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Integrative Medicine In Health and Well-Being

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Integrative Medicine In Health and Well-Being

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Clinical and Mechanism Studies

- For integrative approaches to become part of standard care, research is required to understand clinical effects
 - Studies of mind-body practices, diet/nutrition, supplements/natural products, combined therapies
- Clinical data needs to be supplemented by mechanistic studies
 - Functional neuroimaging
 - Immunological measures
 - Physiological measures

Marcus Institute PET-MR Center

- Siemens PET-MR scanner
- 3T MRI scanner with full MRI and fMRI capabilities
- Standard scans, contrast studies, DTI, ASL, BOLD
- High resolution PET scanner for combined imaging of brain and body
- Metabolic or molecular imaging



Current Applications of PET-MRI

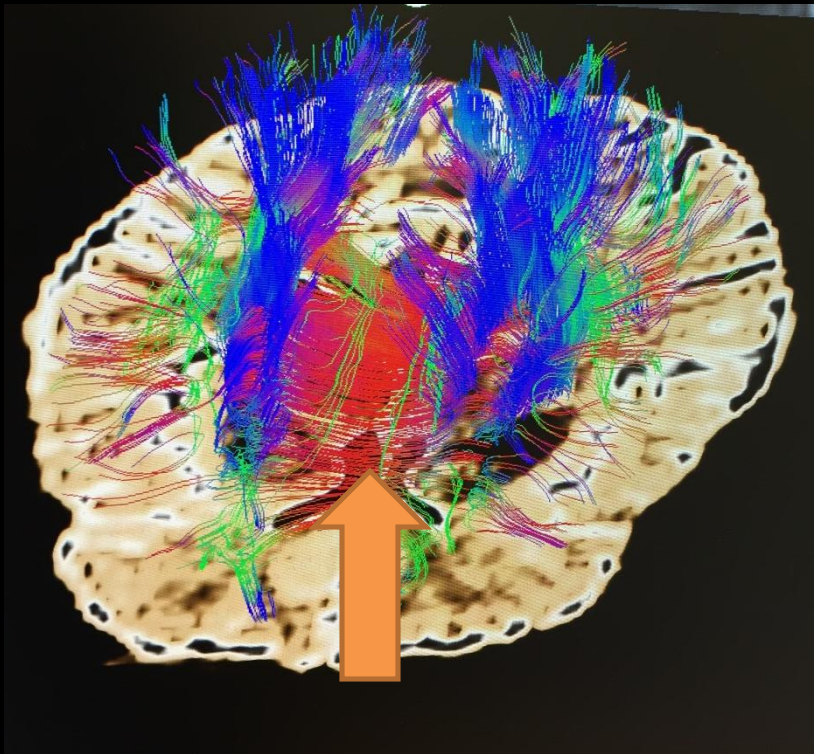
1. Metabolism in Normal/Pathological Conditions of the brain and body – inflammation, infection, cancer, function
2. Cerebral Blood Flow in Normal/Pathological Conditions*
3. Cerebral Activation Studies
4. Neurotransmitter activation studies
5. Neurotransmitter Changes in Pathological Conditions*
6. Molecular imaging of inflammation, disease processes
7. Studying the effects of pharmacological agents and integrative therapies in the brain and body
8. Determining prognosis and directing therapy

Current Applications of PET-MRI

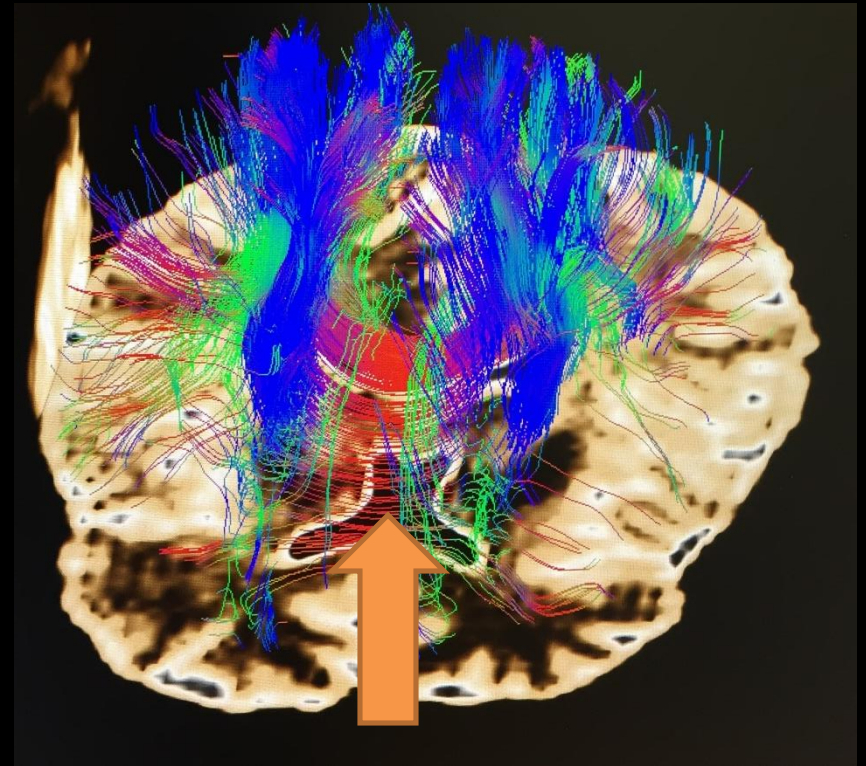
1. Cerebral Blood Flow in Normal/Pathological Conditions*
2. Cerebral Blood Flow is measured with BOLD or ASL
 - a. BOLD is blood oxygen level dependent imaging and measures relative signal during different states
 - b. ASL is arterial spin labeling which measures absolute blood flow by magnetically labeling blood at the level of the neck and observing its flow into the brain
3. Cerebral Activation Studies can use BOLD or ASL
4. Resting BOLD measures variability of different structures compared to each other – Functional Connectivity
5. Diffusion Tensor Imaging (DTI) measures fluid diffusion enabling ability to evaluate white matter tractography
6. Magnetic Resonance Spectroscopy (MRS) allows for the ability to measure the concentration of specific molecules within a part of the brain
7. Studying the Effects of Integrative Therapies and Pharmacological Agents
8. Determining prognosis and directing therapy

