Brain Network Activation during Emotional Response Impacted by Perceived Stress in Adolescents

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Introduction

- Adolescence is a distinct period of development marked by substantial brain remodeling, particularly in networks subserving inhibitory control that are susceptible to stress.[1,2]

- Stress has been shown to negatively impact mental health[3] and peer stress is specifically implicated in the early onset of socio-emotional disorders (e.g. depression, anxiety).[4]

- This study evaluated network activation during performance of an emotional Go-NoGo task[5,6] and associations between network activation and self-reported stress and peer rejection or abuse.

Participants, Procedures and Performance

- *Participants:* 45 healthy adolescents (age = 13.9 ± 0.6 years, 25 biological females). Participants provided consent prior to participation. The study was approved by the McLean Hospital Institutional Review Board.

- *Study visit:* Cognitive testing and emotional questionnaires (NIH Toolbox),[7] Maltreatment and Abuse Chronology of Exposure (MACE)[8] interview, and MRI and fMRI data were collected.[5,6]

Perceived Stress NIH Toolbox (sample questions)

In the past month…	Never	Almost Never	Sometimes	Fairly Often	Very Often
SC011 How often have you been angered because of things that happened that were outside of your control?	1	2	3	4	5
SC014 How often have you felt difficulties were piling up so high that you could not overcome them?	1	2	3	4	5

Perceived Rejection NIH Toolbox (sample questions)

	Never	Rarely	Sometimes	Usually	Always
SOC276 Act like my problems aren't that important	1	2	3	4	5
SOC279 Act like they don't have time for me	1	2	3	4	5

Peer Emotional Abuse (MACE) (sample questions)

26 Swore, called you names/insults more than few times per year
27 Said hurtful things made you feel humiliated more than few times per year
28 Said things behind you back, spread rumors

Go-NoGo Task[5,6]

- Participants were asked to make a button press for every letter except X while ignoring background images.

- Participants had to actively inhibit presses on NoGo trials ('Xs'=25% of trials).

- Background images were selected from the International Affective Picture System (IAPS) and were positive, negative, neutral or scrambled.
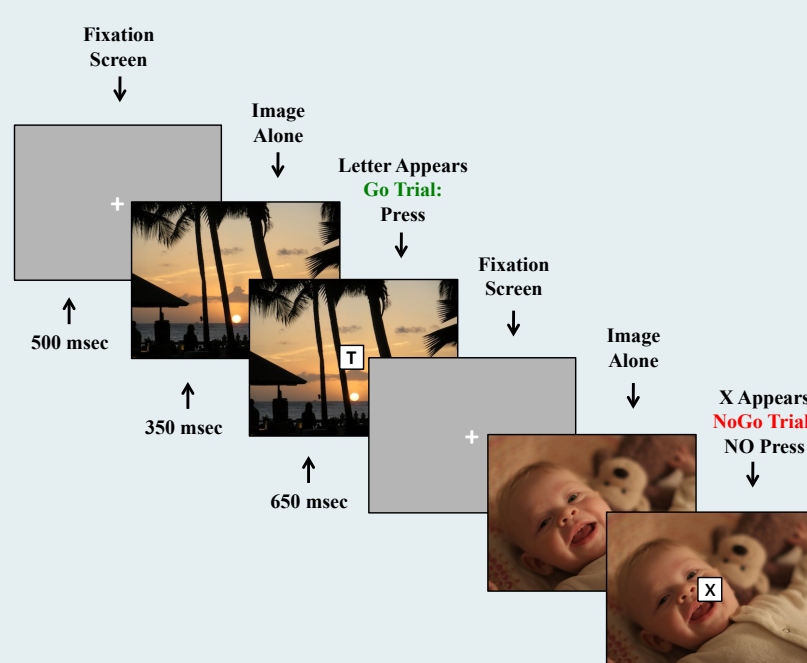

Fixation Screen
Image Alone
Letter Appears Go Trial: Press
Fixation Screen
Image Alone
X Appears NoGo Trial: NO Press
500 msec
350 msec
650 msec

Table 1. Emotional Go-NoGo Performance: Measures & Trial Type

| Measure	Negative	Positive	Neutral	Scrambled
Go Accuracy (%)	97.6 ± 3.2	98.5 ± 2.0	98.7 ± 1.8	98.8 ± 1.6
NoGo Accuracy (%)	51.7 ± 18.1	56.0 ± 16.8	57.0 ± 20.3	61.9 ± 15.8
Go Reaction Time (ms)	367.5 ± 40.3	359.4 ± 39.4	353.0 ± 35.3	355.6 ± 39.0

Data represent mean ± standard deviation.

