

An Update on Depressive Disorders – 2008

**Mood Disorders Association
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Overview of Depression

- 1. One out of five Canadians; lifetime prevalence of major depression-8% (minor depression/dysthymia – 7%; bipolar I/II - ~2%)**
- 2. 1.4 million Canadians afflicted at any one time.**

Depressive disorders have a significant morbidity

- 1. \$83 billion in direct medical costs/\$25 billion in associated medical costs**
- 2. 1,000,000 person-years lost from work**
- 3. second leading medical cause of long term disability**
- 4. fourth leading cause of global burden of disease**

Mood Disorders and the Workplace

30% of disability claims in Canada (\$15-30 billion annually) due to mood disorders (second only to cardiovascular disease)...and increasing!

Mood Disorders and the Workplace

Absenteeism vs Presenteeism

Presenteeism (lost productivity while at work) – likely a more significant problem with mood disorders than previously recognized in Canada

Productivity loss from presenteeism due to depression is 4 hours/week while loss from absenteeism is but 1 hour/week (between \$6-60 billion loss per annum)!

Depression - Mortality

1. 4% of all depressives die by their own hands (i.e. **suicide**)
2. 66% of all suicides are preceded by depression
3. **Depression & cardiovascular disease:**
 - a. risk of MI (heart attack) 2-3 higher in major depression than the non depressed
 - b. depression is biggest risk factor for death after a heart attack

WHAT CAUSES DEPRESSION?

Causes of Depression

1. Genetics
2. Brain Chemical Changes
3. Environment/
Psychological Adversity
4. Personality/Temperament

Causes of Depression - Genetics

1. About “one third” of the ‘variance’ in major depression is related to hereditary factors (in bipolar illness it is likely “two thirds”)
2. What is inherited (e.g. brain biological changes, personality traits, etc) is yet to be determined.
3. Early-onset (before age 30), severe, recurrent depression more likely to have a ‘genetic’ basis.
4. No single gene but likely a complex multi-gene inheritance.

Causes of Depression – Personality/Temperament

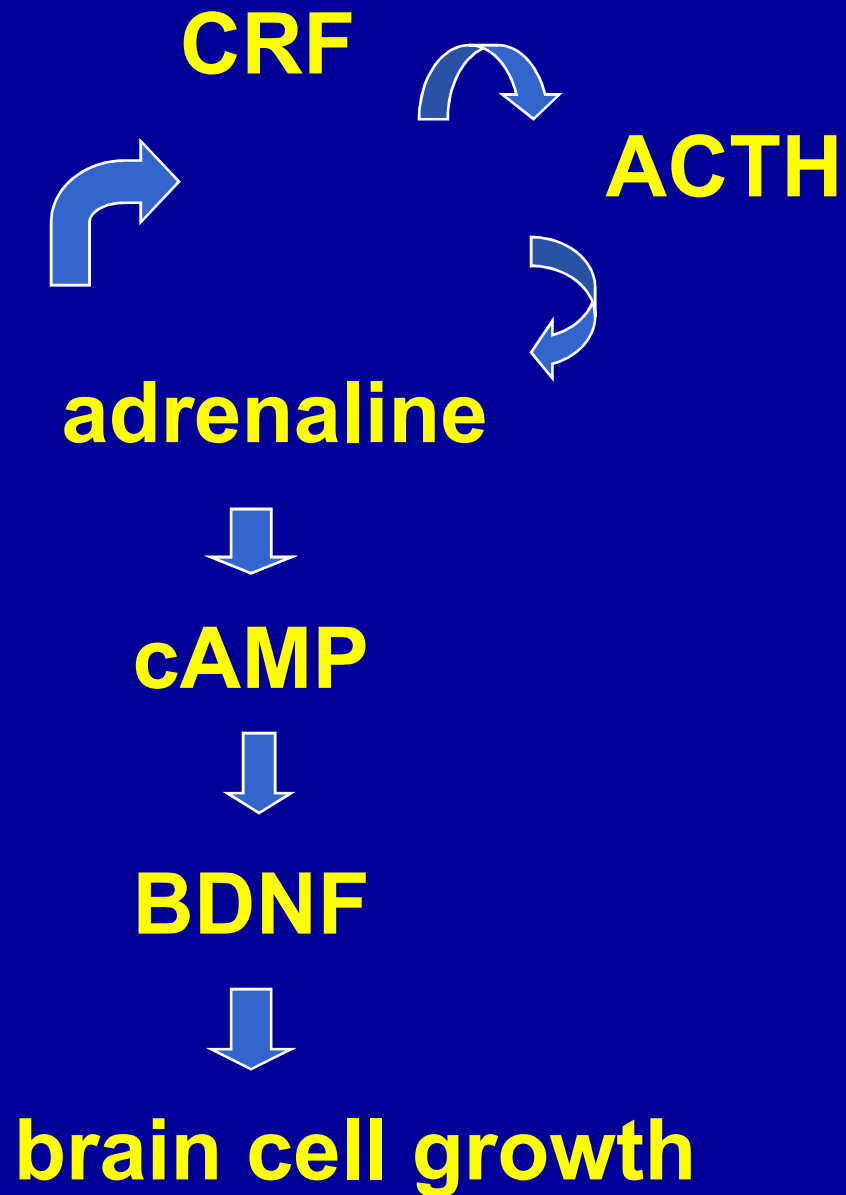
1. Individuals with the **normal** personality traits – avoidance of harm, anxiousness, and pessimism - are slightly more at risk to develop a depressive illness.
2. To a large degree, many personality traits are inherited.
3. How significant this ‘cause’ of depression is, and the relationship between genetics (nature) and/or the environment (nurture) remains unclear.