* Conditions include Neurological, Psychiatric, and Drug Abuse

Comparison Between Genius and Control Showing Increased Connective Tracts Between Left and Right Hemisphere



High Creativity

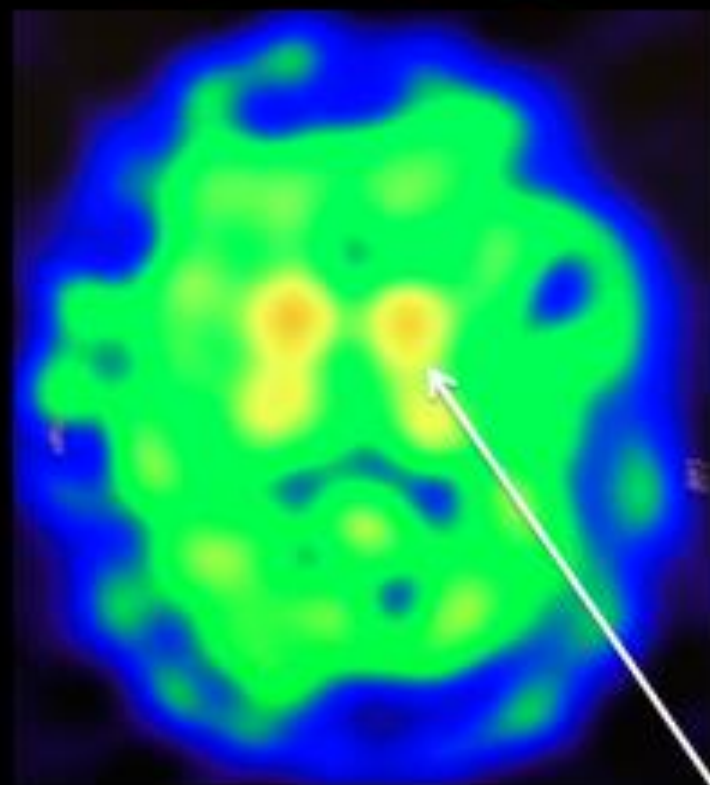


Control

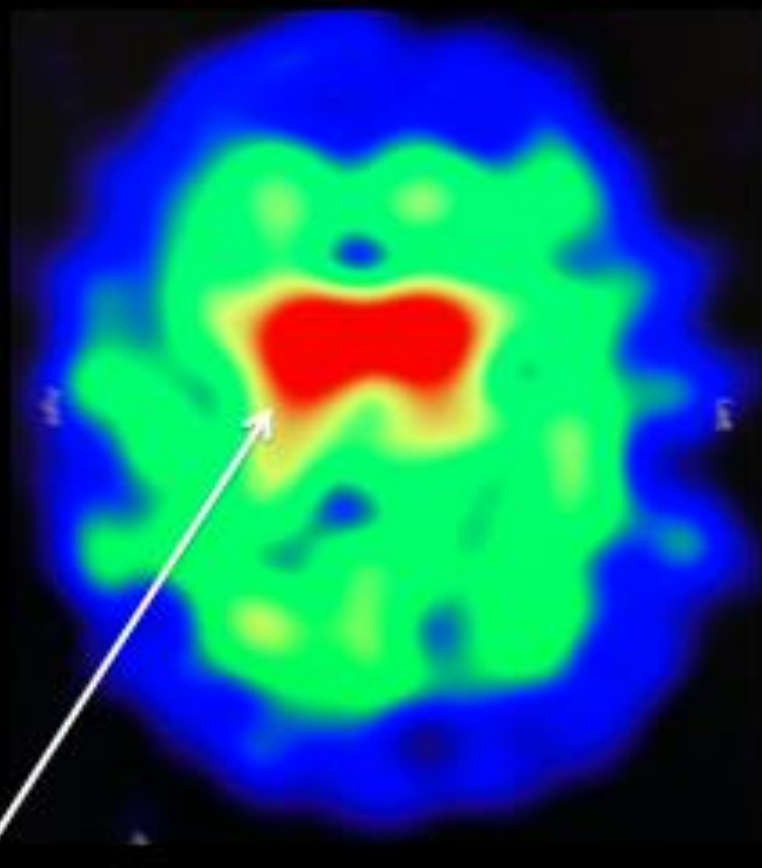
Novel Integrative Therapies for Neuropsychiatric Disorders

