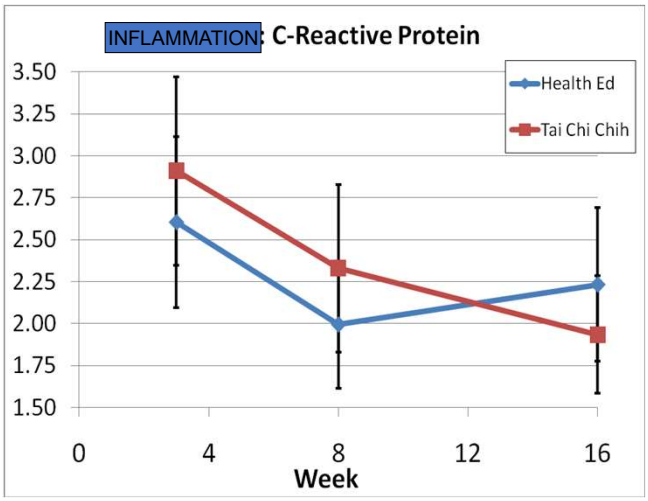
58


HRQOL: SF-36 Physical Functioning
100
98
96
94
92
90
88
86
84
Health Ed
Tai Chi Chih
Baseline
Week 16

59

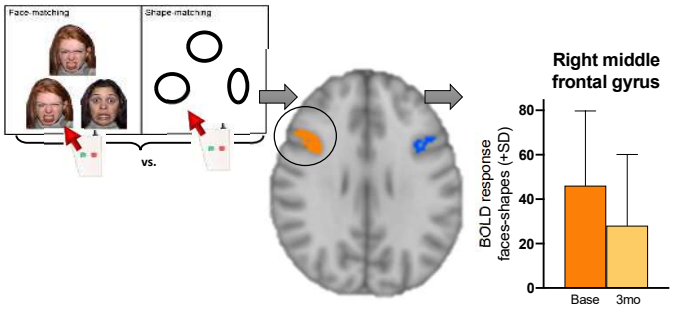

MEMORY: CVLT Long Delayed Recall (Cued)
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
Health Ed
Tai Chi Chih
Baseline
Week 16

60



61

Across groups, brain responses to emotional faces decreased in the right middle frontal gyrus after 3 months

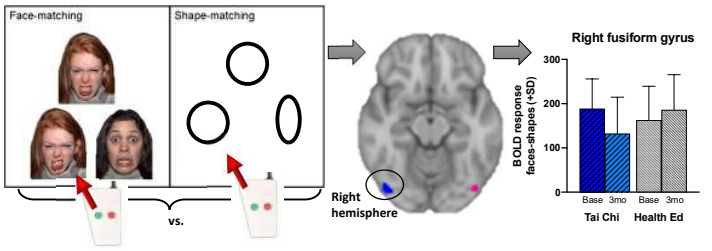


Mixed model main effect of time: f=5.68, p=0.03

62

Tai Chi reduces brain response to emotional faces

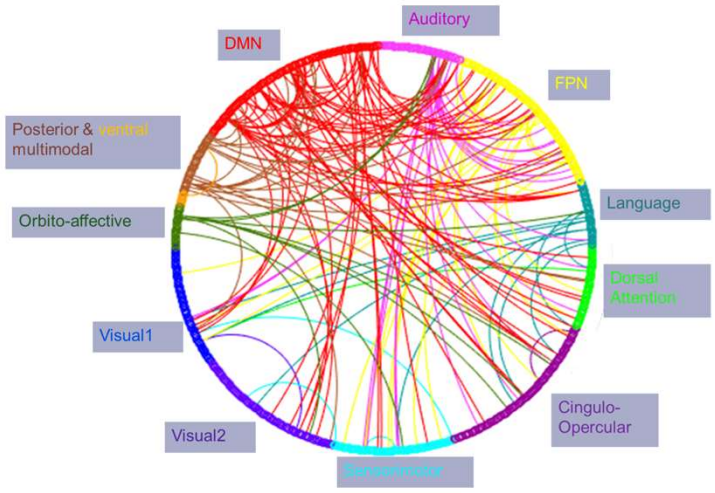
Task fMRI for emotional processing



Mixed model interaction: f=3.16, *p*=0.09

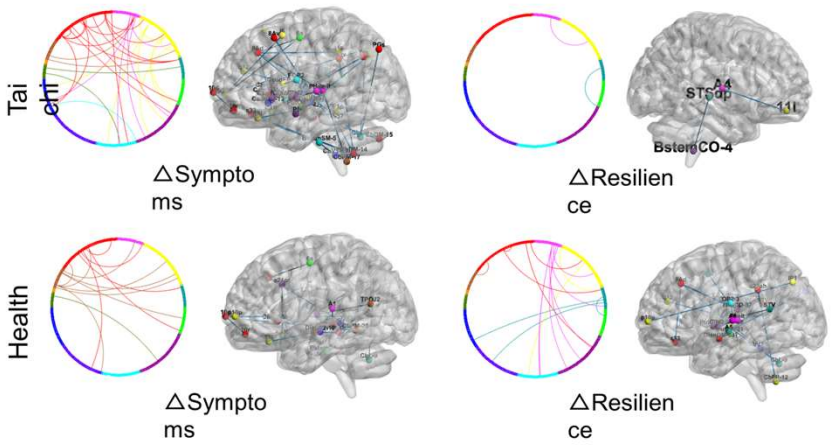
63

Greater increases in resting state connectivity with Tai Chi Chih training than with HEW training (corrected_p < 0.05). The 718 nodes of the Cole-Anticevic Brain Network.



64

Increased connectivity associated with improvements in depression (as assessed by the MADRS) and resilience ($p < 0.05$).



65

Conclusions

- Complementary use of mind-body exercise combined with standard antidepressants may provide additional improvement in clinical outcomes of geriatric depression such as resilience, quality of life, general health, and cognitive function
- **Putative Mechanisms** – via stress reduction, decreased inflammation, epigenetic changes, improved emotion regulation, and direct neuroplastic effects on the brain
- **Personalized approach of Mind-Body Medicine** may improve treatment response to standard antidepressants on multiple outcomes and reduce exposure to multiple drugs
- **Current study of neural mechanisms** underlying response to Tai Chi in geriatric depression; and prevention of cognitive decline (NCCIH/NIA)- shows increase in brain connectivity associated with reduction in depressive symptoms and improvement in resilience

66

Sponsors and collaborators

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- Collaborators:
  - Gary Small and memory and aging program
  - Linda Ercoli and Prabha Siddarth- cognitive analyses
  - Katherine Narr, Lisa Kilpatrick, and Brain Mapping- fMRI
  - Elaine Reed, Michael Irwin, Steve Cole and Immunogenetics Center- inflammatory markers
  - Steve Cole, Stan Nelson, Adrienne Grzenda, and Nelson Freimer- genetic analyses
  - **Coordinators-** Michaela Milillo, Ashlyn Applegate, Raquel Hernandez, Katie Cho, Jillian Yeargin, Natalie St. Cyr,
  - **Postdoctoral students**-Kelsey Laird, Beatrix Krause, Roza Vlasova, Bianca Acevedo, Amber Leaver, Anurag Pant, and Harris Eyre

67

68