A new Anatomy of Melancholy: rethinking depression and resilience

Prof Declan McLoughlin
Dept of Psychiatry & Trinity College Institute of Neuroscience
Trinity College Dublin
St Patrick’s University Hospital
1. Mood and mood disorders
2. Treatment of severe depression
3. Neurobiology of depression
4. Resilience
Some definitions

**Affect** - objective, transient (? blunt, labile)

**Mood** - subjective, sustained

anxious, depressed, elated, euphoric (? appropriate)

**Mood disorder** diagnosis depends on:
• intensity and duration of mood disturbance
  • accompanying symptoms
    • degree to which it interferes with social
      and occupational functioning
Mood disorders: classification

- Mania
- Hypomania
- Normal
- Mild
- Moderate
- Severe
- Psychotic

Bipolar \(\leftrightarrow\) Unipolar

Reactive \(\longleftrightarrow\) Endogenous
Major Depressive Disorder

“indescribable”
“a despair beyond despair”
“grey drizzle of horror”

“torpid indifference”
“my mind was dissolving”

“the libido made an early exit”
“catatonic muteness”

“loss in all its manifestations”
“compelled to destroy themselves”

“those who are suffering a siege...they will pull through”
WHY DID I WASTE SO MUCH TIME?
I DIDN'T HAVE TO KNOW.
WHY SHOULD I BE MAKING MISTAKES AND WHERE DO I GO FROM HERE?
GOD KNOWS
Major Depressive Disorder

Core features (present for > 2 weeks)
- Pervasive low mood (diurnal variation)
- Anhedonia
- Anergia/ tiredness

Additional symptoms
- Insomnia, early morning wakening
- ↓ appetite, ↓ weight
- ↓ libido
- ↓ concentration
- Negative thoughts: hopeless, worthless, guilt, nihilism, passive death wish, suicidal
- Mood-congruent delusions & hallucinations
- Psychomotor retardation or agitation
- Stupor / catatonia
• **Epidemiology**
  - WHO: 2\textsuperscript{nd} most debilitating disorder by 2020
  - 15\% lifetime risk, M:F = 1:2, peaks late 20’s
  - 40-50\% heritability
  - 1-yr prevalence depressive episode = 3.2\%
  - Primary care = 5-10\%; Hospital = 10-14\%
  - Ireland: 300,000 per year; 6,000 hospitalisations
  - cost is 1\% of total European economy

• **Aetiology - multifactorial**
  - genetic (30-40\% heritability); gender
  - Neurochemical, e.g. neurotransmitters, endocrine
  - psychosocial, e.g. loss events, adverse childhood, isolation
Prognosis

• 25% recover, 50% recover but relapse, 25% chronic

• lifetime suicide risk of 6-10% in severe depression (i.e. 20 x general pop); 12-19% for those requiring hospitalisation

• Overall death rate is higher (SMR = 1.4-2.5): suicide, drug/alcohol, accidents, cardiovascular disease, etc

• Risk factor for dementia and stroke
Bipolar affective disorder

MOOD

TIME
Bipolar affective disorder

- **Mania** is sustained period of elevated, expansive or irritable mood

- **Hypomania** = happiness/zest in excess of normal; but usually unproductive; ↓concentration, distractible; no delusions

- **Clinical features:**
  - **Mood:** elation, irritability,
  - **Thought:** pressure of speech, racing thoughts, grandiosity, mood congruent delusion and hallucinations
  - **Behaviour:** disinhibition (financial, sexual), overactivity, reduced sleep
  - **Impairment** is substantial
Bipolar affective disorder

- **Classification**: bipolar I (mania ± depression)
  bipolar II (depression + hypomania)

- **Epidemiology**: 1% lifetime risk, M:F = 1:1, peaks early 20’s; 80% heritability (overlap with schizophrenia)

- **Aetiology**: genetic, neurochemical, puerperal trigger

- **Prognosis**: 90% have manic and/or depressive relapses
Treatment of severe depression

1) Biological

2) Psychological

3) Social
Treatments for depression

**Biological**

- *antidepressants*, e.g. TCAD (nortriptyline, lofepramine), SNRI (venlafaxine), SSRI (fluoxetine, sertraline), MAOI (phenelzine), RIMA (moclobemide), atypical (trazodone, mianserin), NaSSA (mirtazapine), NDRI (bupropion)

**indications**: depressive illness, relapse prevention

**side-effects**: anticholinergic & antiadrenergic (TCAD, MAOI), nausea & headache (SSRI), tyramine interaction aka “cheese effect” (MAOI), weight gain

**toxic side-effects**: cardiac arrhythmias, seizures
Treatments in Psychiatry

- **mood stabilizers**, e.g. lithium, carbamazepine, sodium valproate, lamotrigine

  *indications*: bipolar disorder, unipolar depression, mania, refractory depression

  *problems*: narrow therapeutic range for lithium, hypothyroid, renal function, tremor

-Antipsychotics

-Others, e.g. T3, L-tryptophan, St John’s wort
However...about 30% are treatment resistant.
STAR*D Programme

Remission

28%
18-30%
12-25%
7-14%

Treatment

- Citalopram
- Bupropion/ Venlafaxine/ Sertraline or +bupropion/ buspirone
- Mirtazapine/ nortriptyline or +lithium/T3
- MAOI or Mirtazepine+Venlafaxine
**Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis**

*The UK ECT Review Group*

Lancet 2003; 361: 799-808

**INTERPRETATION**

- ECT is an effective short-term treatment for depression
- probably more effective than drug therapy
- bilateral ECT is moderately more effective than unilateral ECT
- high dose ECT is more effective than low dose
- ECT remains an important treatment option for the management of severe depression

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**Figure 3: Effect of ECT versus pharmacotherapy on depressive symptoms**

Neuroanatomy of depression
Neuroanatomy of depression

STRESS!

IL-6 and pro-inflammatory cytokines raised in depression
Hippocampal neurogenesis

roles in dealing with novelty, complexity, adaptation and stress
BDNF protein levels in the hippocampus following ECS

n=6 per group,  *p<0.05, **p<0.01 compared to control and UBP groups.
Cell proliferation following ECS. BP treatment significantly increased the relative number of BrdU-labelled cells in the dentate gyrus compared to sham-treated control animals (p<0.05)
**Resilience**: an individual’s capacity to adapt effectively to significant adversity and return the body to equilibrium

**Mental capital**
= cognitive ability + learning efficiency + emotional intelligence + resilience

**Mental well-being**: the ability to develop potential, be productive and creative, build strong and positive relationships, contribute to your community
Summary

• Depression is common and is a major socioeconomic challenge

• Depression is readily treatable but many are tx-resistant and/or undertreated

• Understanding the biology of depression will lead to more specific treatments and better diagnosis

• Promoting resilience throughout life is essential for our well-being