- We have conducted an initial pilot study using n-acetyl cysteine in patients with Parkinson's disease (Monti et al., 2016, 2019)
- Patients have improved clinically approximately 5-10% in a short period of time
- Brain imaging has shown significant improvements in dopamine function (the main area affected in PD) by about 5-10%
- PET-MR can further advance these therapies by evaluating dopamine function as well as the neuronal tracts involved

Pre NAC Treatment



Post NAC Treatment



PD NAC Study

Mean pre-to-post changes in DAT binding

*N=NAC, C=Control (waitlist)

	Mean	LCL95%	UCL95%	p-value
Caud pre-to-Post change in group N	0.092	0.013	0.170	0.023
Put pre-to-Post change in group N	0.135	0.056	0.214	0.001
Caud pre-to-Post change in group C	-0.059	-0.171	0.052	0.295
Put pre-to-Post change in group C	-0.110	-0.222	0.001	0.052
Caud pre-to-Post change in group N vs. C	0.151	0.015	0.287	0.030
Put pre-to-Post change in group N vs. C	0.245	0.109	0.382	0.001

PD NAC Study

Comparison of UPDRS scores to changes in DAT binding.

Variable 1	Variable 2	Corr. Coeff.	LCL95%	UCL95%	p-value
Spearman correlation coefficient					
UPDRSdiff	Midbrain	-0.286	-0.540	0.023	0.066
UPDRSdiff	caud	-0.196	-0.470	0.117	0.214
UPDRSdiff	put	-0.493	-0.690	-0.216	0.001
Pearson correlation coefficient					
UPDRSdiff	Midbrain	-0.275	-0.532	0.034	0.078
UPDRSdiff	caud	-0.217	-0.487	0.096	0.169
UPDRSdiff	put	-0.486	-0.685	-0.208	0.001

PD NAC Study

Mean pre and post midbrain SERT binding measures

Group	Time	Mean	LCL95%	UCL95%
C	pre	1.59	1.49	1.69
C	post	1.48	1.38	1.57
N	pre	1.48	1.41	1.55
N	post	1.62	1.55	1.69

NAC in Multiple Sclerosis

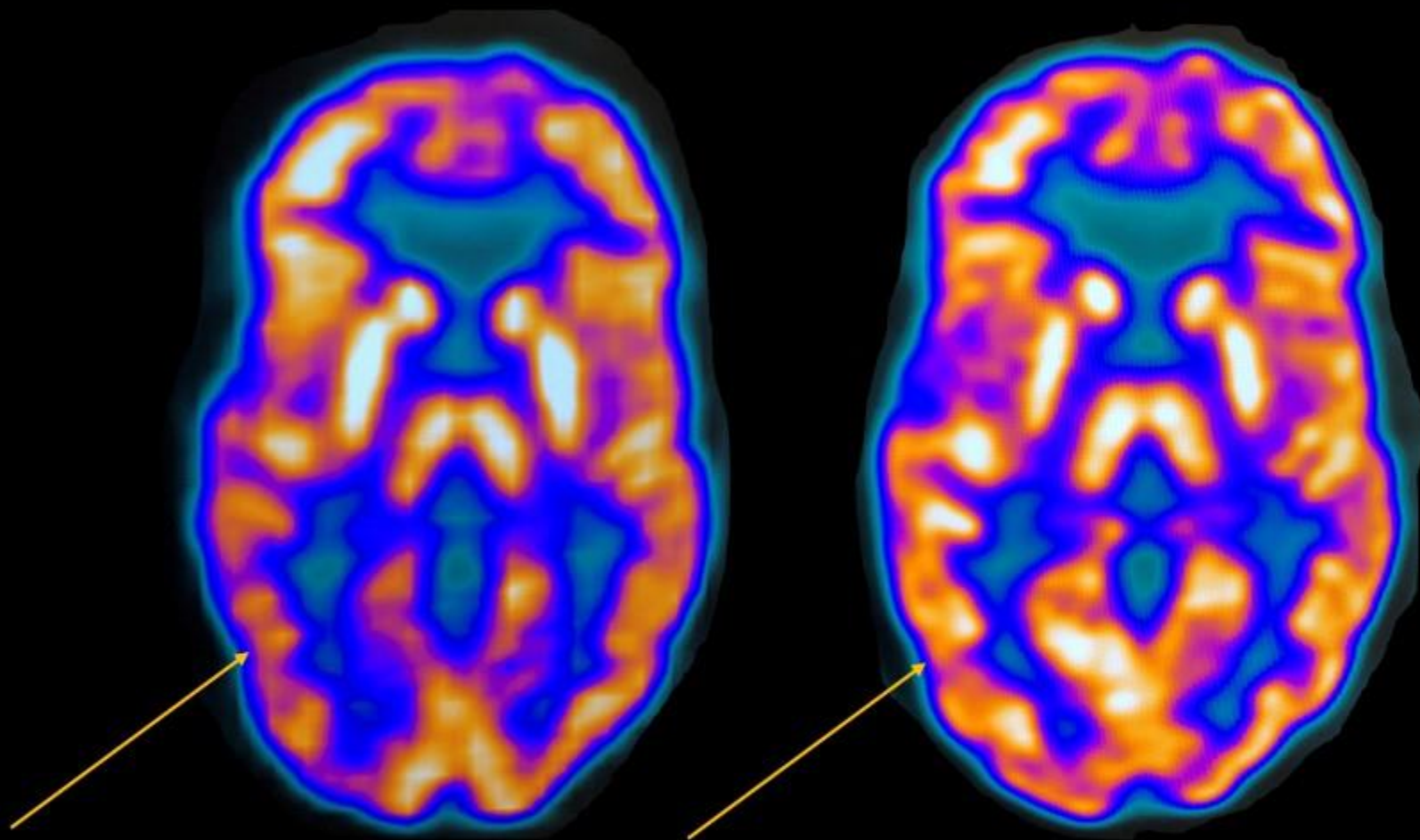
- Multiple Sclerosis (MS) is a progressive neurocognitive disorder with limited treatment options and is associated with a variety of psychological and cognitive problems.
- The purpose of this study was to explore the potential positive effects of n-acetyl-cysteine (NAC) on cerebral glucose metabolism (CMRGlu) in patients with multiple sclerosis (MS), and to elucidate biological mechanisms and potential clinical impact.

