

# How neuroscience is helping to motivate a preventative psychiatry approach

Latent vulnerability and the impact of childhood maltreatment

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*June 2019*



Adversity ⚡

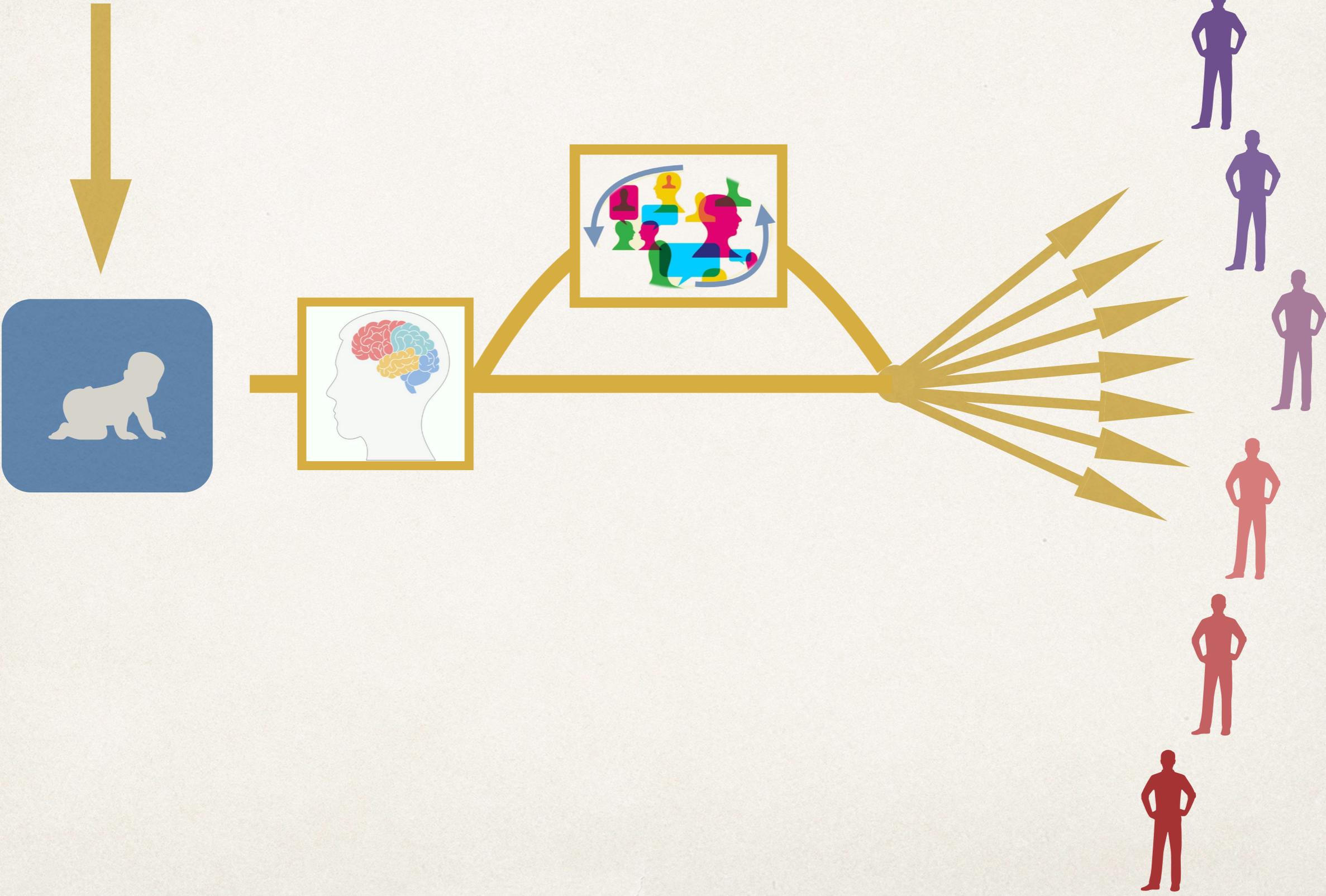
Outcome



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# Stressor Event ⚡





**How does vulnerability unfold?**

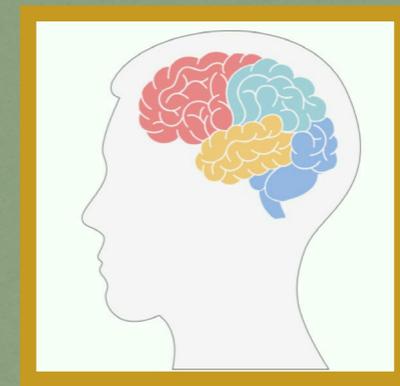
**Dangerous / Unpredictable Environment** ⚡



**Neuro-cognitive Adaptation**



**Normative / Predictable Environment**



**Mismatch / Poor Optimization**

# Latent Vulnerability *McCrary & Viding, 2015*

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- ❖ It is proposed that an array of biological and neuro-cognitive systems adapt to early adverse or neglectful environments in line with the notion of experiential canalization
- ❖ Such adaptations may confer short-term functional advantages in atypical early environments but compromise the ability of the individual to negotiate more normative contexts as well as future stressor events
- ❖ These adaptations may index latent vulnerability such that they can be shown to predict future psychiatric risk before a disorder emerges.
- ❖ We see altered neuro-cognitive function in children exposed to maltreatment, similar to that seen in clinical samples, even in the absence of concurrent psychiatric disorder.
- ❖ However, it is important to note that the ABSENCE of expected inputs associated with neglect can lead to non-optimal development of brain function that confer no adaptive value.

# The impact of neglect *Puetz et al., PsychMed, in press*

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- ❖ Does **abuse** (e.g. physical, emotional and sexual abuse) and **neglect** (physical and emotional deprivation) have different effects of brain function (threat processing)?
- ❖ Four groups of young adults, retrospective report, propensity score matched (PSM) on gender, age, IQ, psychopathology and SES:
  - abuse experiences only ( $n=70$ )
  - neglect experiences only ( $n=87$ )
  - abuse and neglect experiences ( $n=50$ )
  - no maltreatment ( $n=207$ )
- ❖ Experiences of neglect only, were associated with heightened reactivity in a **broadly distributed cortical fronto-parietal network** supporting complex social and cognitive processing as well as in the dorsal amygdala.