**Causes of Depression –
Environment/Psychological
Adversity**

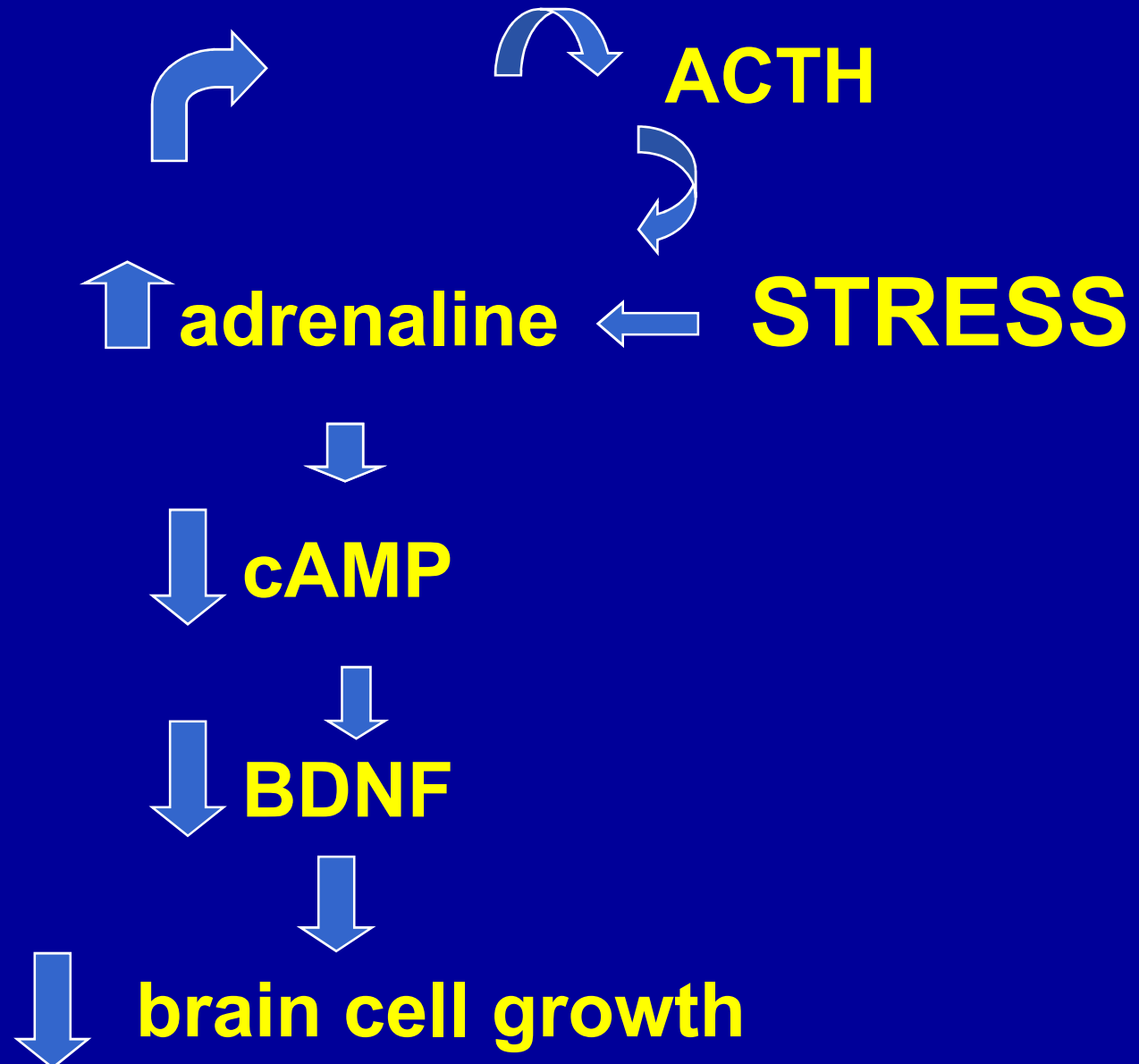
Psychological Stress

1. The effects of stress/adversity dependent:
 - a. the timing of the stressor (prenatal, postnatal, late life)
 - b. severity of the stressor
 - c. repetition of the stressor
2. Stress may be more important in :
 - a. the genetically vulnerable
 - b. lack of social support
3. Resiliency : genetic versus learning

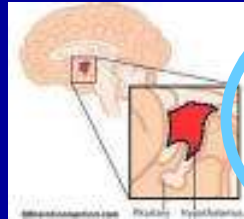
STRESS and the BRAIN :



STRESS and the BRAIN : CRF



Hypothalamus



CRF



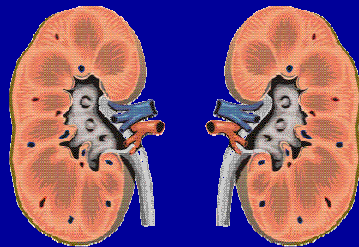
Pituitary



ACTH



Adrenal Cortex



Limbic System

Hippocampal Shrinkage

- Mood dysregulation
- Memory impairment

Apoptosis/neuron death

Cortisol + Adrenaline

New theories of depression

When 'stress' is induced in genetically vulnerable individuals this can lead to an increase or decrease in specific neurotransmitters

OR ...the above events may lead to a decrease in the production of BDNF which results in a cascade of brain effects in different brain areas leading to specific depressive symptoms

Causes of Depression – Brain Chemical Changes

Neuroanatomy in the 21st century

Different neuroanatomical areas are associated with different types of functioning:

emotional

cognitive

somatosensory

sleep

The neuroanatomy of : emotional functioning

BRAIN AREAS

medial prefrontal crtx

anterior cingulate gyrus

orbital prefrontal crtx

amygdala

nucleus acumbens

hypothalamus

FUNCTIONS

depressed mood, guilt,
anxiety, suicidality

as above

as above

loss of pleasure, guilt,
suicidality

as above

loss of pleasure

The neuroanatomy of : cognitive functioning

BRAIN AREAS

dorsolateral prefrontal cortex

hippocampus

amygdala, cerebellum,
frontal cortex

FUNCTIONS

concentration, mental
fatigue, executive
functioning

declarative (factual)
memory

procedural (e.g. riding
a bike) memory

The neuroanatomy of : somatosensory functioning

BRAIN AREA

hypothalamus

striatum

cerebellum

spinal cord

FUNCTIONS

weight change

physical fatigue

physical fatigue

physical fatigue, pain

The neuroanatomy of : sleep

BRAIN AREA

FUNCTION

hypothalamus

sleep

brain stem

sleep

Summary – Brain Chemistry and Psychological Functioning

1. Different brain areas have different functions and result in different symptoms.
2. Different brain areas receive projections from different neurotransmitters which turns on certain pathways and turns off other pathways.
3. “Symptoms” (e.g. pleasure, fatigue, sleep) may be the result of many different brain areas either being turned on or off.
4. Genes and/or ‘stress’ can either turn on or turn off different brain areas.

New theories of depression

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**How do we make a diagnosis
of a Major Depressive
Disorder?**

DSM IV – MOOD DISORDERS

DEPRESSIVE DISORDERS

296.xx Major Depressive Disorder

.2x Single Episode

.3x Recurrent Episode

300.4 Dysthymic Disorder

specify : early/late onset

specify : with atypical features

311 Depressive Disorder NOS

DSM IV : MOOD DISORDERS

BIPOLAR DISORDERS

296.xx Bipolar I Disorder

296.89 Bipolar II Disorder

301.13 Cyclothymic Disorder

296.80 Bipolar Disorder, NOS

293.83 Mood Disorder Due to ...

general medical condition

substance

abuse/withdrawal

296.90 Mood Disorder NOS

Major Depression vs. Dysthymic Disorder

Major Depression :

1. “depressed” mood and >4+ SIGECAPS
2. two week duration

Dysthymic Disorder :

1. “depressed” mood and 2 or 3 SIGECAPS
2. TWO YEAR duration

Detecting depression

1. Individuals at high risk : chronic insomnia or fatigue, chronic pain, multiple unexplained physical complaints, chronic medical illness (RA, DM), acute cardiac events, recent trauma, family history of depression, previous episodes
2. special population – children/adol- irritable mood; geriatric –grief; certain cultures- physical symptoms

Ask about depression:

1. Good screening questions:

a. “in the last month, have you been bothered by little interest or pleasure in doing things?”

b.”...what about feeling down, depressed or hopeless?”

c. **SIGECAPS**

2. Good screening questionnaire:

a. Patient Health Questionnaire(PHQ-9)

www.pfizer.com/PHQ/9

b. www.dbsalliance.org

Diagnosis of major depression

1. A distinct mood change (depressed, irritable, anxious, etc) for at least two weeks

2. Four or more SIGECAPS :

Sleep

Concentration

Interest

Appetite

Guilt

Psychemotor activity

Energy

Suicide

Collateral information and collaboration with family is paramount in the successful treatment of mood disorders.

SIGECAPS

- S** - insomnia/hypersomnia
- I** - interest decreased
- G** – guilt or self blame
- E** – energy loss or fatigue
- C** – concentration problems
- A** – change in appetite/weight
- P** – psychomotor
retardation/agitation
- S** – suicidal thoughts

What should I do if I think my loved one is depressed?

1. Do not minimize or “psychologically” explain it away.
2. Do not be afraid to ask about suicide (this NEVER causes suicidality!).
3. Get back up/confirmation from friends/family.
4. Go with your loved one to your family doctor.