NAC in Multiple Sclerosis

- Twenty-four patients with mild to moderate MS were randomized to either NAC plus standard of care, or standard of care only.
- The experimental group received NAC intravenously once per week and orally the other six days.
- Patients in both groups were evaluated initially and after 2 months (of receiving the NAC or waitlist control) with ^{18}F Fluorodeoxyglucose positron emission tomography to measure cerebral glucose metabolism.
- Clinical and symptom questionnaires were also completed initially and after 2 months.

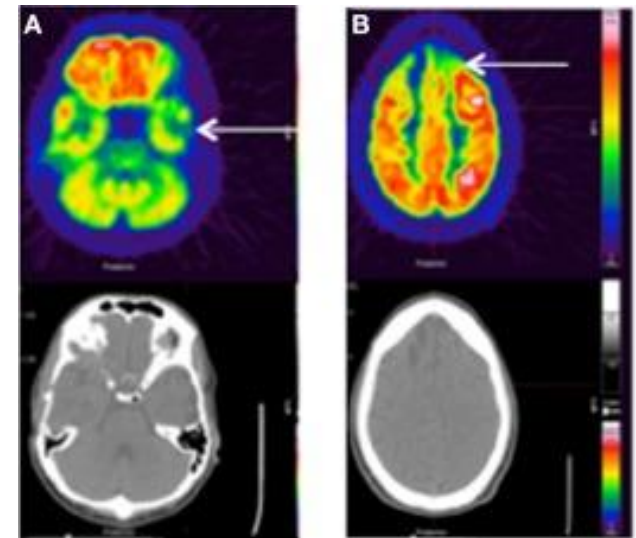
Brain Structure	Group	Post vs. Pre Difference	p value	95% CI
Inferior Frontal Gyrus	Control Group	-0.060	.993	(-0.456, 0.336)
	NAC Group	0.441	.022	(0.044, 0.837)
Lateral Temporal Gyrus	Control Group	-0.805	.039	(-1.579, -0.031)
	NAC Group	0.854	.025	(0.080, 1.629)
Middle Temporal Gyrus	Control Group	-0.774	.072	(-1.595, 0.046)
	NAC Group	0.982	.012	(0.162, 1.803)
Temporal Lobe	Control Group	-0.954	.093	(-2.015, 0.106)
	NAC Group	1.000	.072	(-0.061, 2.061)
Caudate	Control Group	-0.100	.952	(-0.497, 0.297)
	NAC Group	0.606	<.001	(0.209, 1.003)
MHI Cognition	Control Group	-3.056	.744	(-10.188, 4.076)
	NAC Group	8.611	.010	(1.479, 15.742)
PDQ Attention	Control Group	0.917	.305	(-0.413, 2.246)
	NAC Group	-1.417	.031	(-2.746, -0.087)

Pre and Post NAC Showing Increased Right Temporal Lobe Metabolism (arrows)