# Neuro-cognitive Adaptation

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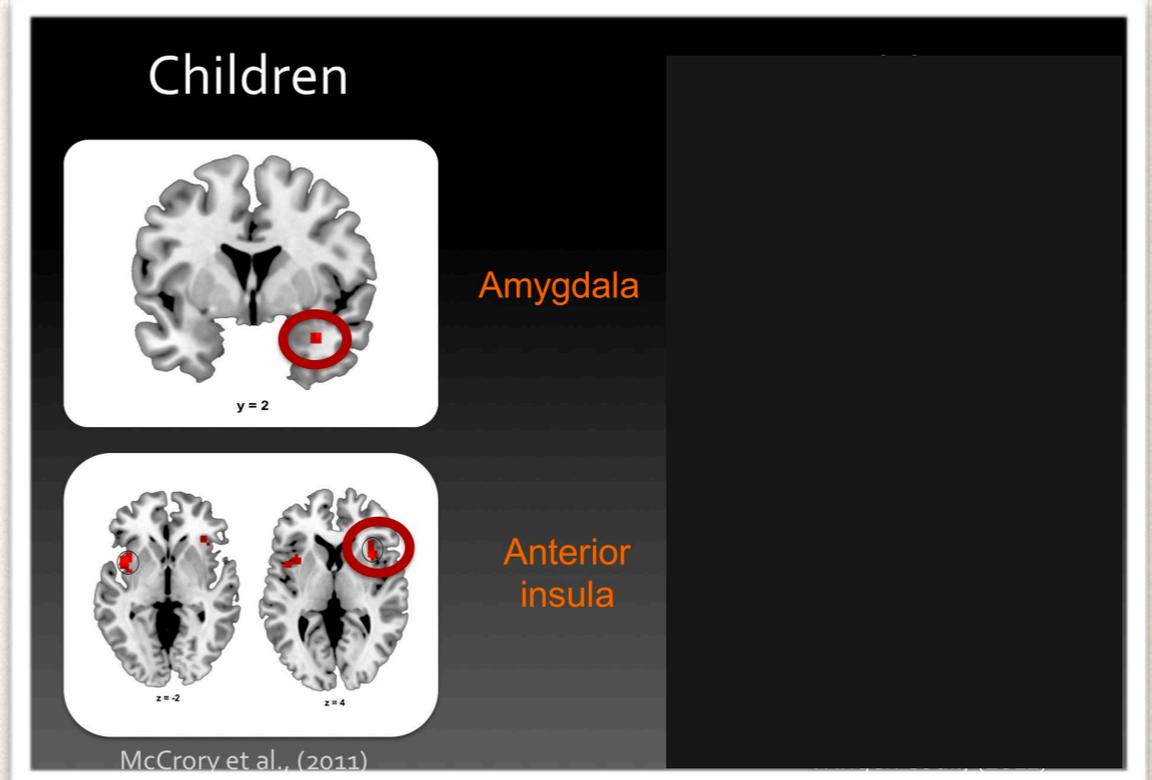
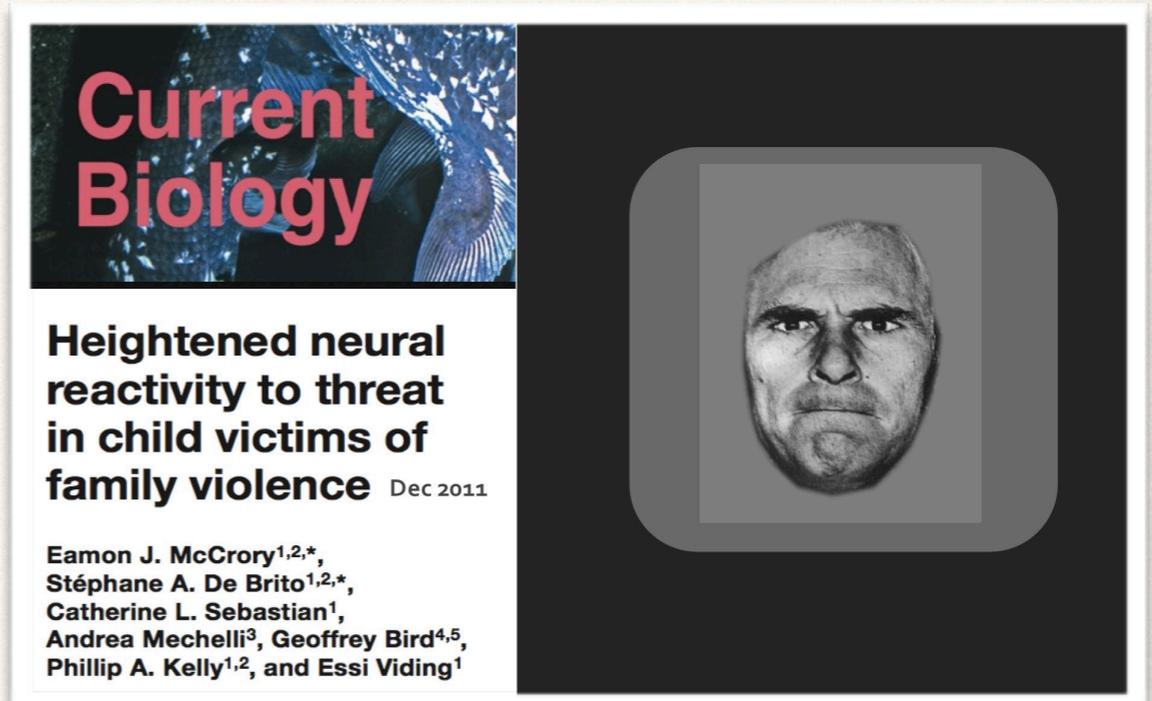
- ❖ Childhood maltreatment has been associated with altered functioning in a number of neuro-cognitive systems:
  - ❖ Threat processing
  - ❖ Memory processing
  - ❖ Reward processing
  - ❖ Emotion regulation
  
- ❖ See McCrory et al., 2017 *Journal of Child Psychology and Psychiatry* for a recent review



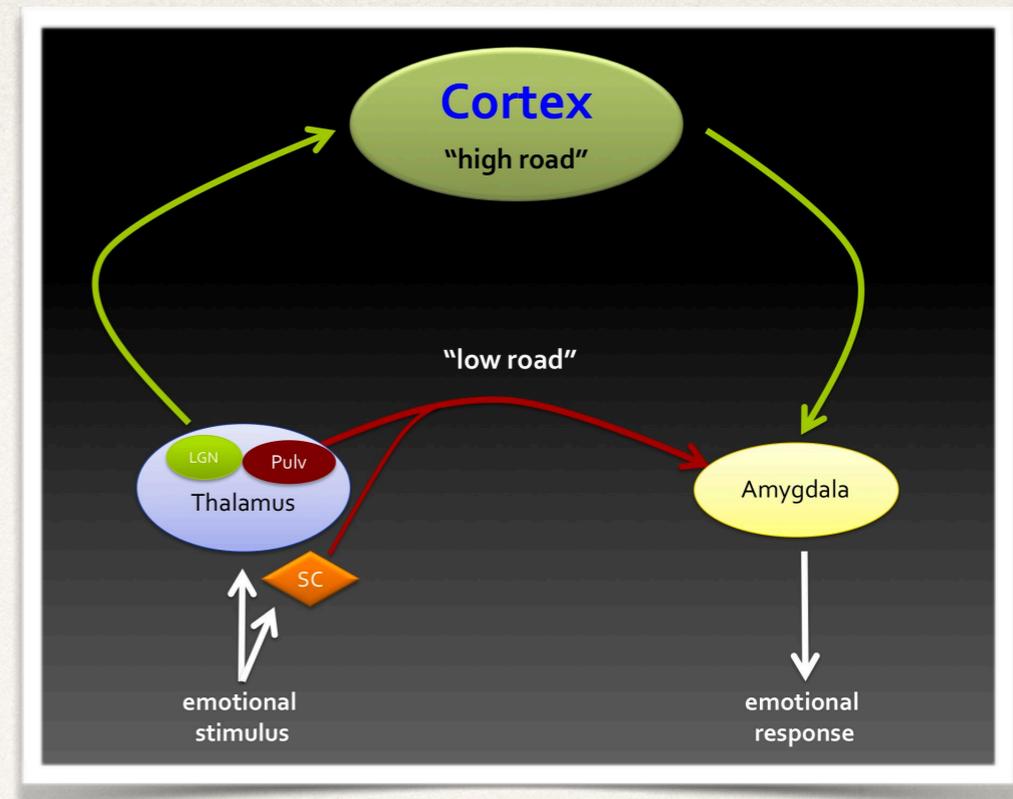


# Threat Processing

- ❖ In children exposed to physical abuse and domestic violence: amygdala and anterior insula activation - similar to what is observed in soldiers before and after combat (McCrorry et al., 2011; Van Wingen et al., 2011).
- ❖ A recent **meta-analysis** found reliable evidence of increased amygdala activation associated with maltreatment, as well as the parahippocampal gyrus and insula (Hein & Monk, 2017).



# Threat Processing



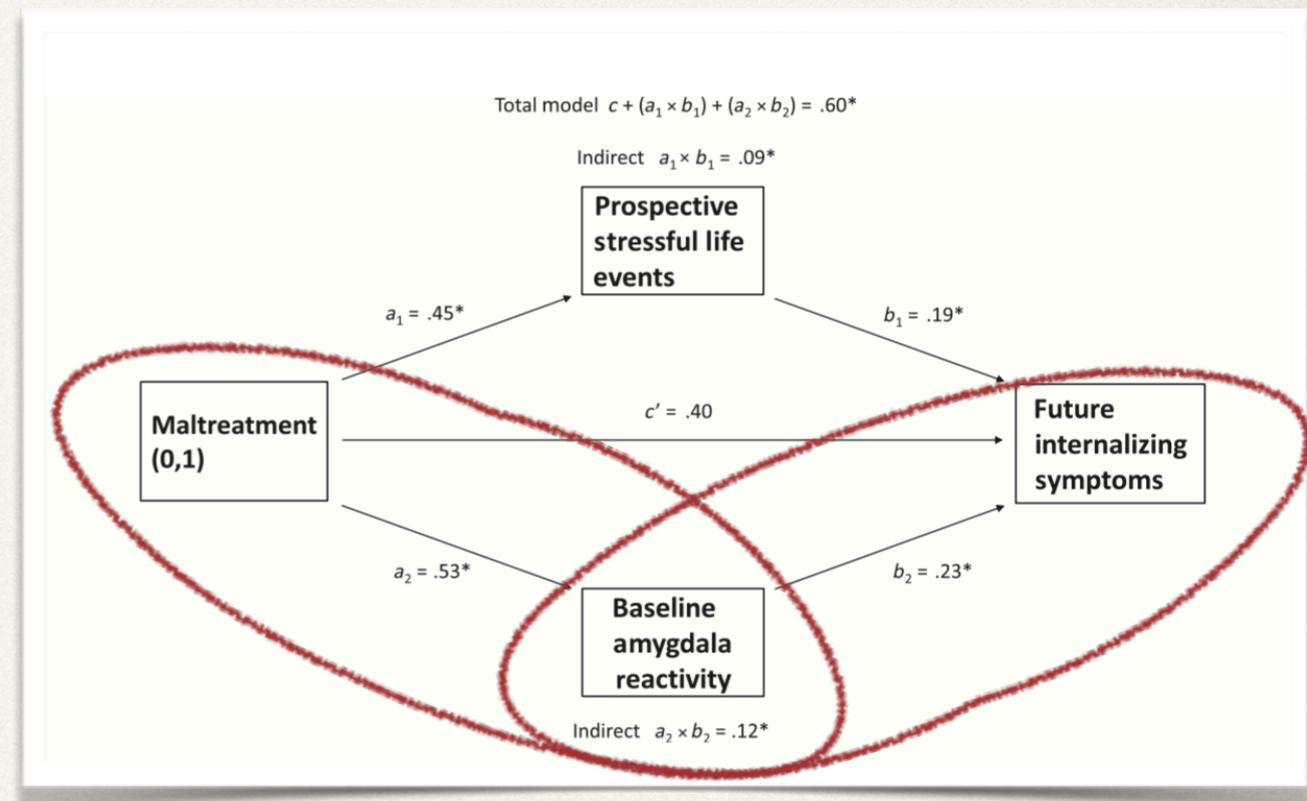
- ❖ Is this hypervigilance to threat under higher order regulatory influence? Evidence of pre-attentive threat processing (McCrorry et al., 2013)