Depression – The Good News

1. Expect full recovery (with treatment) in 65%.
2. Expect marked improvement in 25%.
3. Less than 10% have a protracted chronic course of illness

Treatment of Major Depressive Disorder

Treatment of Major Depressive Disorders

1. **Psychological Treatment** – Cognitive Behavioral Therapy (CBT)

2. **Biological Treatments**

a. antidepressants (26 choices)

b. augmentation of the antidepressant (four choices)

c. electroconvulsive therapy (ECT)

d. others (phototherapy/SAD light, TMS, vagal nerve stimulation, DBS)

Cognitive Behavioral Therapy (CBT)

1. The evidence based psychotherapies (CBT – cognitive behavioral therapy) are **AS EFFECTIVE** as antidepressants in mild/moderate MDD.
2. Cognitive therapy (CBT) is accessible in British Columbia.

Cognitive Behavioral Therapy

CBT response rate(8-12 weekly sessions) – 65%

Core features:

- a. identify automatic maladaptive thoughts and distorted beliefs that lead to depressive moods
- b. learn strategies to modify these beliefs and practice adaptive thinking patterns
- c. use a systematic approach to reinforce positive coping behaviors

Cognitive Behavioral Therapy

CBT is accessible:

a. private psychologist (not covered by medical insurance)

b. Changeways (www.changeways.com) - a group based CBT program offered at many hospitals/mental health centers throughout BC (free – covered by medical insurance)

c. www.carmha.ca/publications - 'anti-depressant skills workbook' (free download)- an outstanding self directed CBT workbook

Antidepressants

1. Antidepressants are also first line treatment for MDD, especially if moderate/severe intensity
2. So many choices!! (>20 meds):
 - a. all are equally effective
 - b. no antidepressant has faster onset of action

Antidepressants

A doctor should choose a specific antidepressant based on :

- a. his/your comfort/familiarity level
- b. your previous good/poor response
- c. side effects
- d. cost
- e. drug-drug interactions
- f. co morbid conditions

Antidepressants

First line

usual dose/d

SSRI

escitalopram (Cipralext)	10-20mg
citalopram (Celexa)	20-60mg
fluoxetine (Prozac)	20-60mg
fluvoxamine (Luvox)	100-250 mg
paroxetine (Paxil)	20-60mg
sertraline (Zoloft)	100-250mg

RIMA

moclobemide (Manerix)	300-600 mg
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Antidepressants

First line

usual dose/d

SNRI :

venlafaxine (Effexor)

75-300mg

duloxetine (Cymbalta)

20-60mg

novel action :

bupropion (Wellbutrin)

150-450mg

mirtazapine (Remeron)

30-60mg

nefazodone (Serzone) – no longer available
in BC

Antidepressants – What you need to know

- antidepressants are not addictive
- take the medicine every day
- it may take 2-4 weeks before you notice improvement
- mild side effects are common, but usually temporary
- do not stop meds even if feeling better
- call doctor if any questions

Antidepressants – What you need to know

- “outer changes” (physical symptoms) improve before “inner changes” (psychological symptoms) so your loved one will likely notice improvement before you do
- “improvement” is a ‘saw tooth curve’ (e.g. you may have a few good days, then a ‘bad’ day, then another few good days, etc) so measure your improvement weekly, not daily

Antidepressant Response

1. typical trajectory of response :
 - a. initial mild symptom improvement in 2-4 weeks
 - b. good clinical response in 4-8 weeks
 - c. remission of symptoms (SIGECAPS) by 8-12 weeks
2. remission of symptoms realistic goal by 12 weeks in 65% of patients; recovery to baseline function may take longer

What should you do if you are not improving on an antidepressant?

1. If no response (e.g. <math>< 20\%</math> improved) after 3-4 weeks, then raise the dose incrementally every week to the maximum tolerated
2. If still no response the doctor and you should re-evaluate diagnostic issues (bipolar, medical/psych co morbidity, substance abuse, personality disorder)

What should you do if you are not improving on an antidepressant?