Treating Traumatic Brain Injury

- Concussions have become a major health problem affecting children, adolescents, and adults
- Brain injury can result from sports, accidents, and personal trauma
- The major problem with brain injury is finding it and helping people recover
- Ongoing post injury inflammation is the primary cause of persistent symptoms
- We have been a pioneer in the use of functional brain imaging in traumatic brain injury
- PET-MR can evaluate for structural damage (MR) and functional damage (PET) from inflammation



Traumatic Brain Injury Study

- Patients are included if they have persistent symptoms (emotional, cognitive, pain, hypersensitivity) for at least 3 months from one or more concussions
- Diagnostically, patients undergo an initial PET-MRI and then follow up MRI at 3 and 6 months
- They receive qEEG at each time point as well as clinical measures/evaluations

Traumatic Brain Injury Study

- Therapeutically, patients are assigned to one of three arms:
 - Diet and nutritional counseling regarding an integrative diet for 3 months
 - NAC given both IV and oral for 3 months
 - Waitlist group which receives nothing for the first 3 months and then oral NAC for the second 3 months
- We are actively recruiting for this study

Insomnia Study

- Used fMRI to evaluate the effects of a vibratory and auditory stimulation program (Theracoustic system)
- Subjects that met the inclusion criteria underwent an initial sleep evaluation along with resting BOLD fMRI.
- Subjects were then randomized in a 2:1 manner into an active intervention group or a waitlist control group.
- The intervention group received auditory and vibratory stimulation for one month and then underwent the same imaging and sleep evaluation as performed during the initial evaluation.
- The waitlist control group was evaluated initially and then had the same imaging and sleep evaluation one month later.

Clinical Results from Insomnia Study

Insomnia Index:

	Mean Diff	p-value	95% CI
Post vs Pre	-3.1	<.001	(-4.281, -1.830)

Minutes Slept:

	Mean Diff	p-value	95% CI
Post vs Pre	+30.6	<.001	(14.457, 46.806)

Additional analyses will compare insomnia patients to controls and also incorporate qEEG measures with respect to clinical response and fMRI results

Functional Connectivity fMRI Results from Insomnia Study

Insomnia group (Vibroacoustic Stimulation Vs control group / Pre Vs Post)			
Brain Structures	FDR Corrected p	T-Test	X, Y, Z Coordinates
Vermis – Sensorimotor	0.009	-4.16	Sensorimotor.Superior Network: [-0.073, -30.535, 67.405]
Vermis – R Auditory Cortex	0.0435	-3.30	Auditory Cortex (R): [46.110, -17.401, 6.961]
R Thalamus – R Caudate	0.032	+3.26	R caudate: [13.301, 10.010, 10.49]
R Cerebellar Hemisphere – R Sensorimotor	0.0375	-2.97	Sensorimotor (R) Network: [56.386, -9.868, 28.818]
R Nucleus Accumbens – R PFC	0.0402	-2.96	FrontoParietal PFC (R) Network: [-43.116, 33.186, 28.244]
L Cerebellar Hemisphere – L Sensorimotor	0.0355	-2.93	Sensorimotor (L) Network: [-55.467, -12.364, 29.489]

NeuroEmotional Technique Study

- NET is an integrative approach combining acupuncture, cognitive therapy, and exposure therapy
- NET study of 25 patients with a history of traumatic memories associated with a cancer diagnosis
- Patients were randomized to NET or waitlist control
- fMRI performed pre and post intervention

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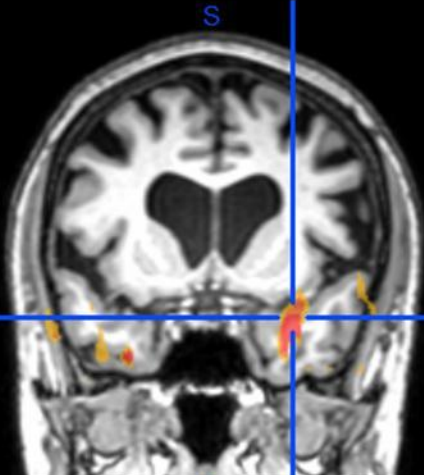
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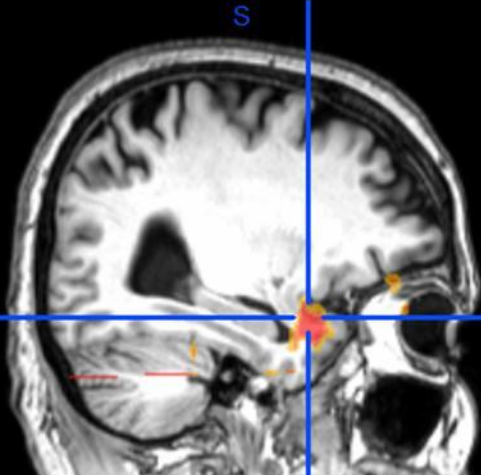
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P



