

## Risk Factors for Major Depressive Disorder

*Age, Sex, Genetics, Culture and Environment*

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## A Century of Mental Health



**Social Psychiatry and  
Early Therapeutics**



- Dilworth Wayne Wooley**
- Graduate of University of Alberta
  - Influenced by LSD research
  - Proposed role for serotonin in Mental illness (1954)
  - Blind at early age from diabetes
  - Died aged 52 while climbing the Andes

**The Monoamine Story**



Influence of life stress on  
depression: moderation by a  
polymorphism of the serotonin  
transporter

(Caspi et al, Science 2003)

**The Gene-Environment Era**



**Diagnostics**

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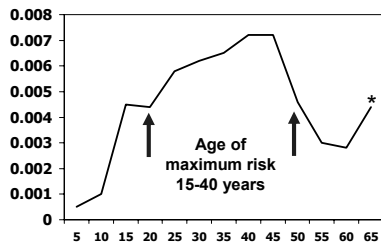
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## Hazard Rates of Major Depressive Disorder by Age



\* Data on first episode depression after 65 years are inconsistent

Hasin et al, 2005

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## Sex and Age in Depression

- Prepubescent boys and girls have comparable rates of depression
- From adolescence through midlife, women have twice the prevalence of depression compared to men
- Marriage has a protective effect for men but not women
- Comorbid Anxiety Disorders and Seasonal Depression are three times more prevalent in women
- Claims for differential pharmacotherapy responses are inconsistent

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## Genetic Factors in Depression

- Genetic factors account for 50% of the variance in the transmission of depression
- Children of depressed parents are 3 times more likely to develop a depressive episode than children of non-depressed parents
- Familial transmission does not necessarily stem from genetic mediation
- Temperamental factors can mediate the genetic risk of depression

### Candidate Genes

- Serotonin
  - Tyrosine hydroxylase
  - Serotonin transporter
  - Various Serotonin Receptors
- Norepinephrine/Dopamine
  - $\alpha_1$ , implicated in childhood depression
  - Catechol-O-methyltransferase
- Glutamate
  - NMDA receptor abnormality
- Brain Derived Neurotrophic Factor
  - Chromosome 11 (working memory as a marker)

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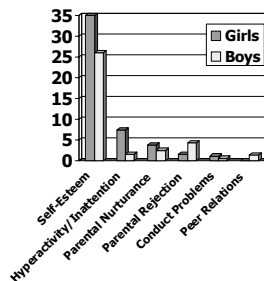
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## Risk factors for Depression in Early Adolescence

- Over 2000 boys and girls in 12-13 age range from 10 Canadian provinces were selected from the National Longitudinal Survey of Children and Youth (Stats Canada, 1999)
- Nine predictor variables from the literature were evaluated
- No data available on parental depression or independent negative life events
- Low self-esteem emerged as the strongest risk factor for both boys and girls



MacPhee and Andrews 2006; University of Calgary

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## Serotonin Transporter (SERT) Polymorphisms and Depression

### SERT polymorphism and Depression

- Individual Differences in Genetic Coding for SERT
  - Short (s) and Long (l) carriers
  - s/s and s/l genotypes are associated with reduced transcription of SERT gene and reduced 5HT uptake



### SERT polymorphism and Early Life Stress

- Short allele carriers subjected to stressful life events have:
  - More depressive symptoms and suicidality (Caspi et al, 2003)
  - More likelihood of developing depression within 2 months (Kendler et al, 2005)

## Social Origins of Depression

- Lack of confiding relationships
- Death of a parent during childhood
- Three or more young children in household
- Absence of paid employment

(Brown & Harris, 1978)

### Depression and Serotonin Transporter Polymorphism: Gene X Environment Interaction

- Examination of Early Childhood Trauma and Recent Life Events
- Childhood maltreatment is associated with high risk of adult depression and chronic course
- Life Events occurring not long before onset of depressive episode confer little risk

(Brown & Harris, 2008)

## The cultural shaping of depression: somatic symptoms in China, psychological symptoms in North America?

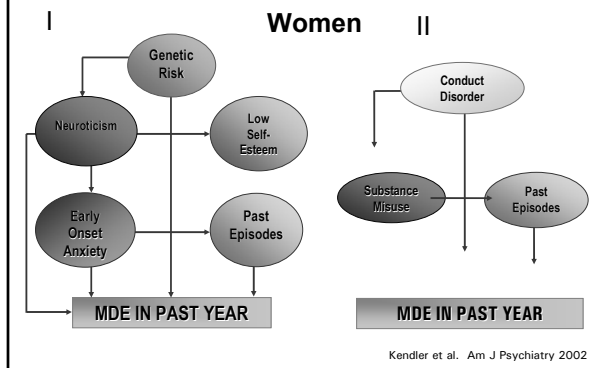
The authors examined symptom presentation in Chinese (n=175) and Euro-Canadian (n=107) outpatients, using spontaneous problem report, structured clinical interview, and symptom questionnaire methods.

**Chinese outpatients reported more somatic symptoms on spontaneous problem report and structured clinical interview compared with Euro-Canadians, who in turn reported more psychological symptoms**

These results suggest that Western psychologization may be more culturally specific than is Chinese somatization.

Ryder AG, Yang J, Zhu X, Yao S, Yi J, Heine SJ, Bagby RM. Department of Psychology, Concordia University, Montréal, Québec.

## Internalizing and Externalizing Pathways




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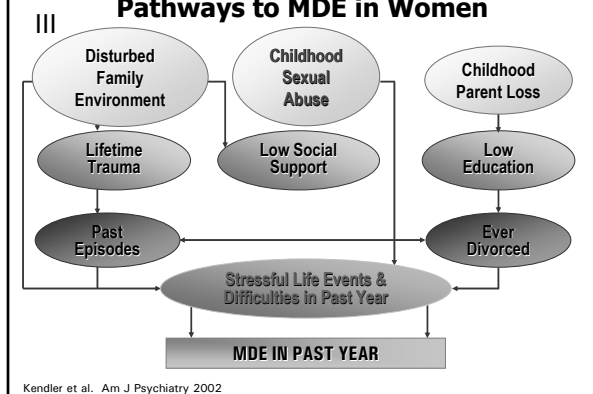
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## Adversity/Interpersonal Difficulties Pathways to MDE in Women




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## Shared Diathesis Model: Diabetes and Depression

- 20 studies on the prevalence of depression in adolescent, adult and older diabetic patients in the past decade
- Significant depressive symptoms in 32.4% of diabetic patients
- < 50% of adolescents with diabetes received treatment for depressive episodes
- Female adolescents with diabetes were at much higher risk for recurrent depressive episodes

Gavard et al (1993)

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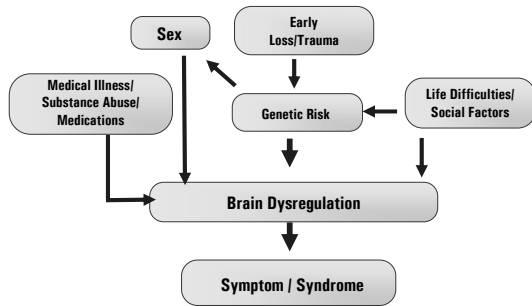
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## Interactions among Risk Factors for Depression



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