THE EVOLUTION OF INTEGRATIVE MENTAL HEALTH

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Faculty Disclosure

- **Faculty:** Scott Shannon, MD

- **Relationships with commercial interests:**
  - **Grants/Research Support:** PI/Researcher for Multidisciplinary Association for Psychedelic Studies - Non profit/Public Benefit B Corp
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  - **Consulting Fees:** none
  - **Other:** Royalties for the sale of four professional books and textbooks.
DISCLOSURE OF COMMERCIAL SUPPORT

• Scott Shannon, MD has received an honorarium from the Highlights in Medicine Conference, and also from the Betty Anne and Wade Heggie Lecture in Integrative Medicine Fund.

• This program has received financial support from College of Medicine, University of Saskatchewan in the form of an educational grant.
MITIGATING POTENTIAL BIAS

- I will not promote my four books
- The presentation will only present published data from Phase II and the clinical design of Phase III.
AGENDA

- Why we need IMH: a look at depression, PTSD and addiction
- The Foundation of IMH
- Roots of IMH
- A quick flight through the decades
- Key arenas and developments
- Future of IMH: the twin pillars
- Closure and discussion
“Never, ever, think outside the box.”
WHAT IS INTEGRATIVE MENTAL HEALTH

It combines the safest and most effective techniques to support the health of body-mind-spirit in an ecologically sound approach that emphasizes prevention, the removal of barriers and the correction of underlying imbalances*

*physical, mental, emotional, social or spiritual issues may predominate…..
WHY WE NEED IMH

- Limitations with Depression
- Limitations with PTSD
- Limitations with Addictions
THE FOUNDATION OF INTEGRATIVE MENTAL HEALTH

allopathic psychiatry vs holistic/integrative psychiatry
Wage war on the illness. Use the most efficacious interventions: collateral damage is acceptable, disease must be conquered.

Support health, remover barriers & enhance healing. First of all do no harm. Use the safest treatment.
SAFETY, EFFICACY AND THE PATIENT

- RCTs = gold standard. Efficacy highly scrutinized
- Safety appears to be less severely scrutinized
- Safety vs Effectiveness: a paradigmatic split
  - CAM vs Conventional
- Patient preference should help to determine direction
- True informed consent rarely provided

Shannon, Weil, Kaplan  *Alternative and Complementary Therapies* 2011, 17 (2): 84-91
ROOTS OF IMH

• Carl Jung
• William James
• Wilhelm Reich
• Human Potential Movement: Maslov, Perls, others
• Osmond, Hoffer and Grof
• Elmer Green
A QUICK REVIEW

selected advances
SELECTED KEY ARENAS AND DEVELOPMENTS

- Meditation
- Biofeedback
- Exercise
- Supplements
- Diet and population
- Positive Psychology
- Assisted Psychotherapy
MEDITATION


EXERCISE


SMILE study: 4 months- 45% response vs. 47% with meds. Superior to placebo. Longer term outcomes superior to medications
NATURAL SUPPLEMENTS


• **Stoll AL et al** Omega 3 fatty acids in bipolar disorder: a preliminary double-blind, placebo-controlled trial. *Arch Gen Psychiatry.* 1999, May;56(5):407-12.

• **Popper CW.** Do vitamins or minerals (apart from lithium) have mood-stabilizing effects? *J Clin Psychiatry.* 2001 Dec;62(12):933-5.

• **Linde K, Berner MM, Kriston L.** St John's wort for major depression. *Cochrane Database of Systematic Reviews* 2008, 4. October

The Twin Pillars of IMH

Neuroplasticity
Epigenetics
ENCODE
ENCyclopedia Of DNA Elements
female yellow mouse (agouti gene unmethylated and active)

- **Diet supplement during pregnancy and nursing with additional methyl groups**
  - Offspring mostly brown and healthy; agouti gene methylated and silenced

- **No dietary supplementation**
  - Offspring mostly yellow and unhealthy; agouti gene unmethylated and active
Excercise
- BDNF

Nutritional Factors
- Calorie Restriction
- Mediterranean Diet
- Polyphenols

Signaling molecules

Transcription factors

Environment
- Clean air, water and soil
- No smoking

Emotional Health
- Religion
- Meditation
Most illnesses are influenced by genetic factors.

The largest international dataset of ADHD, bipolar, depression, autism and schizophrenia found the variation from SNPs explained 17% to 29% of the variance in liability.

Points to dimensional model with no separation between well and sick for depression and ADHD.

“ADHD lies on the spectrum of normal trait variation.”