Perfusion fMRI
 Stressor – Neutral
 Pre NET Treatment

38

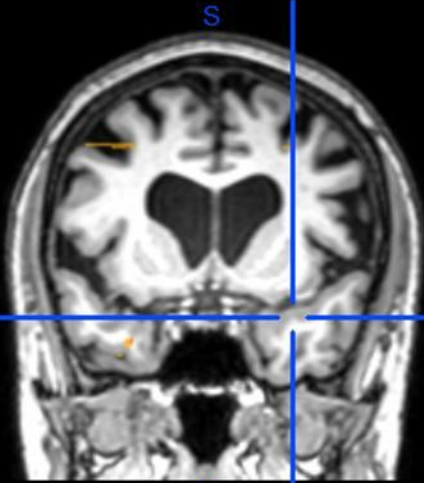
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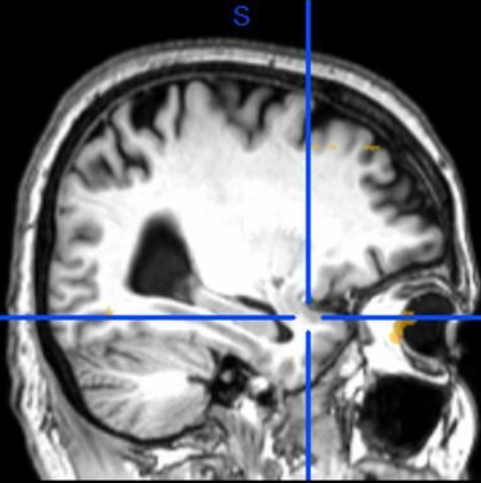
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Perfusion fMRI
 Stressor – Neutral
 Post NET Treatment

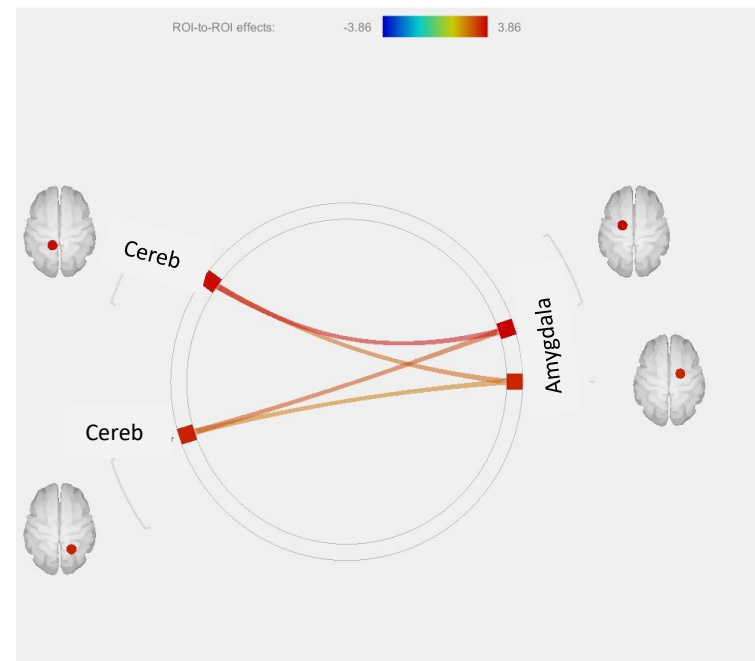
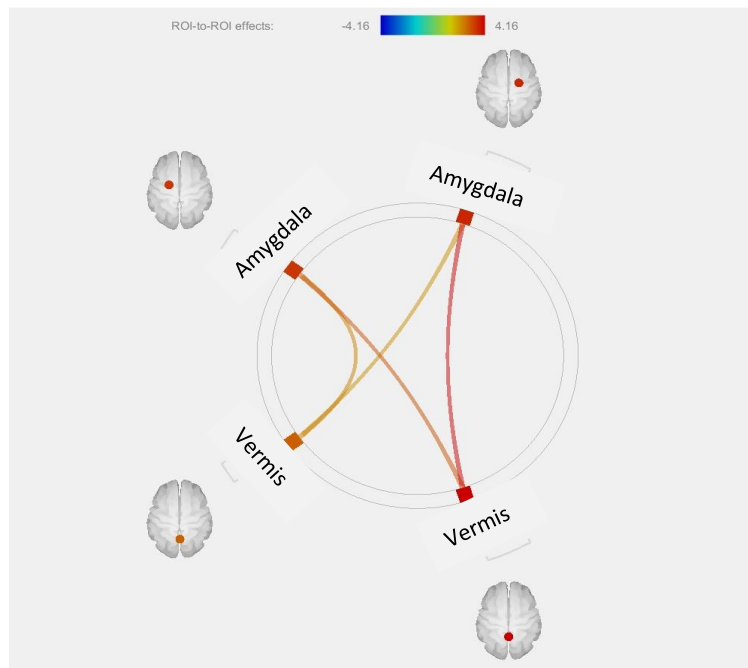
Clinical Results from NET Study