Imaging Methods

- Whole brain multiband echoplanar (EPI) blood oxygen level dependent (BOLD) data were acquired on a 3T Siemens TIM Trio (Siemens, Erlangen, Germany) with a 32-channel phased array head coil (TR: 750ms, TE: 30ms, voxel size: 2.8x2.8x2.8mm).[6]

- Preprocessing (slice scan time correction, linear trend removal, high-pass temporal filtering, spatial smoothing, motion correction) and first-level statistical analyses were performed using FSL. GLM regressors modeled NoGo trials within positive, negative, neutral, scrambled conditions. Contrasts of parameter estimates were calculated between negative and neutral conditions and were averaged across all participants in a second-level GLM in order to identify brain regions recruited in response to increased emotional distraction during inhibitory (NoGo) trials ($p < 0.05$, corrected for multiple comparisons).

- Task-related activation of key brain networks was explored using network template spatial maps[9] derived from Human Connectome Project data (https://www.humanconnectome.org/study/hcp-young-adult).[10]

- Template network maps were regressed against the full set of brain activation maps for Negative NoGo > Neutral NoGo contrast to estimate the impact of negative emotional stimuli during response inhibition on the strength of activation of each associated network. Correlation analysis was done to examine task-related network loadings relative to perceived stress, perceived rejection and peer emotional abuse.

Results

- **Figure 1** shows activated regions observed in response to the presence of negative emotional images during inhibitory control (Negative NoGo > Neutral NoGo contrast).
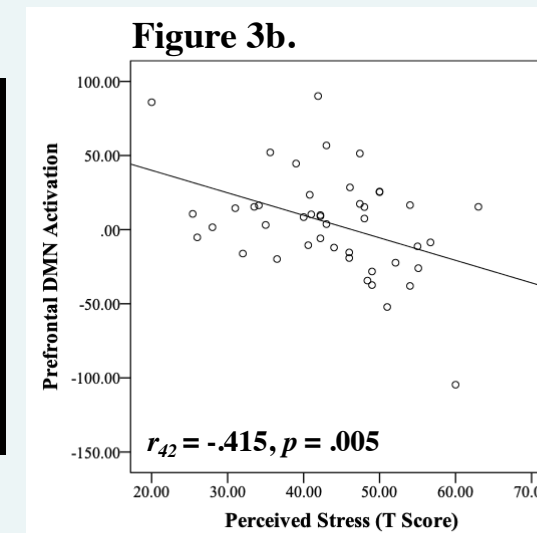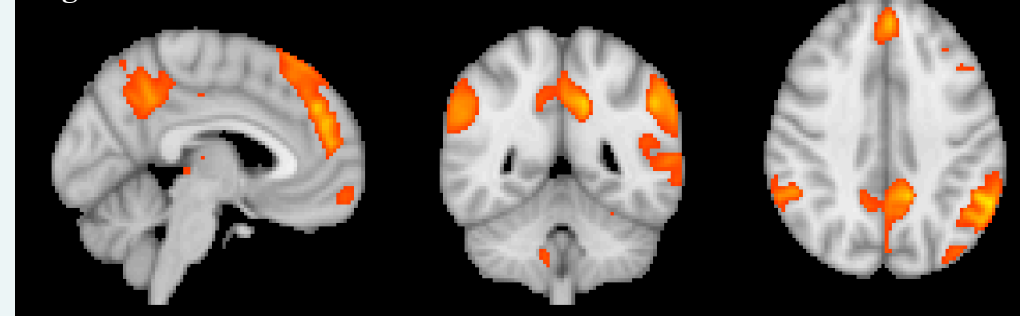