Stergiakouli, E JAACAP 2015 54 (4): 322

Lee, SH Nat Genet. 2013 45: 984-994
“Genetic variations do not cause disease but rather influence a person’s susceptibility to environmental factors.”

“Virtually all human diseases result from the interaction of genetic susceptibility and modifiable environmental factors.”

CDC: The Office of Genetic and Disease Prevention, August, 2000
ADVERSE CHILDHOOD EXPERIENCES

- Surveyed 17,000 adult HMO pts
- Experience of abuse, neglect, DV, crime, alcoholism. 8 categories/10 questions.
- ACEs correlate in graded fashion with every negative outcome in affective, somatic, memory, substance abuse, aggression and sexual disorders

ABUSE CREATES EPIGENETIC CHANGE IN HPA AXIS

- Post mortem study of suicide victim’s brains
- Compared abuse survivors versus controls
- Structural changes in NR3C1 receptor vs controls
- NR3C1 responsible for deactivation of HPA axis
- Links to schizophrenia, mood disorders and suicide
- Most research finds continuum of stress and abuse

McGowan, P Nat Neuroscience 2009, 12:342-348
NEUROPLASTICITY

The power of change
NEUROPLASTICITY

Includes:

- New cells (neurons, glial cells)-
  neurogenesis
- New connections-synapses,
  dendrites
- Axonal sprouting
- Pruning
127 adults with mild cognitive impairment

Intensive multi-disciplinary brain fitness program

12 week program: 5 hours per week

Q-EEG, MRI, neurocognitive tests: pre and post

Coaching on exercise, cognitive skills, diet, supplementation (omega 3 EFAs), mindfulness

2 hours per week of Neurofeedback

84% demonstrated significant improvement in 3 of 10 components on cognitive testing (p < .05)

Post study MRI: 65% improvements in hippocampal growth above baseline

**Crucial proof of concept**

NEUROFEEDBACK

The essence of neuroplasticity

All demonstrated significant improvements in attention, hyperactivity or impulsivity as compared to controls.
Examples of Electrical Neuroimaging After Neurofeedback

Pre-Treatment

Post – 10 Treatments

S #1

S #2
NEW WAYS OF THINKING
“On Chorea and Choreiform Affectations” (1894), Osler described obsessive-compulsive behavior in SC.  
Acute or abrupt onset of symptoms  
Can be chronic or relapsing  
Movement issues, anxiety, OC behaviors,  
“a changed child”  
Marcerollo, A *Tremor Other Hyperkinet Mov* 2013 Sep 25;3.
Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections

Pediatric Acute-onset Neuropsychiatric Syndrome

Psychiatric or Neurological symptoms following Group A Beta Hemolytic Strep infection (GABHS)

Molecular mimicry-rheumatic fever/Syndenham’s chorea-antigens in GABHS similar to proteins in heart and basal ganglia

Swedo SE. *JAMA* 1994 272: 1788–1791

Chang, K et al. *J Ch Ad Psychopharmacology* 2014 October 17th
RANGE OF SYMPTOMS

• Emotional lability (66%)
• School performance (60%)
• Personality change (54%)
• Hyperactivity (50%)
• Separation anxiety (46%)
• Handwriting change (36%)
• Oppositionality (32%)

All of these documented in SC
ANTI-NMDA RECEPTOR ENCEPHALITIS
Depressed?
Over Worked?
Job Suck?
Unappreciated?
Family Problems?
Money Worries?

Well Here is a pill for you!

FUKITOL®
1000 mg

When Life Just Blows.... FUKITOL®!

www.fukitol.com
NEW APPROACH: MITOCHONDRIAL MODULATION

Known Modulators:

1. N-acetyl Cysteine (NAC)
2. Acetyl-L-Carnitine
3. S-adenosyl Methionine (SAM-e)
4. CoQ10
5. Alpha-Lipoic Acid
6. Creatine Monohydrate
7. Melatonin

Nierenberg AA  *Aust NZ J Psychiatry* 2012, June 18
CRP LEVEL AND FRONTAL LOBE

• Elevated hs-CRP previously linked to MI and stroke.
• Used DTI imaging technique for detail and early identification
• 447 elderly, no prior stroke (MA-63)
• Hi CRP linked to worse Executive Function and microstructural WM abn in Frontal Lobe

Wersching, H. Neurology 74 (13), 2012
Survival plot (Kaplan-Meier) showing the probability of remaining free of de novo major depressive disorder for women stratified into tertiles of hsCRP.