	NET	NET	Controls	Controls		
Clinical measure	Pre	Post	Pre	Post	P-value	P-value(*)
BSI Anxiety Score	30.5	14.6	25.1	23.7	0.0083	0.025
BSI Depression Score	31.1	14.1	24.9	23.8	0.0039	0.023
BSI Anxiety Score	30.5	14.6	25.1	23.7	0.0083	0.025
BSI Global Severity Index	32.4	11.8	26.3	23.3	0.0013	0.011
IES Score	33.1	10.4	26.8	23.5	0.0018	0.013
PTCI Score	32.6	19.7	22.5	19.6	0.0204	0.025
STAI State Score	25.4	9.9	29.1	25.5	0.0223	0.025
STAI Trait Score	29.2	12.0	26.8	22.0	0.0246	0.025

(*) adjusted to control for family-wise type I error

Evaluation of Novel Psychological Interventions – The NeuroEmotional Technique

- Functional connectivity showed influence of the cerebellum, a novel and important finding



Monti et al. Journal of Cancer Survivorship, 2019

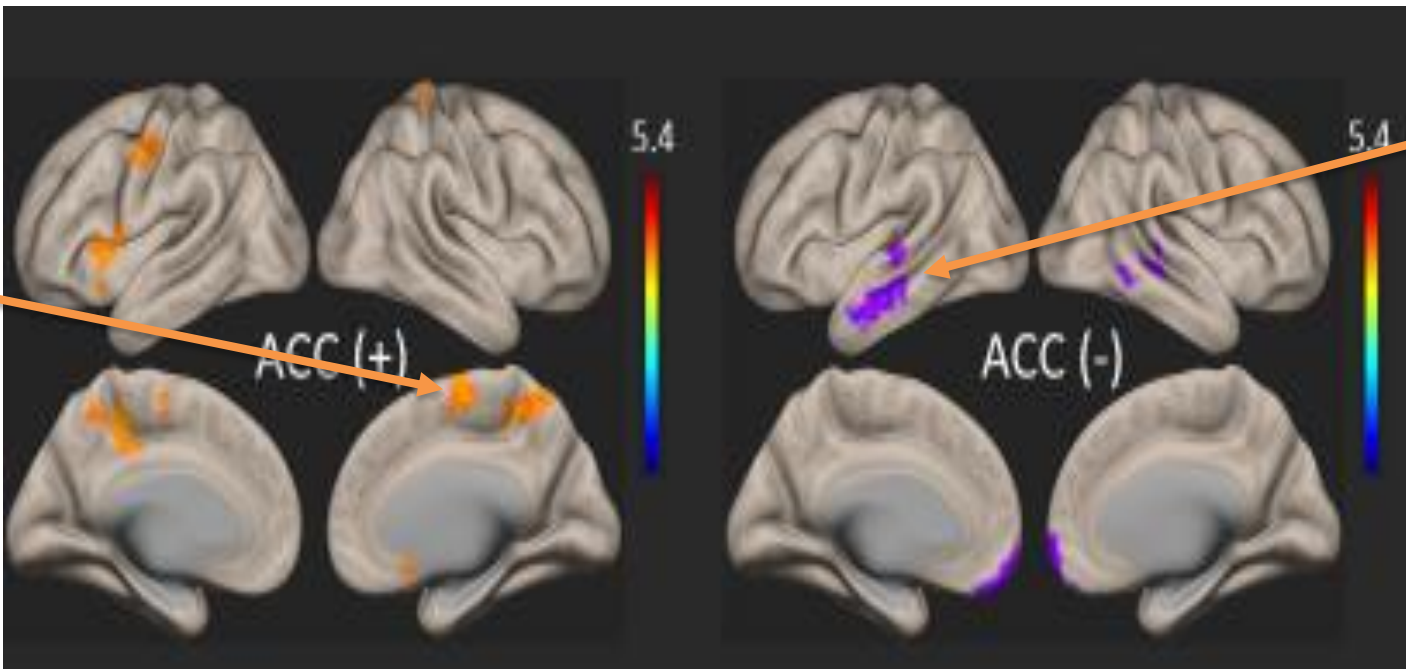
Evaluation of Meditation/ Spiritual Practices

- Meditation
 - Mindfulness: MBAT study, Reibel Elderly study
 - Transcendental, Kirtan Kriya
 - Moving meditations – Tai chi, yoga
- Prayer
 - Meditative prayer, Centering Prayer
 - Charismatic practices
 - Different traditions: Judaism, Christianity, Islam, etc.
- Drumming
- Rituals
 - Standard rituals, liturgy, personal practices

