Why are there such large differences in boys' and girls' rates of emotional and behavioural disorders – and why does it matter?

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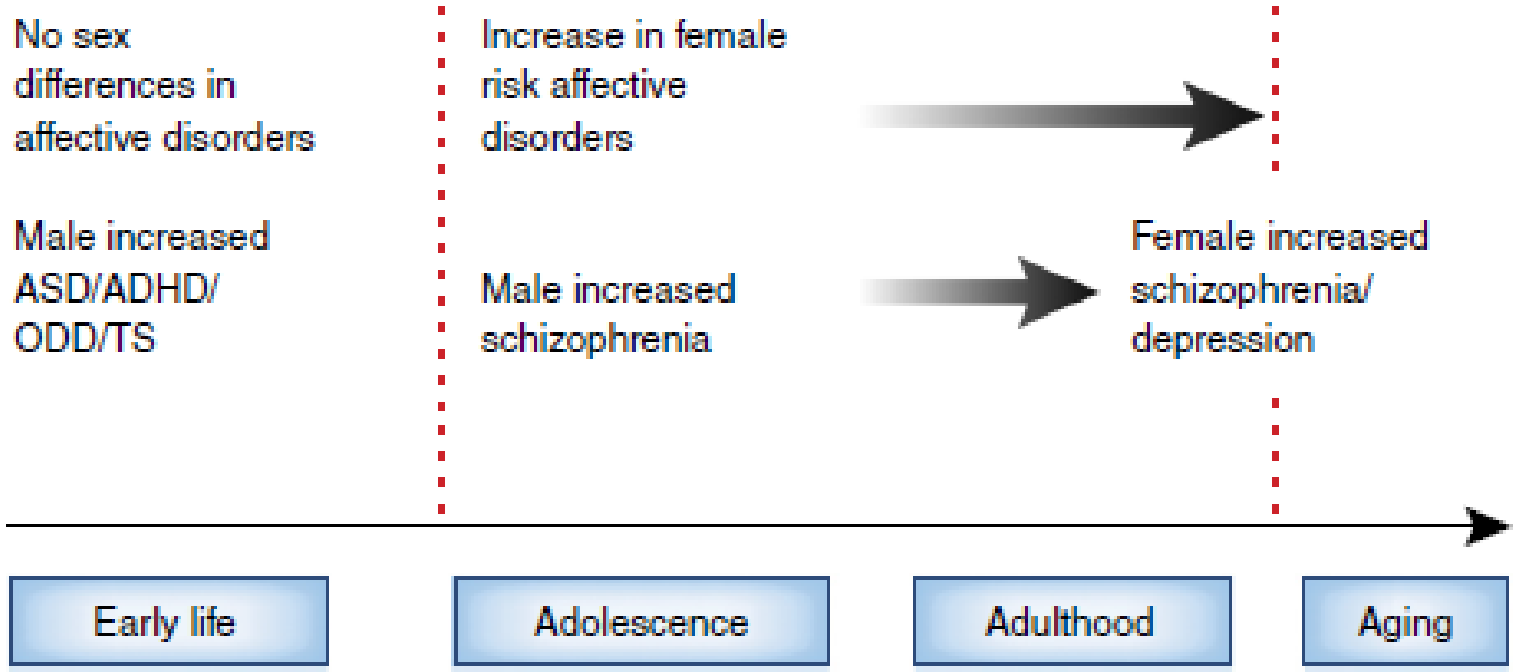
Sex differences in stress-related disorders across the lifespan



Bale & Epperson, 2015

Sex/gender differences in rates of psychiatric disorders

Male preponderance 1.5:1 - 5:1	Female preponderance 1.5:1 - 3:1
Autism spectrum disorders ADHD Dyslexia Tourette syndrome Early onset conduct problems ODD Developmental language disorders	Depression Eating disorders Anxiety
Early onset **Neurodevelopmental impairments**	**Adolescent onset**

Also some sex/gender differences in

developmental course
recurrence
comorbidities
long-term outcomes

Questions

- real differences, that might hold important clues for aetiology?
- partly reflect differing expectations/biases re behaviour of boys and girls?
- some children with serious problems going unrecognized and untreated?

Across disorders, concerns re whether

- diagnostic criteria are equally valid for males and females
- behavioural definitions might be biased towards features more characteristic of one sex
- parents/teachers 'interpret' some behaviours differently in boys and girls
- the sexes differ in willingness to report some types of symptoms

And as a by-product

- impact on research samples (and findings…) in some areas
  - ASD: brain imaging studies: ~8:1 males : females

Why *might* rates of disorders vary so markedly between boys and girls?

- same/different risk factors for girls and boys?
- one sex more exposed - or more vulnerable - to those risks?
- one sex protected/buffered in some ways?
- might same factor work in different ways in boys and girls?