Congruent	Duration (ms)
	500
	17
	68
	1100

# Threat Processing

Gerin et al., JCPP, 2019

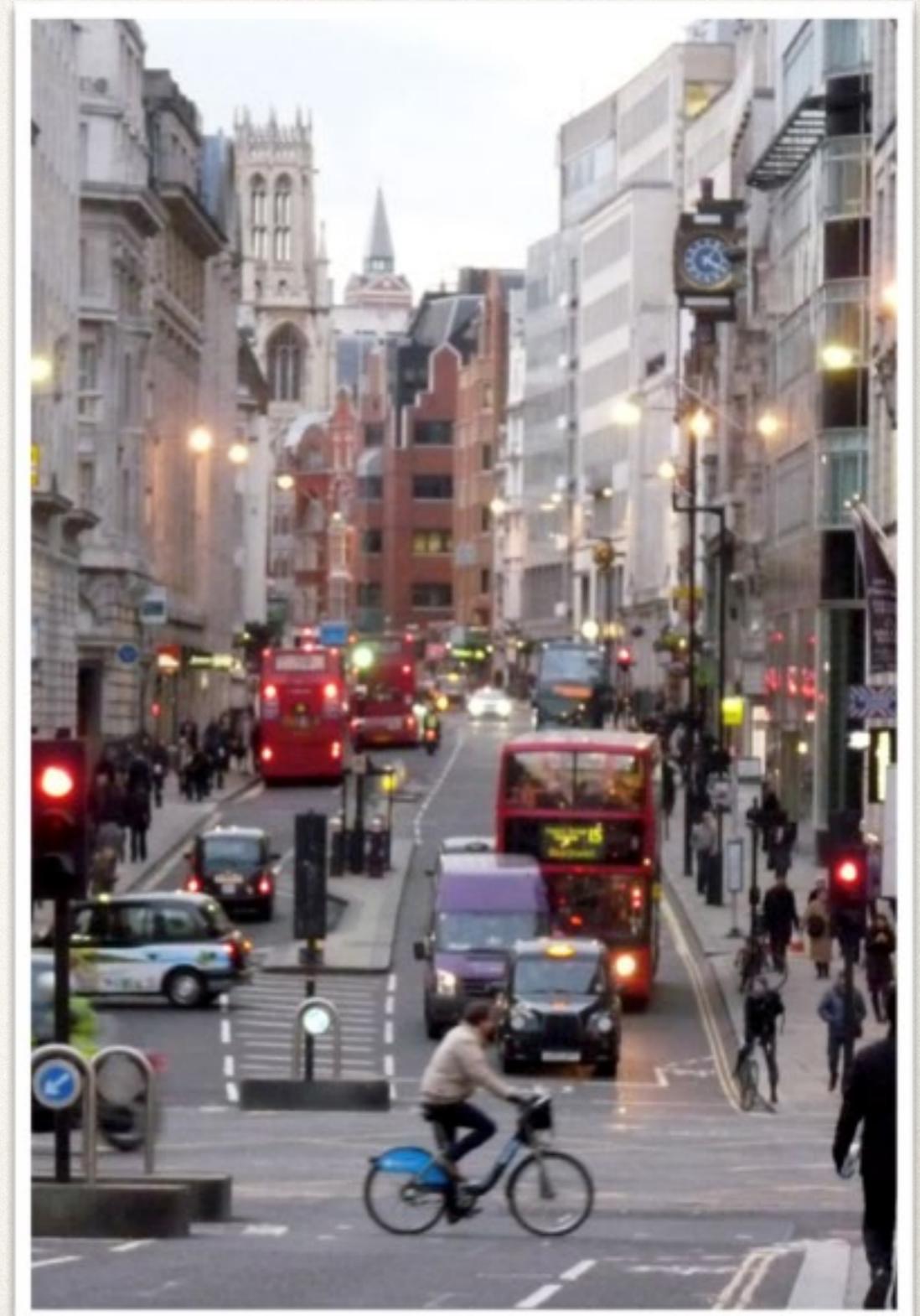
- ❖ Contribution of **baseline threat-related amygdala reactivity** to **internalizing symptoms severity** 1 year later maltreated sample (n=100) and non-maltreated peers (n=96) (Total n=1144)
- ❖ Even after stringent propensity matching - including baseline internalizing symptoms - childhood maltreatment predicted increased amygdala reactivity at baseline.
- ❖ Moreover, amygdala reactivity at baseline partly mediated the association between a history of maltreatment and future internalizing symptoms.



# Memory Processing

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- ❖ Provides data to help us simulate the future more effectively
- ❖ Impaired Autobiographical Memory (ABM) -> poorer social problem solving
- ❖ 'Overgeneral' ABM predicts future PTSD and Depression symptoms: involved in *pathogenesis* of disorder
- ❖ Traumatic material is aversive and is thought to promote encourage a more avoidant recall style leading to overgeneral ABM (Williams et al., 1996).
- ❖ Maltreatment associated with overgeneral ABM (Valentino et al., 2009)

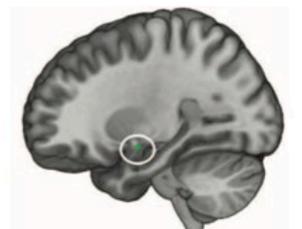
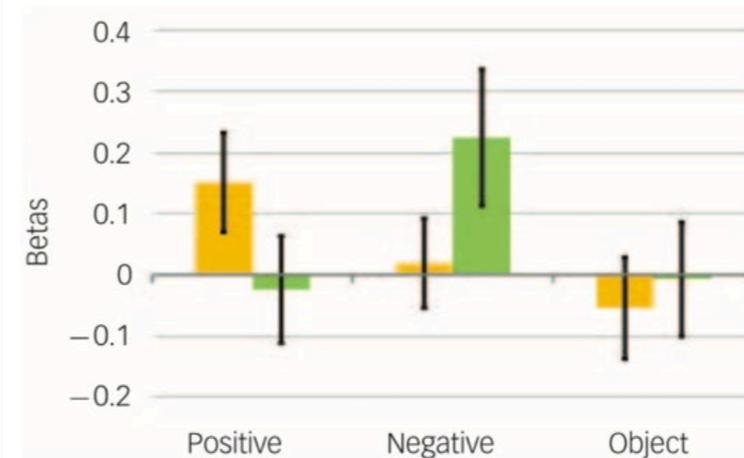


# Memory Processing *McCrary et al., BJP, 2017*

- ❖ Behaviourally, children with maltreatment histories showed overgeneral ABM
- ❖ **POSITIVE** memory recall - *reduced activation in the hippocampus* consistent with reduced memory specificity
- ❖ **NEGATIVE** memory recall - increased activation of the amygdala / connectivity between amygdala and the mACC
- ❖ This indicates heightened salience of negative memories
- ❖ On 2-year follow up greater overgeneral memory associated with poorer prosocial functioning (Puetz et al., under review).

