Chapter 7 & 3 (gene environment interaction) Caspi (2003)
We will go over this in class.

Depression is among the top five leading causes of disability and disease burden throughout the world. Across the life span, stressful life events that involve threat, loss, humiliation, or defeat influence the onset and course of depression. However, not all people who encounter a stressful life experience succumb to its depressogenic effect. Diathesis-stress theories of depression predict that individuals' sensitivity to stressful events depends on their genetic make-up . Behavioral genetics research supports this prediction, documenting that the risk of depression after a stressful event is elevated among people who are at high genetic risk and diminished among those at low genetic risk.

(How could we tell if someone was at high or low genetic risk?)

However, whether specific genes exacerbate or buffer the effect of stressful life events on depression is unknown. In this study, a functional polymorphism in the promoter region of the serotonin transporter gene (*SLC6A4*) was used to characterize genetic vulnerability to depression and to test whether 5-HTT gene variation moderates the influence of life stress on depression.

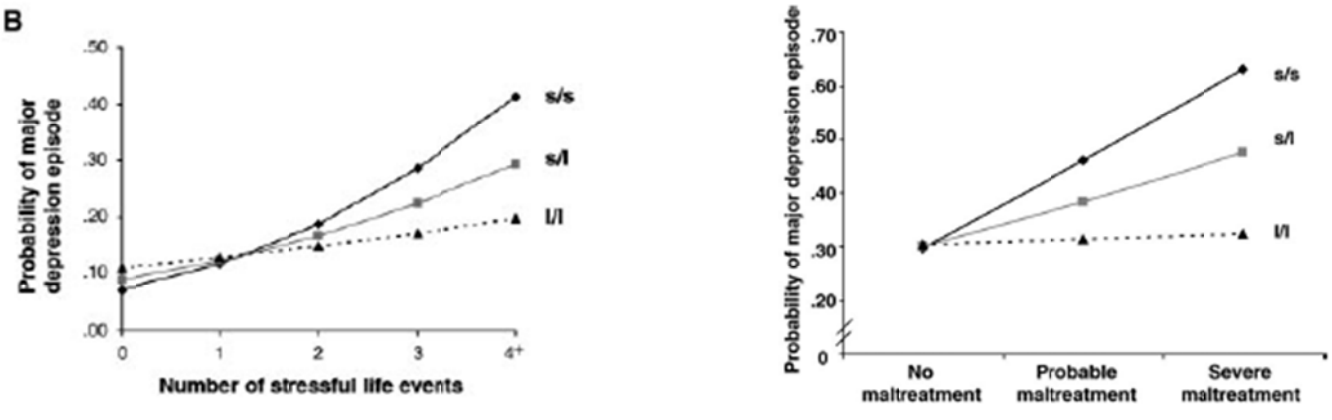
The serotonin system provides a logical source of candidate genes for depression, be cause this system is the target of selective serotonin reuptake–inhibitor drugs that are effective in treating depression. The serotonin transporter has received particular attention because it is involved in the reuptake of serotonin at brain synapses. The short ("s") allele in the 5-HTTLPR is associated with lower transcriptional efficiency of the promoter compared with the long ("l") allele.

(The authors provide evidence that the long/short alleles have something to do with risk for stress in rats, monkeys, and humans.)

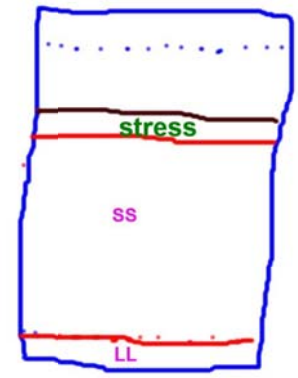
A representative birth cohort of 1037 children (52% male) has been assessed at ages 3, 5, 7, 9, 11, 13, 15, 18, and 21 and was virtually intact (96%) at the age of 26 years. Stressful life events occurring after the 21st birthday and before the 26th birthday were assessed with the aid of a life-history calendar.

Study members were assessed for past-year depression at age 26 with the use of the Diagnostic Interview Schedule, which yields a quantitative measure of depressive symptoms and a categorical diagnosis of a major depressive episode according to *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV).

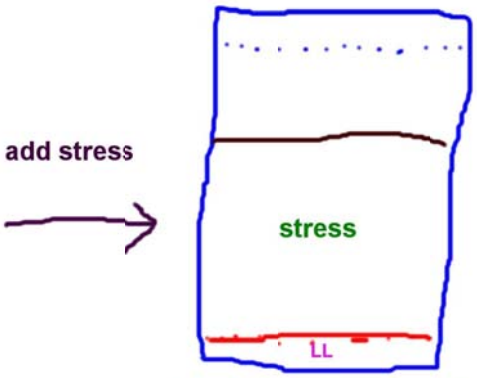
The G x E interaction showed that stressful life events predicted a diagnosis of major depression among carriers of an s allele but not among l/l homozygotes ($P = 0.056$, Fig. 1B).



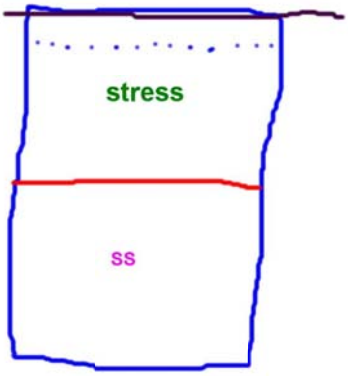
Caspi as a Diathesis-Stress Model



even with bad genes (ss) small stess isn't enough for depression



big stress? No depression if good genes



but big stress AND bad genes is over the line