Time Course of Brain Reactivity in Anxious Youth Performing an Attentional Bias Task: A Pupilometry Study

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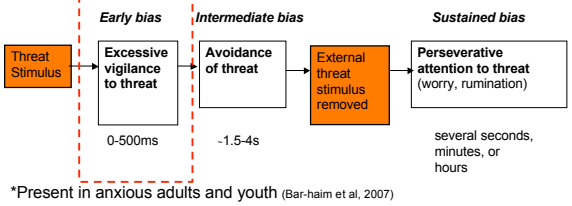
Attentional Bias

- Altered attention to threat is a transdiagnostic feature of clinical and non-clinical forms of anxiety
- Findings might implicate a role for biased attention in perpetuating anxiety:

  Excessive focus on danger cues in the environment-> more anxiety -> more excessive focus …..
- Understanding these processes in youth could inform early intervention and alter life-long trajectories of mental health

Three Forms of Bias

Time course is a critical factor in attention bias, with alternate forms of bias emerging at different points in time following threat presentation



*Present in anxious adults and youth (Bar-haim et al, 2007)

*Younger samples may show vigilance irrespective of anxiety (Vasey & MacLeod, 2001)

*May be causally related to anxiety symptoms (MacLeod et al, 2002; Amir et al, 2009; Eldar et al, in press)

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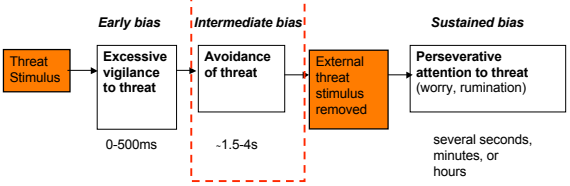


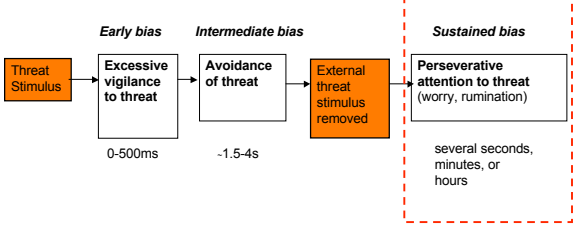
*Present in anxious adults (e.g., Mogg et al, 2004)

*One study supports vigilance-avoidance in anxious youth (In-Albon et al, 2010)

*May be related to clinical manifestations of avoidance

Three Forms of Bias

Time course is a critical factor in attention bias, with alternate forms of bias emerging at different points in time following threat presentation

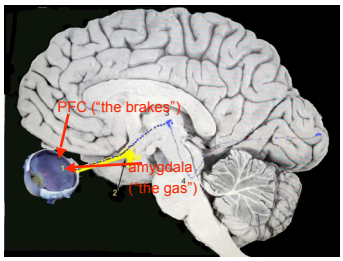


Sustained neural bias/ perseverative cognition

- fMRI studies of adult depression:
  - Depressed adults show increased sustained activity in the amygdala (an emotional processing region) following negative stimuli--correlates with self-reported rumination[8]
  - Depressed adults show sustained deficits in a prefrontal regulatory region[9]
- Pupilometry study of adults with GAD[10]

[8]Siegle et al, 2002, *Biol Psychiatry*; [9]Siegle et al, 2007, *Biol Psychiatry*; [10]Oathes et al, 2011, *Emotion*

Pupil dilation



- Pupil diameter provides a summative index of neural reactivity in cognitive and affective brain regions ("cognitive-affective load")

Sustained neural bias/ perseverative cognition (cont.)

- Pupilometry studies:
  - Adults with high levels of worry show decreased sustained pupil dilation to negative stimuli, possibly consistent with decreased regulatory control[10]
  - Depressed youth show decreased sustained pupil responses to negative stimuli[11]
- Sustained neural alterations may:
  - promote perseverative thinking patterns (worry, rumination)
  - in youth, confer neurocognitive risk for adult psychopathology (e.g., depression)[12]

[11]Silk et al, 2007, *Am J Psychiatry*; [12]Pine et al, 1998, *Arch Gen Psychiatry*

Current study goals

- Investigate *sustained* forms of bias in anxious youth using pupillary reactivity
- Concurrently collect behavioral measures of *early* and *intermediate* bias
- Gain insight into potential neurocognitive targets for early intervention

Current sample

- 74 youth (age 9-13; mean=10.5) with generalized anxiety disorder (GAD; 68%), separation anxiety disorder (SAD; 26%), and/or social phobia (SP; 25%)
- 20 youth with no lifetime DSM-IV diagnoses

Methods

- Dot-probe task

500ms

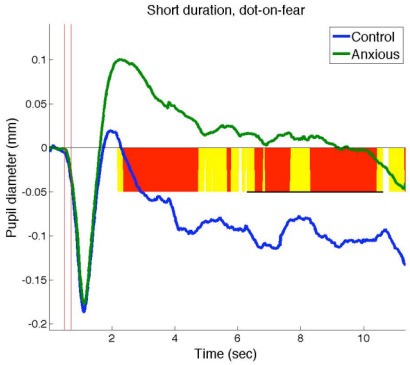
200ms or 2s

8.8 or 10.6s

Methods

- Dot-probe task
  - Sustained bias measure:
    - Pupil dilation collected during the extended post-stimulus dot period
    - *Hypothesis: Sustained alterations (increases or decreases) in anxious youth*
  - Early and intermediate bias measures:
    - Reaction times for short and long face presentations--comparison of dot-on-fear to dot-on-neutral trials