## Right Hippocampus

## Right Amygdala

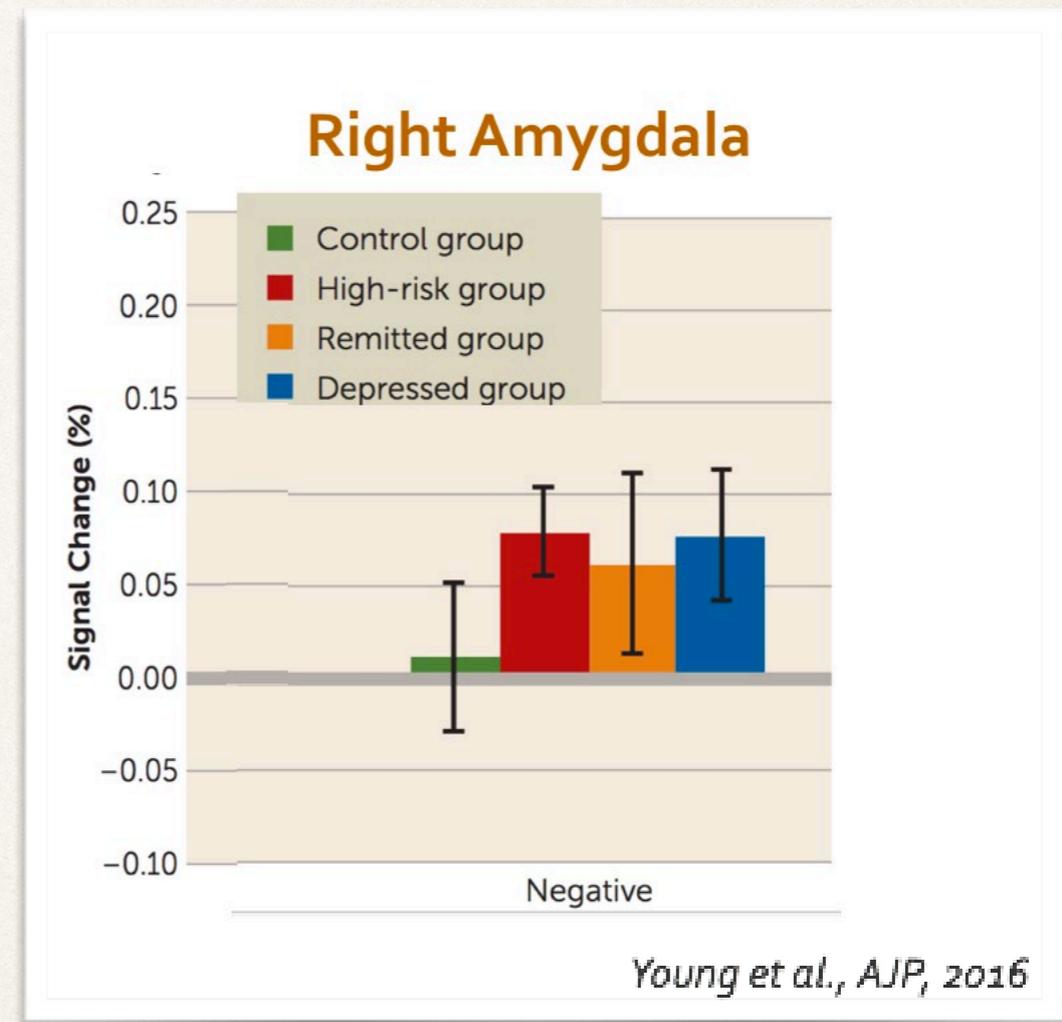


- Non-Maltreatment group
- Maltreatment group

# Memory Processing

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- ❖ Individuals at high familial risk of depression also show increased amygdala activation, and functional connectivity with regions implicated in salience processing during negative ABM recall
- ❖ Heightened salience of negative memories may therefore represent a trait-like marker of depression.