Why *might* rates of disorders vary so markedly between boys and girls?

Levels of explanation

- **Genetic influences: sex chromosomes**
- **Consequences of being male or female – including*:***
  - *slower rate of biological maturation in males*
  - *increased vulnerability to insults*
  - *variations in prenatal hormone production: organizational effects on brain development*
  - *pubertal variations in sex hormone production: activational effects on brain*
  - *culturally-influenced variations in life-styles*
- **Proximal risk/protective factors**
  - *variations in temperament/personality features that predispose to disorder*
  - *variations in **exposure** to 'risky' environments*
  - *variations in **susceptibility** to risky environments*

Rutter, Caspi & Moffitt, 2003

Emphasizes

- wide range of processes that might be implicated
  - genetic, epigenetic, hormonal, neuronal, psychological, social/cultural
- need for developmental perspective
- need to begin with influences very early in development

Methodologically

- does factor X vary between males and females?
- does factor X predict outcome?
- does including factor X in analyses affect estimates of gender difference?

Autism spectrum disorder

- male: female ratio 2-5:1
- early onset (age at diagnosis typically later in girls)
- heritability high
- interest in genetic influences
  - *male-specific risks via Y-chromosome genes (eg SRY)*
  - *female-specific protections from increased X-chromosome gene dosage*
  - *associated epigenetic mechanisms*