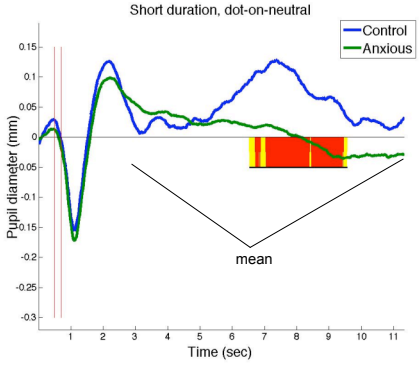
Results--Sustained bias: Pupil dilation



Increased pupil diameter=

increased cognitive-affective load

Results--Sustained bias: Pupil dilation

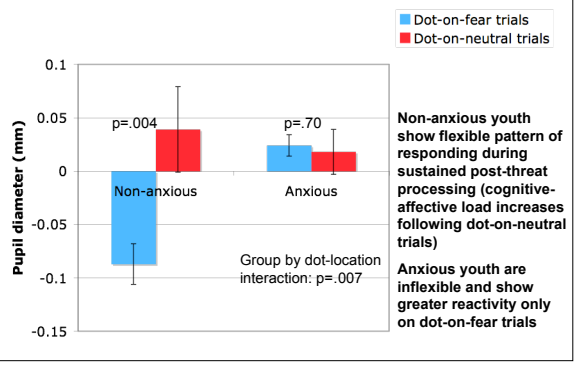


Increased pupil diameter=

increased cognitive-affective load

Results--Sustained bias: Pupil dilation

Average pupil diameter during sustained processing

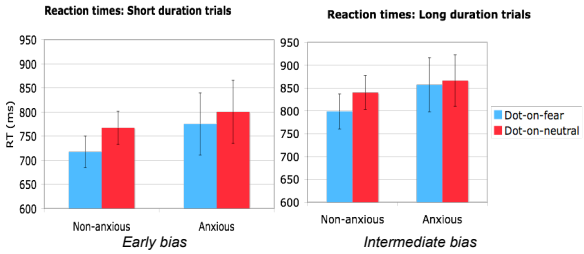


Non-anxious youth show flexible pattern of responding during sustained post-threat processing (cognitive-affective load increases following dot-on-neutral trials)

Anxious youth are inflexible and show greater reactivity only on dot-on-fear trials

Results

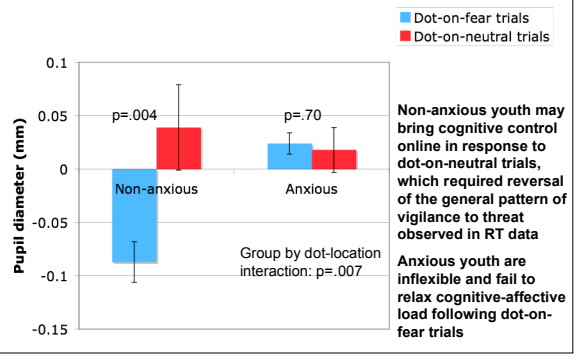
Early and intermediate bias: Reaction times



Vigilance to threat **seen in both groups at early and intermediate timepoints (main effect of dot location: *p*=.003)**

Results--Sustained bias: Pupil dilation

Average pupil diameter during sustained processing



Non-anxious youth may bring cognitive control online in response to dot-on-neutral trials, which required reversal of the general pattern of vigilance to threat observed in RT data

Anxious youth are inflexible and fail to relax cognitive-affective load following dot-on-fear trials

Summary of findings

- An inflexible pattern of sustained post-threat processing was found in anxious youth
- A *vigilant* pattern in RTs was found in all participants
- Non-anxious youth may have flexibly brought cognitive control on-line only when the dot appeared in the unattended/unexpected location
- This resulted in increased cognitive-affective load in anxious youth observed specifically following dot-on-fear trials

Conclusions: sustained bias

- Altered neural reactivity to threat in anxious youth persists well beyond the timeframe of stimulus presentation and responses
- Sustained bias is dissociable from the peri-stimulus biases more commonly studied in anxiety
- Approaches to directly modify attentional bias in order to reduce anxiety vulnerability are being developed
  - Will these approaches effect sustained bias?
  - Or do sustained patterns require a targeted intervention of their own?

Conclusions: early and intermediate bias

- No evidence of excessive vigilance or avoidance in anxious youth
  - Consistent with a subset of previous findings, RT vigilance to threat was seen in this age group irrespective of anxiety
- The ability to inhibit attention to threat may develop in non-anxious individuals at a later age
- Only one previous study has shown a vigilant-avoidant pattern in anxious youth
- Many more studies in youth are needed to counteract a potential “file drawer problem”

Future Directions

- Use observed pupil pattern to guide future neuroimaging analysis--identify the neural substrate of sustained patterns
- Determine the developmental trajectory--e.g., do sustained pupil alterations in anxious youth confer risk for later development of depression?
- Develop new interventions, or tailor selection of existing options (e.g., CBT, early bias modification) to the individual patient

Questions?