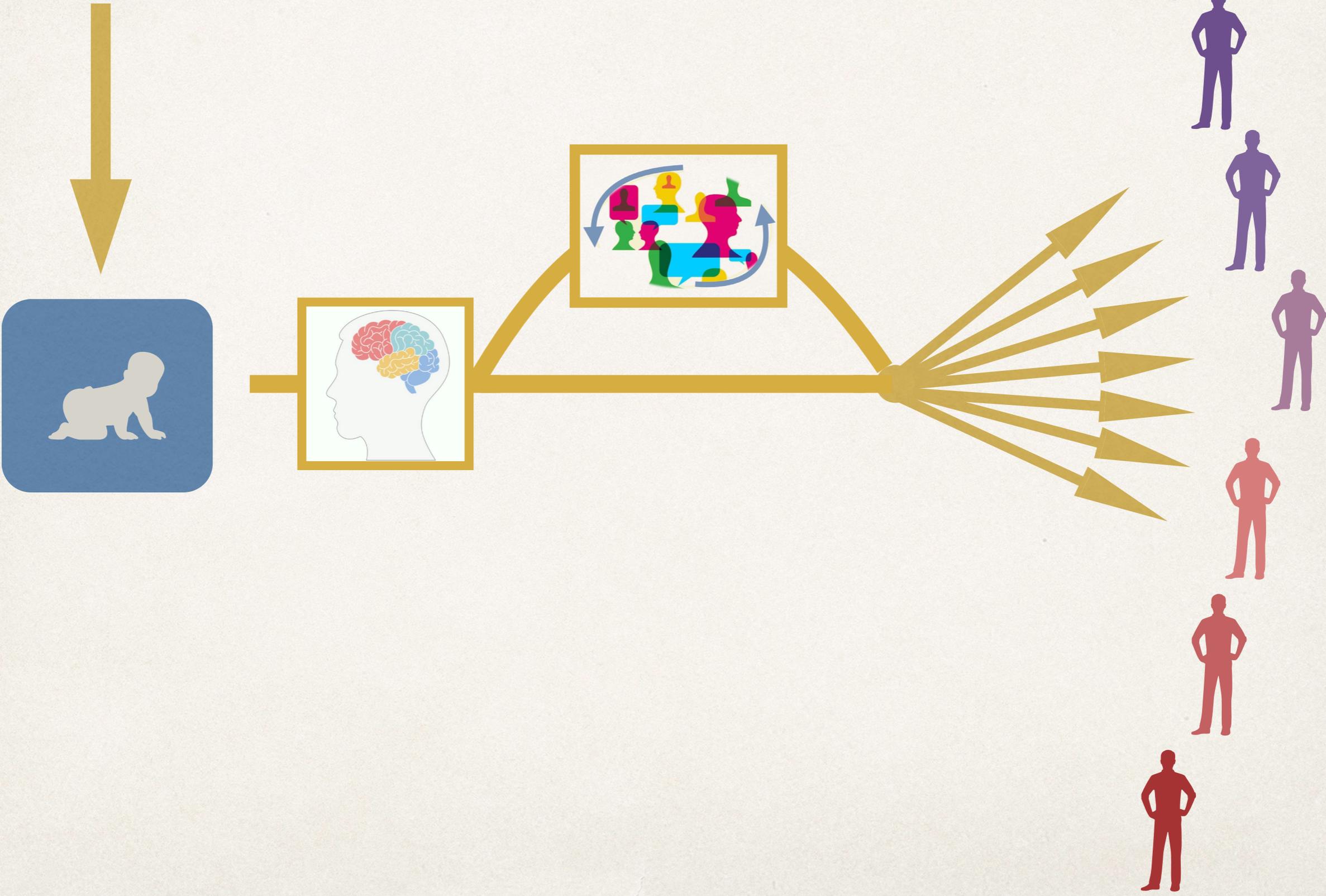


# Latent Vulnerability *McCrary et al., JCPP 2017*

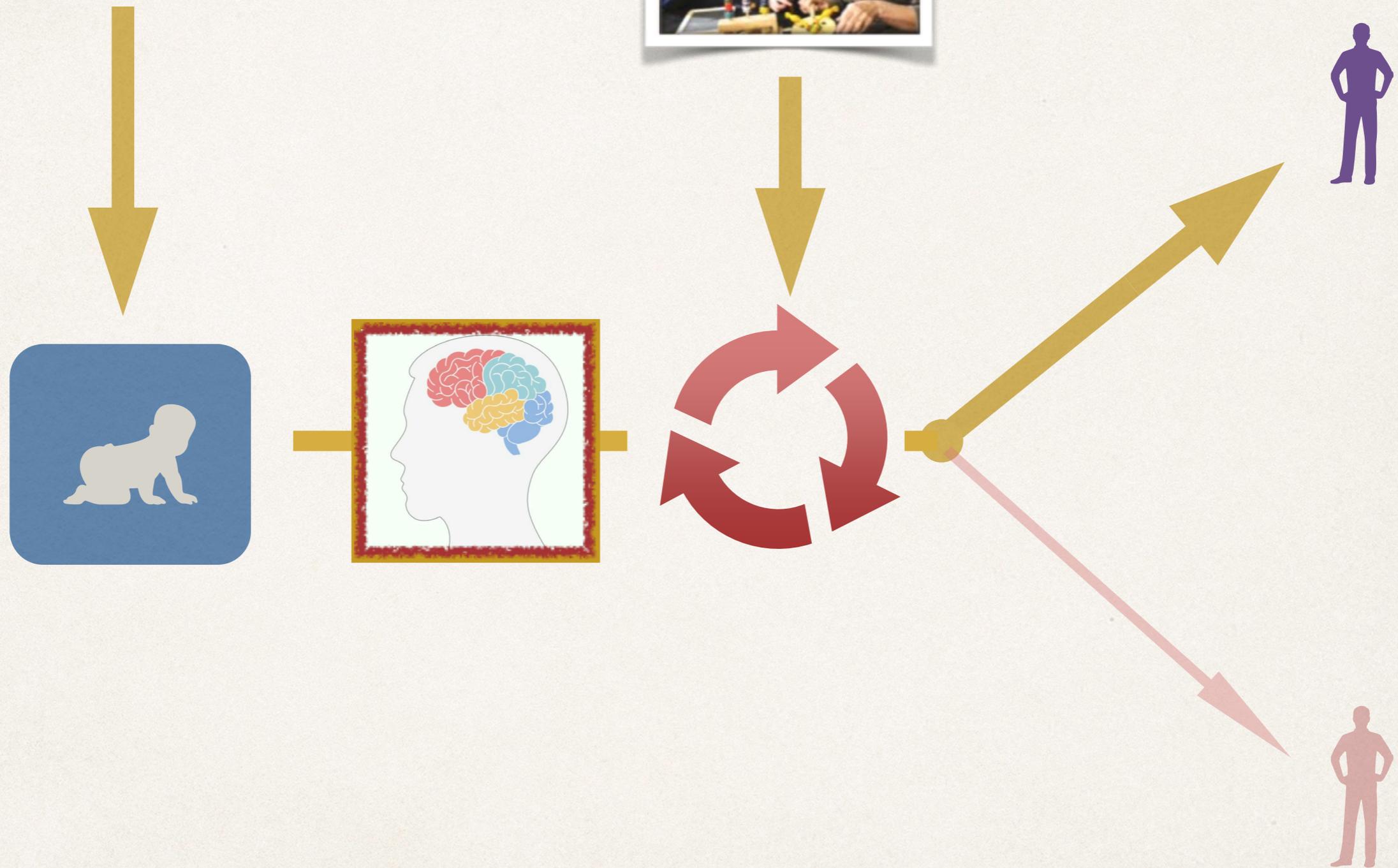
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- ❖ fMRI research has demonstrated that childhood maltreatment is associated with altered functioning in a range of neurocognitive systems including: threat processing, reward processing, emotion regulation and executive control.
- ❖ Such changes are observable **even in the absence of psychiatric disorder** and in some cases, predict future symptomatology. They are thought, in part, to reflect adaptations to early adverse environments.
- ❖ These changes are strikingly consistent with those seen in individuals presenting with psychiatric disorder suggesting such neurocognitive 'adaptations' embed latent vulnerability to future psychiatric disorder.
- ❖ If we are to move towards a **preventative** model of help, how can we move to a more precise mechanistic understanding of the pathogenesis of psychiatric disorder following maltreatment?

# Stressor Event ⚡



# Stressor Event ⚡



# 1. Stress Susceptibility:

## *Life takes a greater toll*

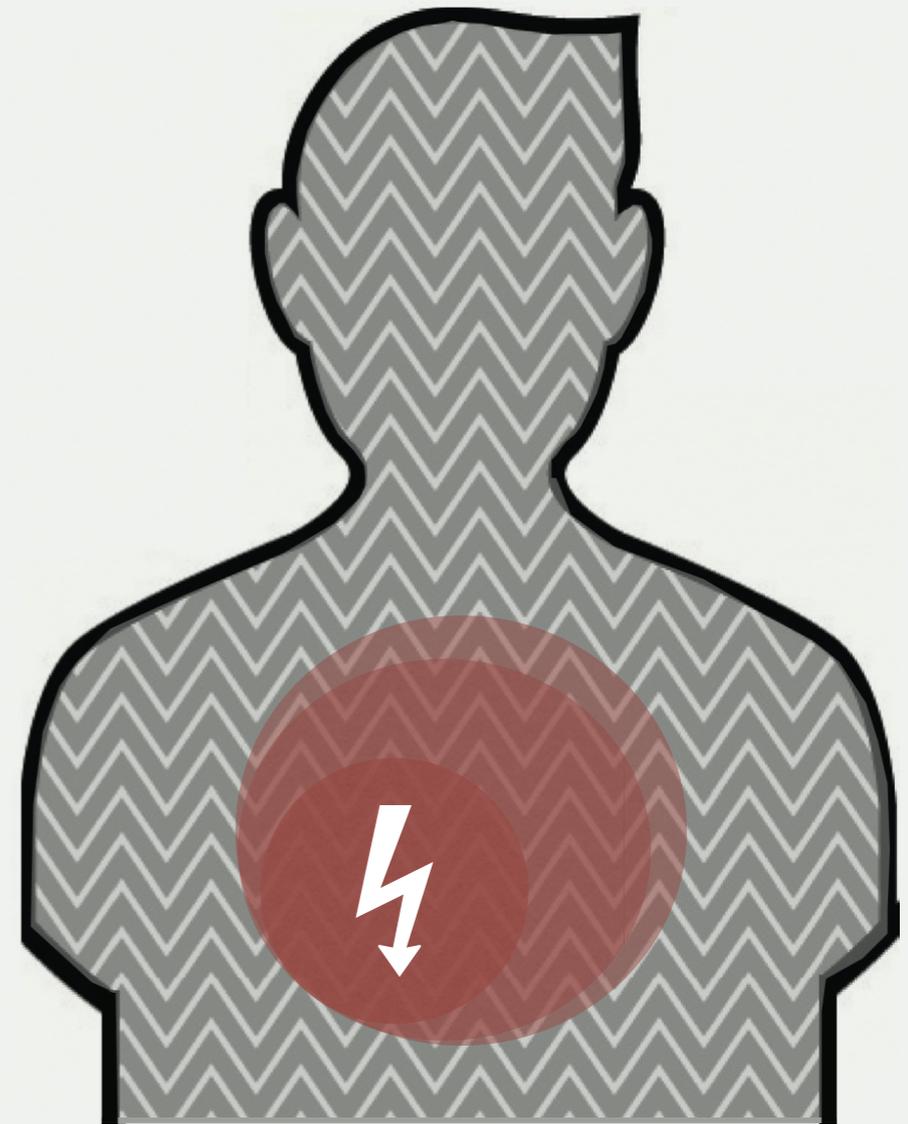
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- ❖ Children exposed to maltreatment show heightened stress reactivity, for example:
  - ❖ Increased threat reactivity (McCrory et al., 2011, 2013);
  - ❖ Increased sensitivity to social rejection (Puetz et al., 2014);
  - ❖ Negative self-schemas and biases (van Harmelen et al., 2010; Zeanah & Zeanah, 1989);
  - ❖ Poor emotion regulation (e.g. Shields et al., 2001; Jennissen et al., 2016);
  - ❖ Increased inflammatory response in women (Baldwin et al., 2018)
- ❖ Reactivity applies to **internal** cues (e.g. memories) AND **external** cues (e.g. interactions)
- ❖ These changes are consistent with adaptation an early dangerous or unpredictable early environment
- ❖ The **Allostatic Load model** (Danese & McEwen, 2011) postulates that adverse childhood experiences are associated with changes in biological systems responsible for maintaining physiological stability, or allostasis
- ❖ Heightened stress reactivity, poorer emotion regulation and chronic activation of allostatic systems leads to progressive wear and tear.