MBSR in the Elderly

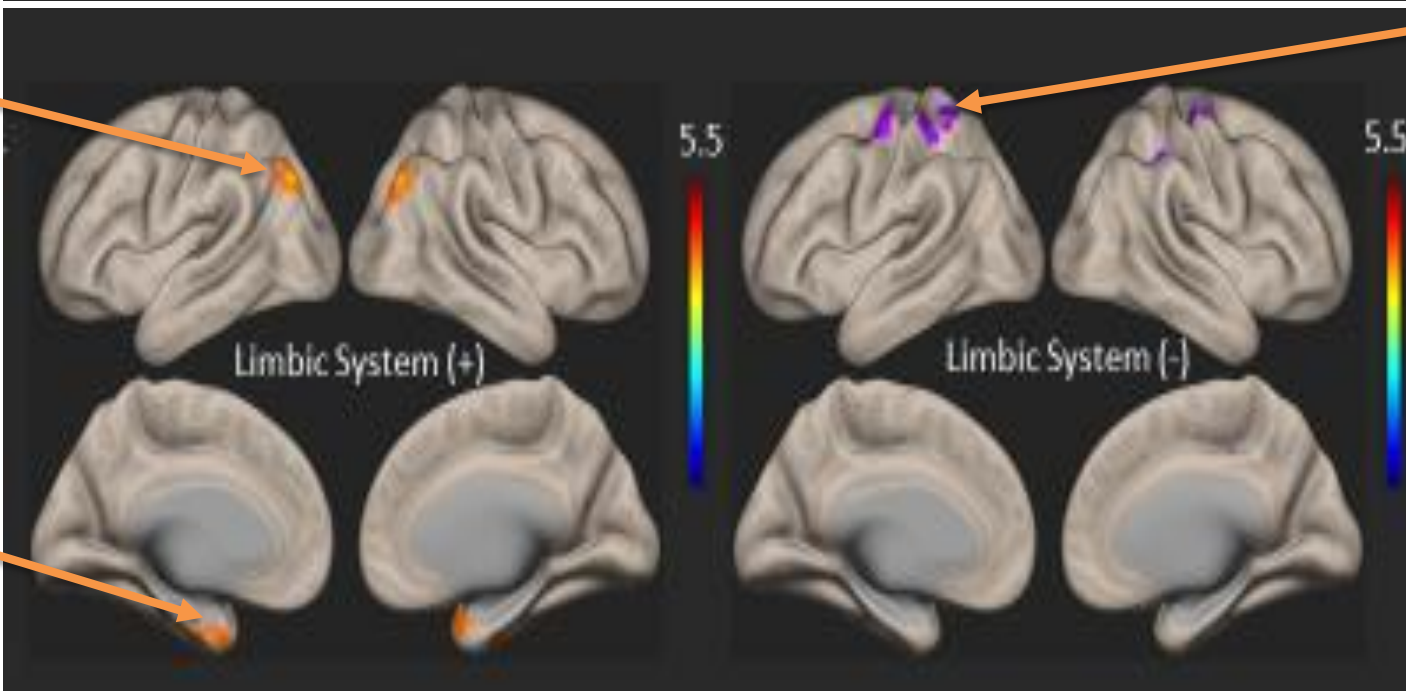
- 11 subjects who participated in the fMRI study completed the 8-week MBSR program undergoing both and pre- and post-program scans.
- 9 of them attended all 8 classes and 2 attended 7 classes.
- MBSR participants also had a high level of compliance with home practice.
- On average they practiced 5.6 times per week for 26 minutes per session, listening to guided meditations on compact discs over the course of the 8-week program.

Post Cent
Gyrus



Temporal

Occipital



Sup Parietal

Temp Pole

PET Imaging Pre and Post NET in Patients with Chronic Pelvic Pain

IMPACT:

This 2 year study will change the way chronic pelvic pain is understood, evaluated, and treated using the NET program.

Such findings will also transform how the medical field conceptualizes the relationship between chronic pain and brain function.

These results can also revolutionize how the medical field recognizes the importance of integrative approaches to chronic pain based on physiological data from PET-MR imaging.

AIM #1: To use PET-MR to define abnormal brain activity in subjects with chronic pelvic pain that improves when treated with NET.

AIM #2: To define areas of inflammation in the body based on PET-MR in subjects with chronic pain syndromes which are altered when treated with integrative therapies.

Evaluation of an Integrative Medicine Approach to Treating Irritable Bowel Syndrome

IMPACT:

To change the way irritable bowel syndrome is understood and diagnosed utilizing PET-MRI technology.

To revolutionize how to evaluate and treat IBS using integrative approaches, which could help thousands of people with this debilitating and chronic condition.

AIM #1. To evaluate the ability of FDG PET-MRI to detect reductions in GI tract inflammation in the in patients with IBS receiving 3 months of an integrative medicine treatment program.

AIM #2. To correlate FDG PET-MRI findings with various physiological and clinical parameters at baseline. This will further help evaluate the utility of FDG PET-MRI for assessing patients with IBS, helping to target future therapies.

Conclusions

- ✔ Integrative medicine and general medicine have multiple areas of intersection
- ✔ Studies can evaluate mental and physical disorders such as depression or anxiety or chronic pain and fatigue
- ✔ Studies can evaluate psychological symptoms associated with other medical and neurological disorders
- ✔ Important to establish efficacy and also mechanism
- ✔ Future collaborations are very welcome!

The End

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