Research Directions for the Future: Along the Clinical Continuum

Sidney H Kennedy, MD, FRCPC
Professor of Psychiatry, University of Toronto
Psychiatrist-in-Chief, University Health Network

Research Directions : Clinical

Modifications of Existing Concepts

- **Earlier detection and Treatment**
- **Making CBT available**
- **Other psychotherapies**
- **Stigma and Adherence**
- **Current Antidepressants**
- **Combined Approaches**

Paradigm Shifts

- **Atypical Antipsychotics**
- **Agomelatine**
- **Neuromodulation therapies**
- **CRF antagonists**
- **Ketamine**
- **Mifepristone**
- **NK Antagonists**
- **Neurogenic compounds**

Future Research Questions

Q1. How can we improve early interventions?

- Mental health curriculum starting in early grades
- Targeted psychoeducation
- Development and implementation of screening tools in primary care(at risk population)
- Identify treatment seeking predictors (and those who do not seek treatment)

Treatment Seeking for Depression in Canada and the United States

- Sought treatment from any provider- 56%
- Saw a psychiatrist- 10%
- GP referral to psychiatrist or psychologist- 28% (double US referral rate)
- Factors associated with treatment seeking
  - ***-Female***
  - ***-Higher education***
  - ***-Widowhood***
  - ***-Regular medical doctor***
  - ***-Severe impairment in functioning***
  - ***-Greater severity***
  - ***-Longer episode duration***

* Individuals of minority race/ethnicity are significantly less likely to seek treatment

Mojtabai & Olfson, 2006

Managing Depression in Primary Care

- Modified from National Institute for Clinical Excellence

Severity/Type	Action or Treatment
Mild	Watchful Waiting; Guided Self-help; Exercise
Moderate to Severe	Medication; Psychotherapy; Social support
Treatment Resistant	Combination treatments
Risk to life	ECT; Experimental options

Tylee J Clin Psychiatry, 2006

Future Research Questions

Q2. How can we resolve diagnostic boundary issues?

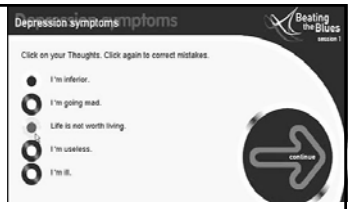
- DSM-V?
  - Diversity of symptom clusters
  - Confounds of comorbidity
- Implications of mild, moderate, and severe for treatment
- Integrating neurobiology into diagnosis
  (symptom positive/marker positive or negative)

Future Research Questions

Q3. How can we improve outcomes for depression?

- Optimize resources to deliver existing treatments
  - Stigma - Adherence - Mega-trials
  - The next STAR*D?
- Paradigm shifts
  - Internet based psychotherapy
  - New psychosocial therapies
  - Circadian rhythm restoration
  - Neurogenesis therapies?
  - Neuromodulation

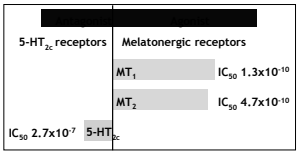
CBT on Internet

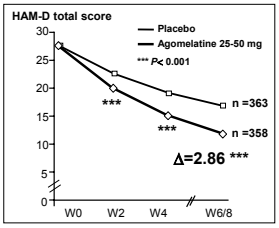


- For Depression– the MoodGym
  - http://moodgym.anu.edu.au
  - Useful for depression and anxiety
- For Panic and Phobias
  - www.fearfighter.com (UK prescription)
  - www.paniccenter.net (free)

Agomelatine

- Acute and long-term efficacy
  - Superiority to placebo in 3 trials
  - Comparative efficacy to venlafaxine in 2 trials
- Not yet available in Canada

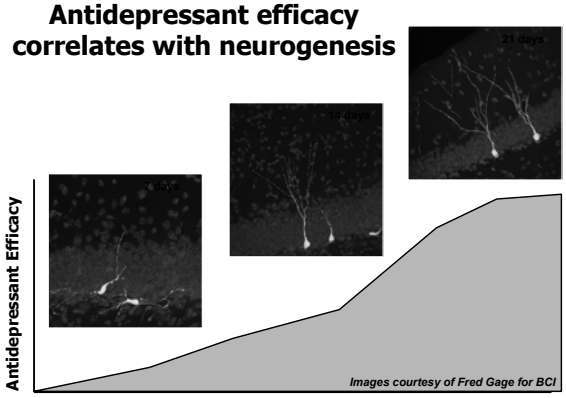




- Minimal side effect profile
  - Restorative sleep
  - Favourable sexual function
  - No weight gain

Montgomery and Kasper 2007

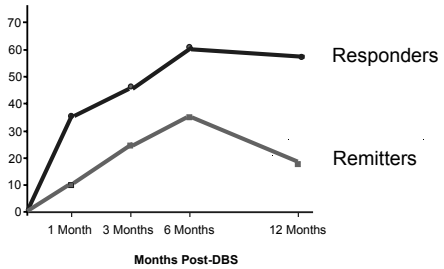
Antidepressant efficacy correlates with neurogenesis



PRIORITY COMMUNICATION

Subcallosal Cingulate Gyrus Deep Brain Stimulation for Treatment-Resistant Depression

Andres M. Lozano, Helen S. Mayberg, Peter Giacobbe, Clement Hamani, R. Cameron Craddock, and Sydney H. Kennedy



Lozano et al. Biol Psychiatry 2008

Disentangling the Heterogeneity of Depression

Symptom Profiles
- Melancholic
- Atypical
- Psychotic
- Seasonal

Comorbidities
- **I.** Anxiety Disorders Substance Abuse
- **II.** Personality Disorders
- **III.** Diabetes/ Cardiovascular

Depression

Etiological Pathways
- Preexisting Anxiety/Neuroticism
- Conduct Disorder/Substance Abuse
- Childhood Abuse/Deprivation

Markers of Gene Expression
- Monoaminergic Dysregulation
- Circadian Rhythm
- HPA Axis/Immune Function
- Neurotrophic Signaling
- Brain Structure and Function