# 1. Stress Susceptibility

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- **Altered threat processing**
  - Increased reactivity to physical threat
  - Increased reactivity to social rejection
  
- **Altered autobiographical memory processing**
  - Privileging negative memories relative to positive memories
  - Greater ruminative processing
  - Development of negative self-schema



Total model  $c + (a_1 \times b_1) + (a_2 \times b_2) = .60^*$

Indirect  $a_1 \times b_1 = .09^*$

**Prospective  
stressful life  
events**

$a_1 = .45^*$

$b_1 = .19^*$

**Maltreatment  
(0,1)**

$c' = .40$

**Future  
internalizing  
symptoms**

$a_2 = .53^*$

$b_2 = .23^*$

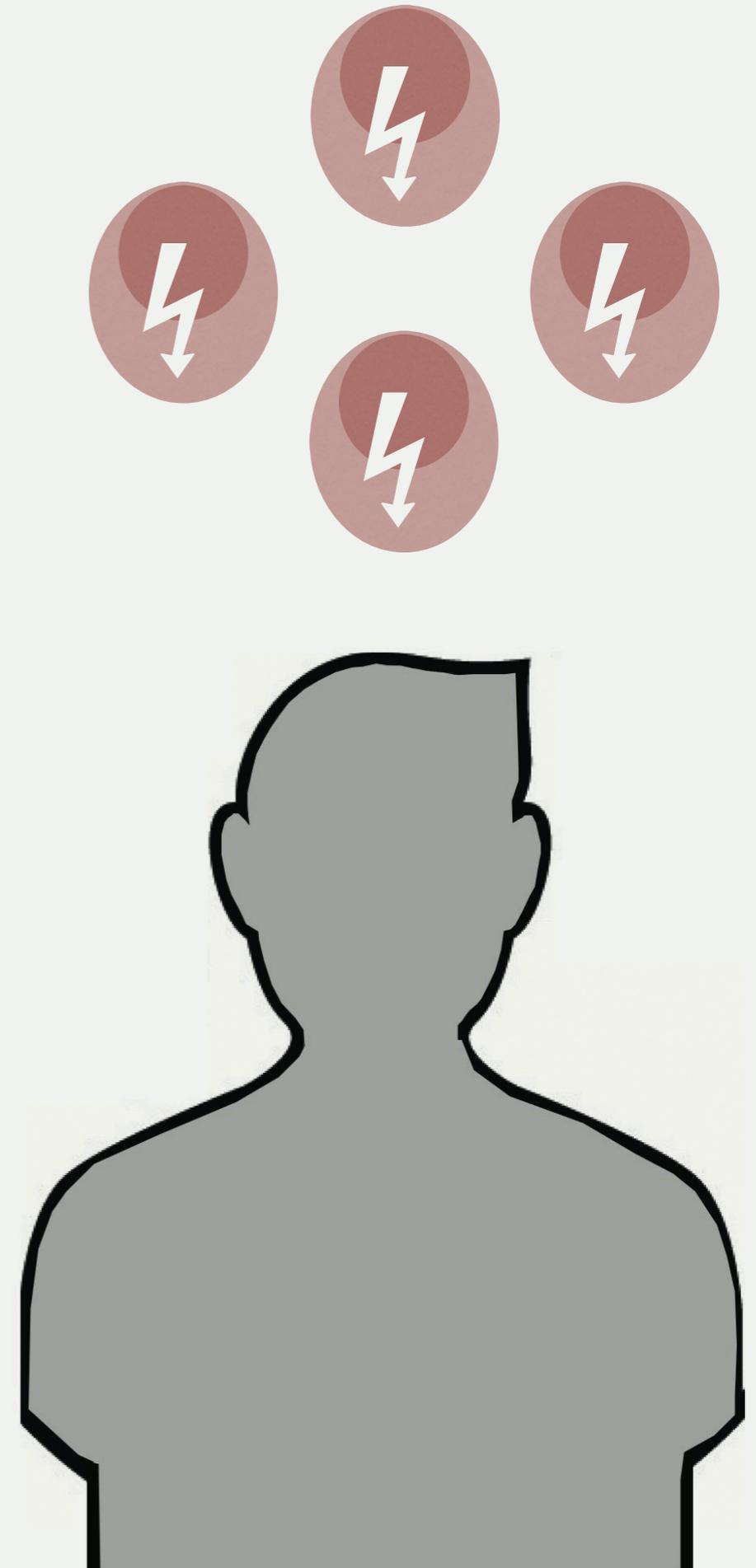
**Baseline  
amygdala  
reactivity**

Indirect  $a_2 \times b_2 = .12^*$

## 2. Stress Generation

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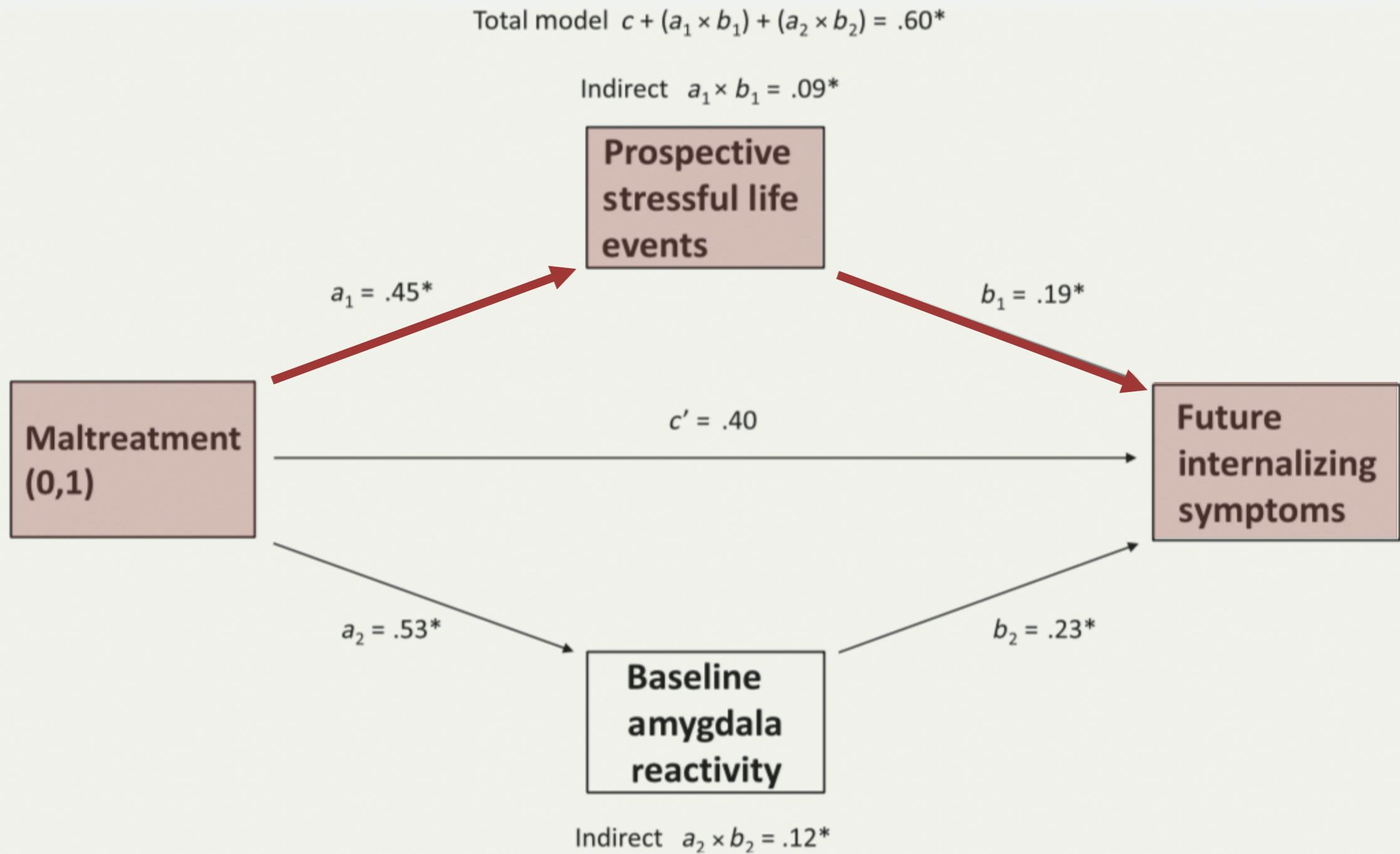
- ❖ Individuals with childhood histories of maltreatment are at great risk of *future* stressful life events:
  - ❖ Benedini et al., 2013: Increased risk of bullying
  - ❖ Widom, Czaig & Dutton, 2008: Increased lifetime risk of revictimization
  - ❖ Finkelhor et al., 2007: Abuse and revictimization risk
- ❖ However, are these associations due to confounding mental health symptoms?