Pasco JA et al. BJNP 2010; 197: 372-377
PSYCHEDELICS AS CATALYSTS OF EMOTIONAL GROWTH AND RECOVERY

• Ketamine-Depression and Bipolar Disorder
• MDMA-PTSD
• Ibogaine-Substance Abuse
• Ayahuasca-Substance Abuse
• Psilocybin-End of life issues

Review of Research completed and in Progress: Multidisciplinary Association for Psychedelic Studies  www.maps.org
MDMA PHARMACOLOGY

**Increases release of:**
- serotonin (5-HT)
- norepinephrine (NE)
- dopamine (DA)

**Enhances release of hormones:**
- oxytocin
- prolactin
- vasopressin
- cortisol
SURVEY OF PSYCHIATRISTS

20 psychiatrists with long-term experience with MDMA

- Altered perception of time 90%
- Enhanced ability to be open 85%
- Decreased defensiveness 80%
- Decreased fear 65%
- Increased awareness of emotions 50%
- Less aggression 50%

Liester, MB J Nervous Mental DO 1992 180:345-52
THERAPEUTIC APPROACH

• Non-directive, supporting emerging experience
• **Inner healing intelligence**
• Reclining, headphones with music, eyeshades
• Alternating inner focus & talking to therapists
• Allows for therapists’ individual variation
• **Importance of preparation and integration**
Crime related PTSD
Failed psychotherapy & psychopharmacology
Required to taper off psychiatric meds

The safety and efficacy of ±3,4-methylenedioxymethamphetamine-assisted psychotherapy in subjects with chronic, treatment-resistant posttraumatic stress disorder: the first randomized controlled pilot study

Michael C Mithoefer, Mark T Wagner, Ann T Mithoefer, Lisa Jerome and Rick Doblin

Abstract
Case reports indicate that psychiatrists administered ±3,4-methylenedioxymethamphetamine (MDMA) as a catalyst to psychotherapy before recreational use of MDMA as 'Ecstasy' resulted in its criminalization in 1985. Over two decades later, this study is the first completed clinical trial evaluating MDMA as a therapeutic adjunct. Twenty patients with chronic posttraumatic stress disorder, refractory to both psychotherapy and psychopharmacology, were randomly assigned to psychotherapy with concurrent active drug (n = 12) or inactive placebo (n = 8) administered during two 8-hour experimental psychotherapy sessions. Both groups received preparatory and follow-up non-drug psychotherapy. The primary outcome measure was the Clinician-Administered PTSD Scale, administered at baseline, 4 days after each experimental session, and 2 months after the second session. Neurocognitive testing, blood pressure, and temperature monitoring were performed. After 2-month follow-up, placebo subjects were offered the option to re-enroll in the experimental procedure with open-label MDMA. Decrease in Clinician-Administered PTSD Scale scores from baseline was significantly greater for the group that received MDMA than for the placebo group at all three time points after baseline. The rate of clinical response was 10/12 (83%) in the active treatment group versus 2/8 (25%) in the placebo group. There were no drug-related serious adverse events, adverse neurocognitive effects or clinically significant blood pressure increases. MDMA-assisted psychotherapy can be administered to posttraumatic stress disorder patients without evidence of harm, and it may be useful in patients refractory to other treatments.

STAGE 1: MEAN CAPS-4 SCORES BY GROUP

Time*Group Interaction
\( p = 0.015 \)

Ketamine

C$_{13}$H$_{16}$CINO
THE ANTI ANTIDEPRESSANT

Depression afflicts 300 million people. One-third don’t respond to treatment.

A surprising new drug may change that

BY MANDY OAKLANDER
KETAMINE AND DEPRESSION

“The marked acute antidepressant efficacy of ketamine, even in medication-refractory patients, now seems beyond doubt. A meta-analysis of 9 ketamine RCTs (pooled N = 234) found that ketamine attenuated depression significantly more than did control treatment. The antidepressant benefits were apparent at 40 minutes, peaked at day 1, and were lost by days 10–12.”

Andrade, C  J Clinical Psychiatry 2017 Apr;78(4):e415-e419.
"I’m getting bored, Mom — let’s cut to the chase."
CLOSURE
• NIMH: Treatment of Depression Collaborative Treatment Program (TDCRP)
• 112 pts with Major Depression, 9 psychiatrists
• Compared medication, practitioner and placebo effects
• Beck Depression Inventory: proportion of variance
  Medication: 3.4%
  Psychiatrist: 9.1%

The psychiatrist was more important than the medication.