Figure 1. Activation on Negative NoGo > Neutral NoGo Contrast
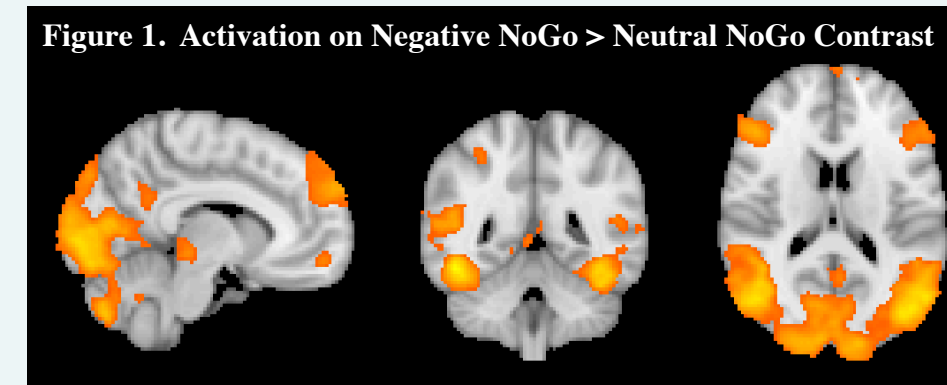
- **Figure 2:** Greater perceived stress was significantly associated with lower accuracy on inhibitory trials.

Figure 2. Go-NoGo Performance
$r_{75} = -.321, p = .004$
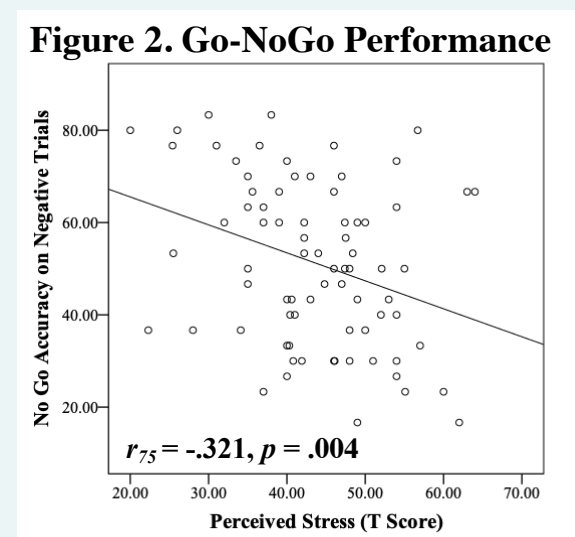
Networks Associated with Self-Report Measures

Figure 3a. Anterior DMN Sub-Network

Figure 3b.
$r_{42} = -.415, p = .005$

- Weaker activation of the anterior DMN sub-network (**Figure 3a**) was associated with greater perceived stress (**Figure 3b**) and greater peer emotional abuse (p = .03).