## 2. Stress Generation Gerin et al., 2019, *JCPP*

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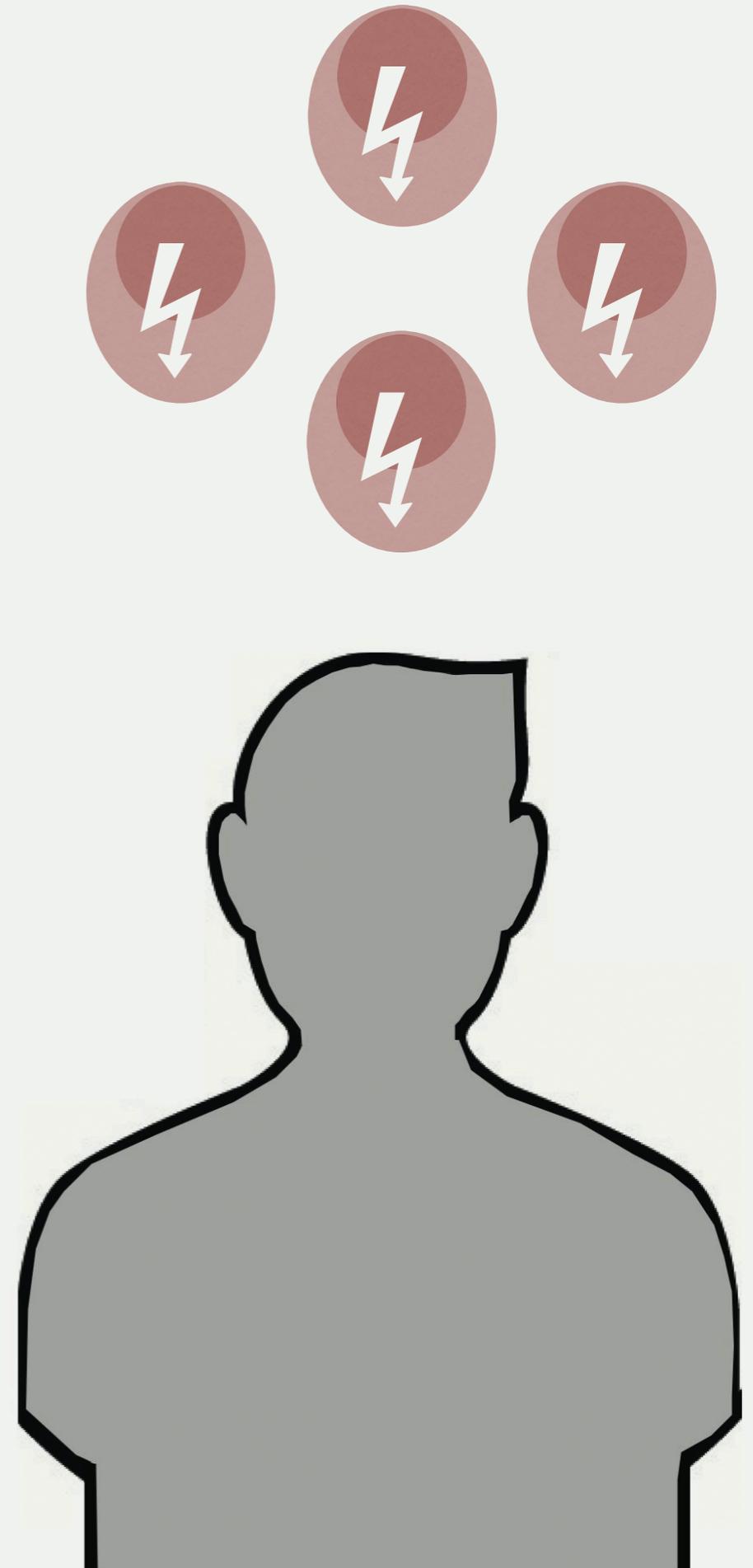
- ❖ 1144 young adults: contribution of **prospective major stressful life events** on **internalizing symptoms severity** 1 year later (on average) in individuals with a history of maltreatment (n=100) and non-maltreated peers (n=96)
- ❖ After propensity score matching - including baseline internalizing symptoms including baseline internalizing symptoms, socioeconomic status and IQ – childhood maltreatment status **predicted elevated post-baseline exposure to major stressful life events** at follow-up.
- ❖ Moreover, post-baseline exposure to major stressful life events mediated the association between a history of maltreatment and future internalizing symptoms



## 2. Stress Generation

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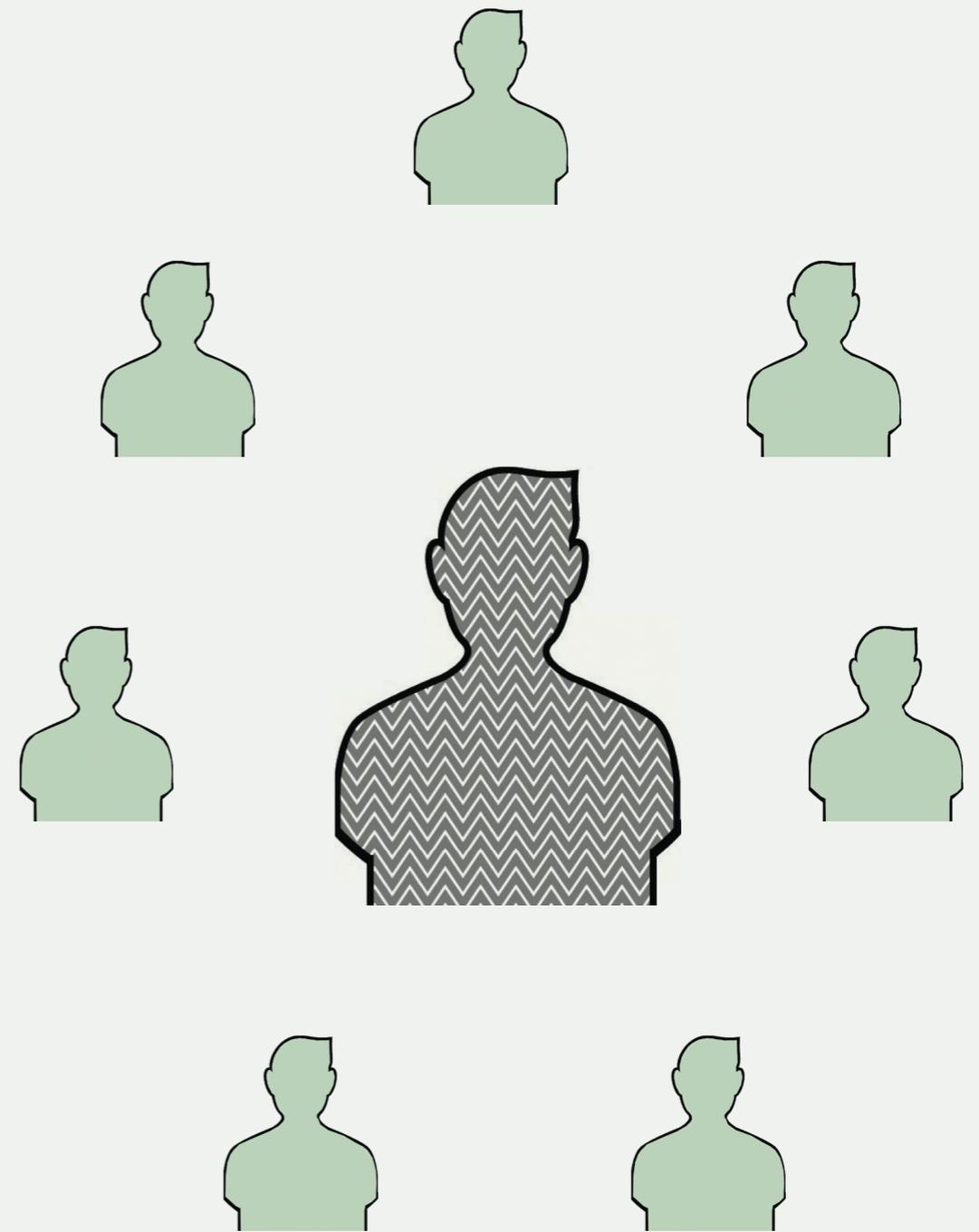
- Altered autobiographical memory processing
  - Poorer social problem solving. Less able to resolve relationship difficulties?