McKay, KM  J Affective DO 2006; 92 (2-3): 287-290
SUMMARY

• Our current model of psychiatry is failing on many levels.
• IMH with its focus on health offers a new model with strong support from epigenetics and neuroplasticity.
• Over the last 50 years developments using the IMH model have enriched our view of the human psyche and mental health care.
• As we move forward IMH has the potential to lead us to a new model of mental health.
Larsen, J. *Seven Weeks to Sobriety*  Ballentine Books: NY 1997
RESOURCES

Culbert and Olness (ed) Integrative Pediatrics  Oxford Univ Press: NY, 2010
Doidge, N  The Brain That Changes Itself, Penguin: NYC, 2007
Greene, R  The Explosive Child  Harper Collins, NY, 2005
Kemper, K  Mental Health Naturally  AAP Press: Elk Village, Il, 2010
Newmark, S  ADHD without Drugs  Nurtured Heart Tucson, 2010
Shannon, S  Mental Health for the Whole Child  Norton: NY, 2013
Shannon, S  Parenting the Whole Child  Norton: NY, 2014
PSYCHIATRIC DX: LOW RELIABILITY

- Large meta-analysis
- 38 studies
- 16,000 patients
- Low correlation between clinical evaluations and standardized diagnostic interviews (SDIs)
- K value: 0.27 overall (poor)

Rettew, DC et al *Int Methods Psych Res* 2009, 18:169-184
12,564 patients and 74 FDA registered studies reviewed

- 94% of published trials positive  (only=51% positive by FDA)
- 37 positive published, 1 positive not
- Vast majority of unpublished: negative
- FDA: effect size distortion- increase ranged from 11 to 69%.
- **Average distortion = 32%**

Turner, E  *NEJM*  2008, 17;358(3):252-60
ANXIETY: LESS EFFECTIVE RX?

- Review of all FDA studies (57)
- 9 Second Gen. Anti-depressants
- Huge publication bias (5x) (p=.001)
- Spin (abstract not consistent with data) : p=.02
- “reporting biases led to significant increases in the number of positive findings in the literature”

Roest, A et al JAMA Psychiatry 2015 online March 25th.
STEP-BD
STUDY OF BIPOLAR RELAPSE

- 1,469 patients with Bipolar Disorder
- 48.5% relapse within two years
- Depression more common than mania
- Lamotrigine better than antidepressants
- “Recurrence common and highlights the need for more treatment options”

Largest US study of Major Depression.
3,671 patients over one year.
No medication better than another.
37% remission after 1 trial, 67% after 4.
Massive drop out rates= 21, 30 and 42%
More than one med= more likely to relapse
“The 67% rate is almost certainly an over estimate of what would happen in the real world”

Over 50 publications

Numbers reported are different in different publications.

29% drop out right away (4041 - 2876 = 1165)

Initial remission rate with Citalopram - 37% (790)

Relapse - 40% in the first year (316)

In remission at the end of year after all the steps - (from 3671 only 556) 15%

Or 85% are treatment resistant after 4 steps

ST. JOHN’S WORT

- Common roadside plant
- Traditional use for centuries
- Few side effects (headache, nausea, rash)
- Non-fatal in overdose
- Three to four week onset of action
ST JOHN’S WORT: COCHRANE

- 29 studies from a variety of countries with 5,489 patients, randomized and double blind.
- Major Depression only
- Placebo or antidepressants
- **Superior** to placebo in treating patients with major depression and are "similarly effective" as standard antidepressants
ST. JOHN’S WORT

- Safe, effective treatment for depression (mild to major)
- No Black Box warning
- Use quality product; 0.3% hypericins is a general marker
- Cost $8–20 per month
- BID dosing best: 900mg/day total, age 8 up
S-ADENOSYL-L-METHIONINE (SAM-e)

\[ B_{12} \]

Folate $\rightarrow$ 5MTHF + Homocysteine
$\rightarrow$ Methionine $\rightarrow$ SAM-e

Methyl Donation

SAM-e $\rightarrow$ DA
5HT
NE
DEPRESSION TREATMENTS: SAM-E

- S–adenosyl methionine (crucial methyl donor)
- Enhances methylation in body
- Profound, effective and synergistic antidepressant
- Stimulating, works quickly (2 weeks)
- Headache, insomnia, nausea
- 200-800 mg twice daily, start low, give on empty stomach
- Can induce mania
OPINION: DEPRESSION

- SJW, SAMe, Saffron or SSRI based on patient
- B Complex 50mg (B-6 and 1 mg folate)
- EPA: 1 gram or more
- Exercise and higher protein, high quality diet
- Psychotherapy or education
- If low energy think mitochondrial support
- Check thyroid, vitamin D (target 40-45 ng/dl), DHEA, ferritin/CBC, CRP. Consider MTHFR if chronic.