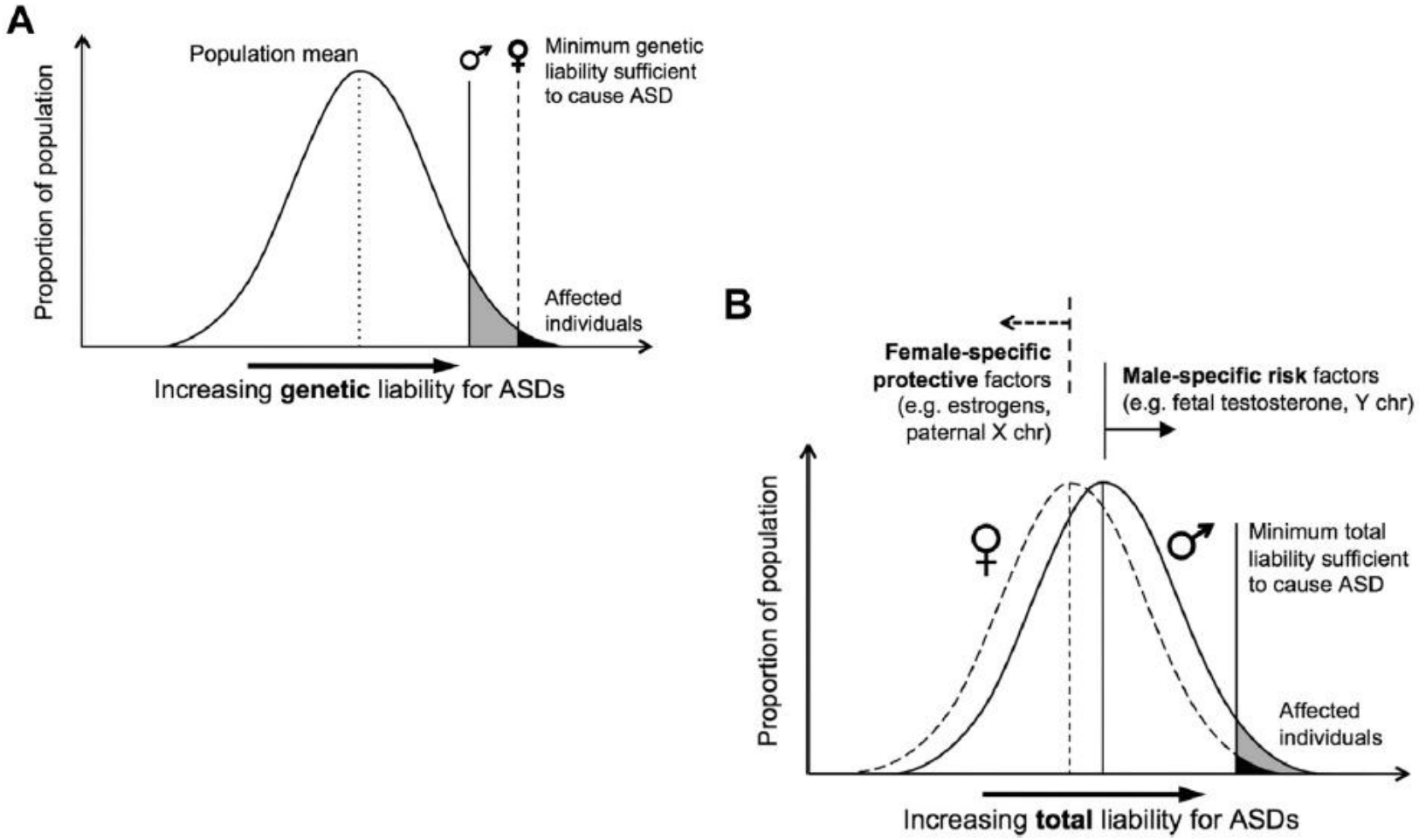
but

- sex chromosome genes unlikely to account for major proportion of effects

- possible sex differences from more general aetiological models

Lai et al, 2015

Multi-factorial multi-threshold vs sex/gender-differential liability models



Lai et al, 2015

Autism spectrum disorder

- *pre- and perinatal environmental mechanisms*
  - pre-natal androgen exposure
  - pre-natal testosterone predicts cognitive/behavioural characteristics related to autism in typically developing samples
  - maternal immune activation: possible joint effects of hormonal and maternal-immunological factors
- *possible social/cultural mechanisms*
  - culturally-influenced gender role expectations may impact definition and recognition
  - ? protective effects from increased opportunities for reciprocal social interaction for girls
  - developmentally, social influences on how individuals maintain/modify autism-related characteristics over time

Lai et al, 2015

Depression

- rates low, and similar/slightly higher in boys pre-puberty
- early adolescence: marked rise in girls: ~2:1 ratios in adolescence and adulthood worldwide
- difference mainly affects first onset
- heritability 30-40%
  - *no evidence for female-specific susceptibility genes on X-chromosome*
  - *GWAS-related findings similar for men and women*
  - *GxE (individual susceptibility to stress moderated by genetic factors): some evidence for stronger effects in women*
- pre-natal influences
  - *androgen exposure may contribute to protective effects in males (negative response bias in affective tasks)*
  - *maternal stress later in pregnancy: increased risk of internalizing symptoms in girls*
  - *low birthweight (ie sub-optimal intrauterine environment): increased risk of depression in girls post-puberty*

Altemus et al, 2014; Kuehner, 2017

Depression

Puberty

- dramatic increase in androgens in males, oestrogens in females
- timing of puberty more responsive to adversity (eg poor parent-child relationships, CSA) in girls
- more advanced pubertal stage and early maturation associated with increased risk of depression (and conduct problems) in girls
  - *? direct effect of hormone exposure*
  - *? indirect effects via eg hormonally-induced body changes*
- sex differences in HPA axis activation start in adolescence
- men typically show larger physiological responses to variety of stressors – including greater HPA axis activation
- oestrogen can exert activating or blunting effects on HPA axis
  - *evolutionary hypothesis for attenuated stress response in women: pressure to protect foetus from adverse effects of stress*
  - *could confer risk for depression*

Depression

Temperament, personality, coping styles

From early childhood, consistent sex differences in:

- *effortful control* (girls better able to regulate attention and inhibit impulses)
- girls: more *fearful and anxious*
- girls: higher levels traits indicating *interpersonal orientation – empathy and prosociality, agreeableness and warmth*

Later in development

- negative affectivity and *neuroticism* similar in childhood, increase more markedly in girls in adolescence (NB: magnitude of gender gap in neuroticism varies between cultures – highest in developed countries)
- self-cognitions: boys: higher *self-esteem* from adolescence
- *body shame and dissatisfaction*: evidence for some mediation of gender difference
- *ruminative response style* predicts depressive symptoms and interacts with stress; gender gap higher in adolescence than childhood or adulthood
- *coping styles*: under threat, men tend to escape/take action, women express affiliative behaviours and seek support from others (cultural variations in size of gender difference)

Depression

Exposure to stress and adversity

- CSA more common in girls
  - *increased risks of depression, anxiety, inflammatory illnesses*
  - *often occurs in context of other childhood adversities*
  - *women report higher levels exposure to multiple childhood adversities*
  - *increased risk for re-victimization and adult sexual abuse*
- Adolescence
  - *girls have greater number of interpersonal stressors, and more susceptible to them, than boys*
- Adulthood: gender-specific stressors contribute to depression risk
  - *women: interpersonal stress and absence of social support*
  - *men: work-related, financial, legal problems*
- Macro-level factors
  - *structural gender equality (eg opportunities for political participation, economic autonomy, reproductive rights) associated with gender ratio in depression*

Why *might* rates of disorders vary so markedly between boys and girls?

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Why does it matter…?

- because it is one of the most widely observed and consistently reported findings in our field
- because it challenges us to think hard about
  - *diagnostic assessment criteria and methods*
  - *diagnostic decision-making*
  - *aetiological factors*
  - *how best to design appropriate treatments/interventions*
  - *how best to design research studies*