# 3. 'Social Thinning'

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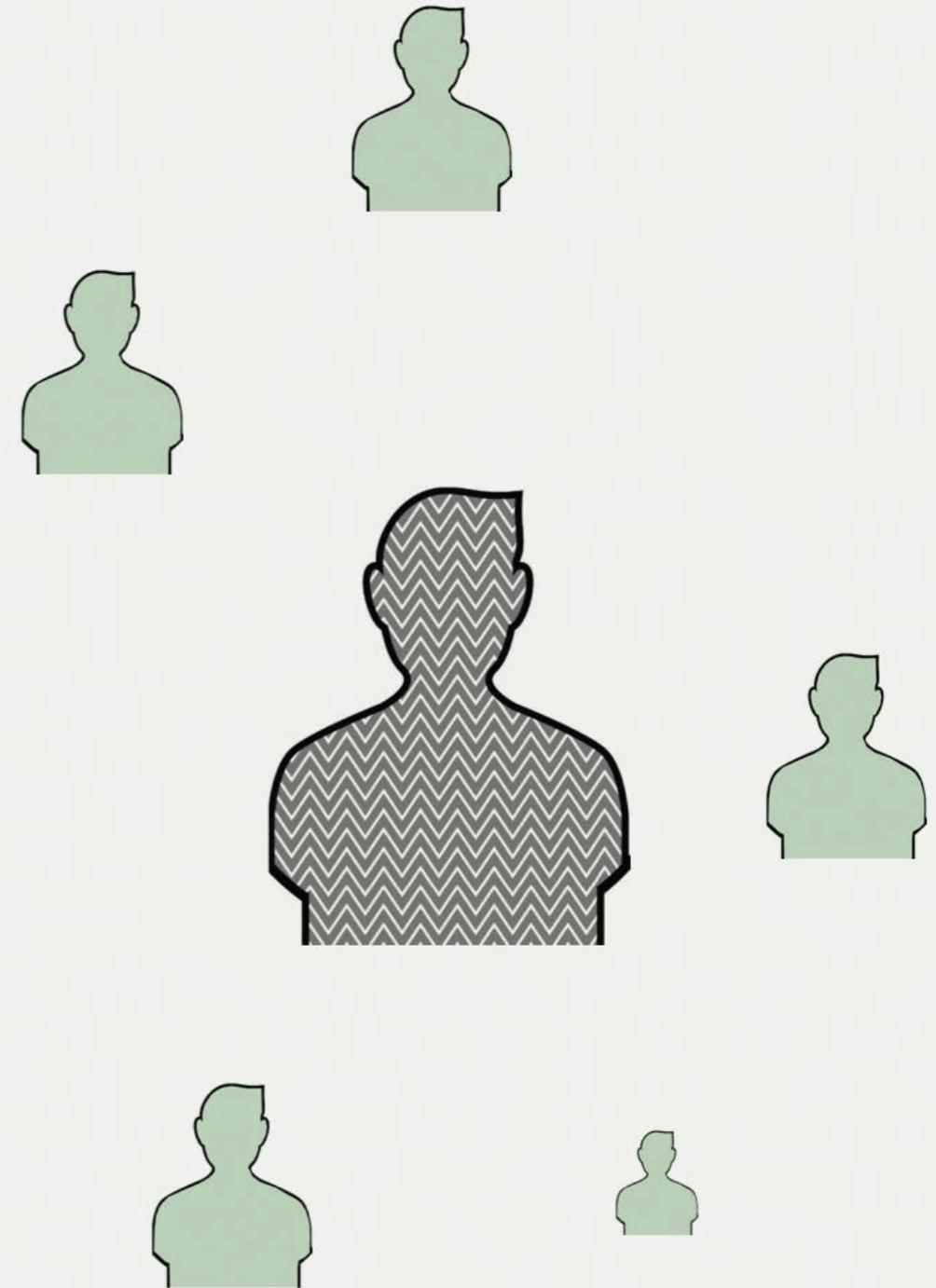
- ❖ Degraded social support emerges over time, as frequency and strength of trusted social connections diminish
- ❖ For example, **Sperry and Widom (2013)**, using data in a prospective cohort design (N=696), compared children with documented histories of physical and sexual abuse and neglect at age 0–11yrs (N=388) with a matched control group (N=308). Participants were followed up and interviewed in adulthood with social support assessed at mean age 39.5 yrs.
- ❖ Adjusting for age, sex, and race, maltreatment was associated with significantly **lower levels of social support in adulthood.**



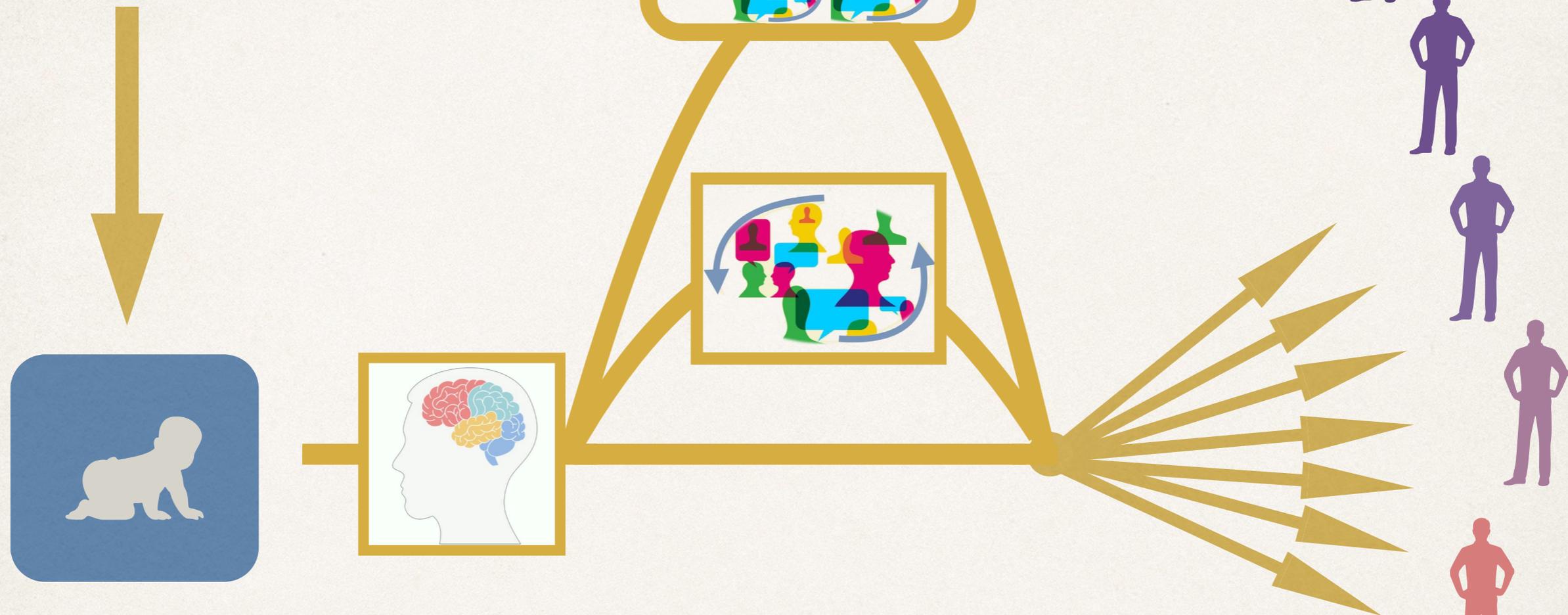
# 3. 'Social Thinning'

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- ❖ In a sample of children (10-15 years) we found that documented severity of abuse and neglect (rated by social services) was significantly associated with child related social support (Kelly et al., *in preparation*).
- ❖ Inspection of the data indicated that the relationship was largely driven by *classmate and friend* social support.
- ❖ That is, the more severe the maltreatment experience, the more less children feel supported by their peers.



Stressor Event ⚡



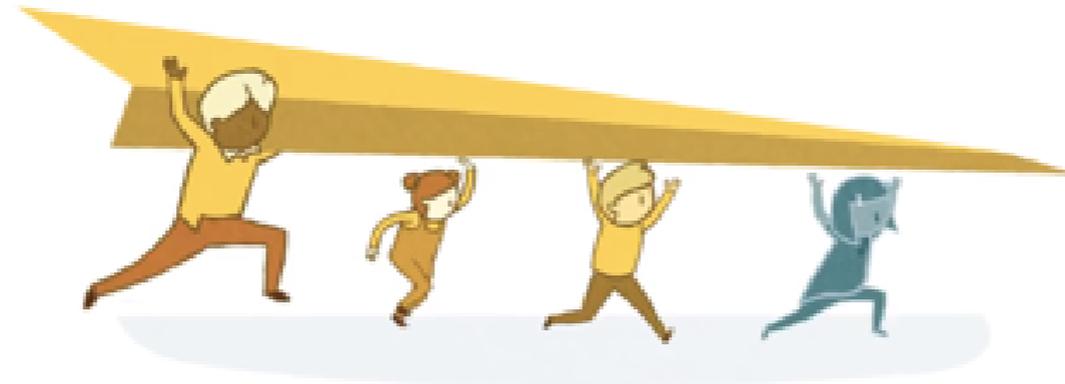
Early neurocognitive adaptation, from the earliest years, is likely to influence how an individual shapes their social ecology and social experience over time. This is proposed to play out at both an **interpersonal** level and a **systems** level (*Emanuel, 2002; Sutton, 1991*).

# Conclusions

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- ❖ Early adversity leads to neuro-cognitive adaptation. This can provide short term benefits but long term costs for the individual.
- ❖ Brain changes do not mean that vulnerability is simply located in the child. Rather, vulnerability plays out in a relational context and very possibly in a systemic context
- ❖ We need to begin to systematically investigate the ways that neuro-cognitive adaptation impacts specific aspects of social functioning in order to better inform how children can be supported
- ❖ Adults and systems around the child need to frame their understanding of infant and child behaviour in the context of the impact of their early experience and respond in ways that:
  - ❖ Promote a child's ability to regulate emotion
  - ❖ Do not inadvertently increase the likelihood of future stressors, but rather create opportunities to learn
  - ❖ Promote number and strength of trusted social connections

# Thank-you!



Developmental   
Risk and Resilience Unit



**NSPCC**