2. b. Reassess treatment issues
(compliance, side effects)

c. Consider **SWITCH** (if < “30%”
response) to different drug (another SSRI
or different class) or

AUGMENT (if > “30%” response)

Antidepressant Augmentation

rationale – 30% response in 2 weeks

a. lithium 150mg x 5day and increase to 300mg for 5day, and then 450mg for 10day trial

b. Cytomel (thyroid) 25ugm for 5day, then 50ugm for 10day trial

c. dextroamphetamine 2.5-5mg for 3 days, then increase by 2.5-5mg every 3day to max 15mg for 7d trial

d. olanzapine (Zyprexa)- At this time, I do **not** recommend

Maintenance antidepressant treatment

Once you are better:

1. continue antidepressants at least six months
2. consider longer (2years to indefinite) treatment:
 - a. chronic (>2 yr duration) depression
 - b. frequent(>2 episodes/5yr) episodes
 - c. age >50
 - d. severe (suicidality/psychosis) episodes

Other Treatments for Major Depressive Disorders

- 1. electroconvulsive therapy (ECT)**
- 2. phototherapy (light box)**
- 3. Transcranial magnetic stimulation(TMS)**
- 4. vagal nerve stimulation (VNS)**
- 5. deep brain stimulation (DBS)**

What is a mood swing?

1. distinguish a mood state from a mood state with concurrent additional symptoms (i.e. a diagnosable syndrome)
2. distinguish whether there is a diagnosis that is either subsyndromal or syndromal in duration and intensity

Depressive Temperament vs. Medical Syndrome

1. The diagnosis of a mood disorder is risky at best without collateral information.
2. A diagnosis of a mood disorder is a constellation of symptoms not just a mood state.
3. A diagnosis of a mood disorder requires a minimum duration of persistent symptoms.
4. A DSM IV diagnosis requires significant distress or impairment.

Depressive Temperament vs. Medical Syndrome

1. Not all people are happy all the time...actual very few are!
2. Dysthymia can be effectively treated (60% respond to cognitive therapy-CBT; 60% respond to antidepressants-AD).
3. Obsessive compulsive disorder (OCD) and obsessive personalities with their serious, somber demeanor are often misdiagnosed as having a mood disorder.

Depressive Temperament vs. Medical Syndrome

4. Borderline personality disorder (BPD) (affective instability with reactivity of mood with intense dysphoria, irritability, anxiety; chronic feelings of loneliness; excessive inappropriate anger; impulsive suicide attempts) : the key to the differential diagnosis is BPD mood swings lasts hours, rarely days.

A few topical issues in mood disorders today

1. antidepressants and an increase in suicidality
2. antidepressants are no more effective than a placebo

antidepressants and an increase in suicidality

1. There is likely an increase in suicidal ideation, in 1-3% of individuals (particularly adolescents) prescribed antidepressants
2. In 2004 health Canada issued such a 'black box' warning on most antidepressants.
3. A recent Manitoba study : in 2005
 - a. 14% decrease in antidepressant prescriptions
 - b. a 25% increase in completed suicides!

antidepressants are no more effective than a placebo

1. a recent research study suggested these findings and received a great deal of coverage in the lay press
2. However, the findings have been criticized by most researchers for:
 - a. including all types of 'depression' in their findings (i.e. not just major depressive disorders)
 - b. using a very 'unusual' study design to determine drug response and no response

SUMMARY

1. Depression is a very common medical disorder with significant morbidity and mortality risks.
2. There is increasing research and understanding of the psychological and biological factors that trigger the onset and lead to the ongoing course of depressive disorders.

SUMMARY

3. Nearly 90% of individuals suffering from a major depressive disorder can expect significant if not full recovery with a variety of psychological and biological treatment interventions.

4. **Be informed.**

5. **Get help!**

Resources

The Mood Disorders Association of BC offers:

- Over 65 General and Special Interest Support groups throughout BC
- Support and information via our website at: www.mdabc.net
- A weekly walk-in psychiatric clinic
- For more information about the Mood Disorders Association of BC call our office at 604.873.0103