Figure 4a. Medial Temporal Lobe DMN Sub-Network

Figure 4b.
$r_{42} = -.348, p = .02$

Figure 4c.
$r_{42} = -.348, p = .02$
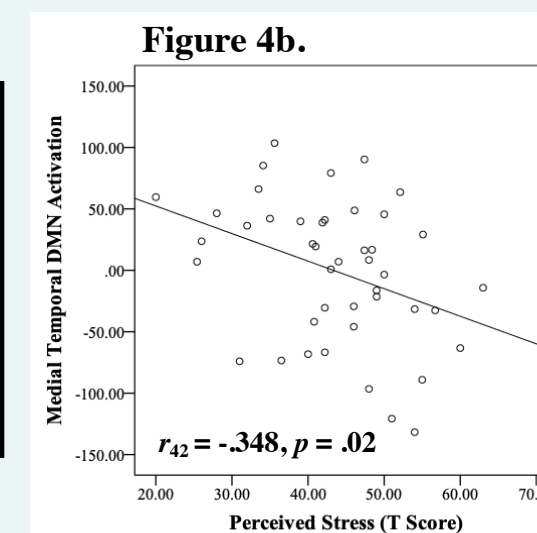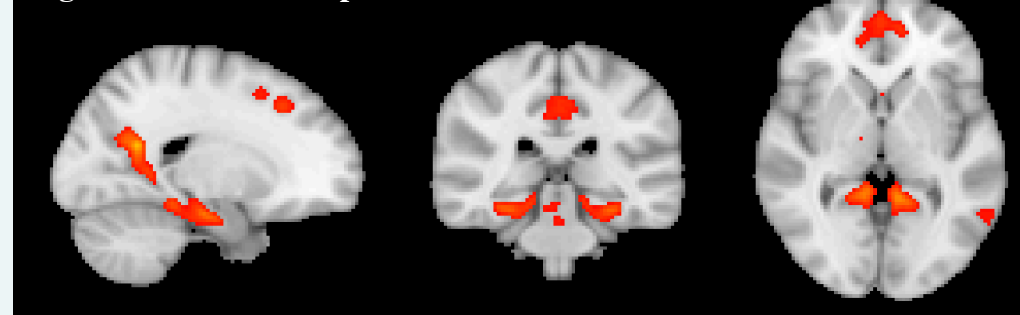
- Weaker activation of medial temporal DMN (**Figure 4a**) was associated with lower perceived stress (**Figure 4b**), perceived rejection (**Figure 4c**) and peer emotional abuse (p = .009).
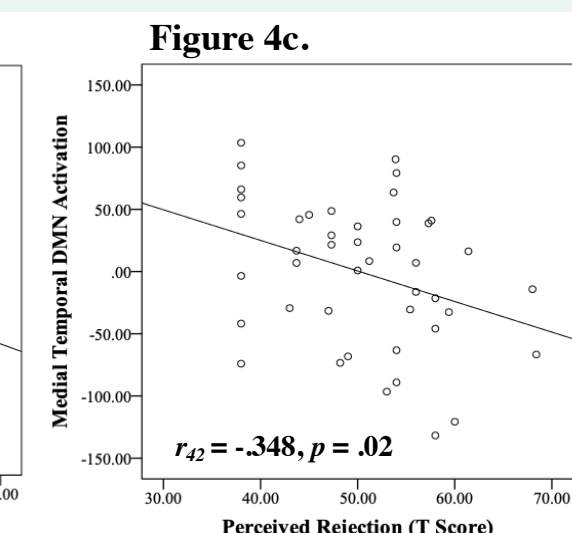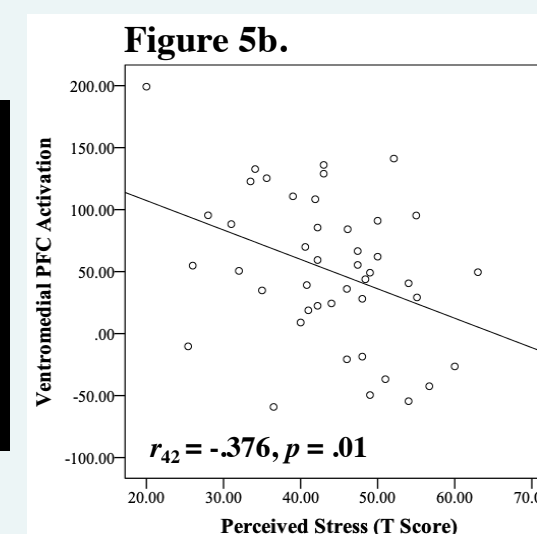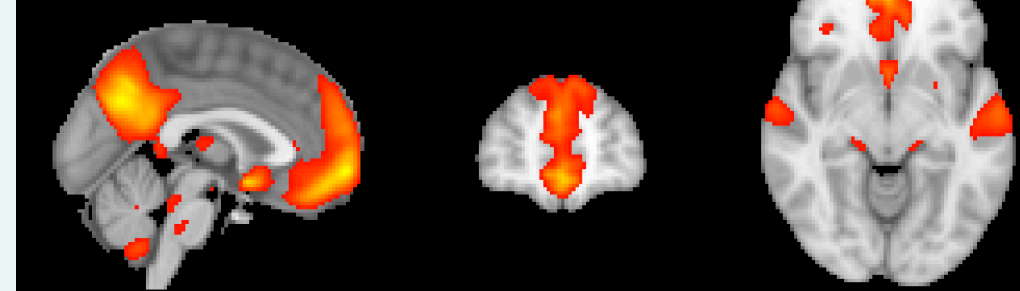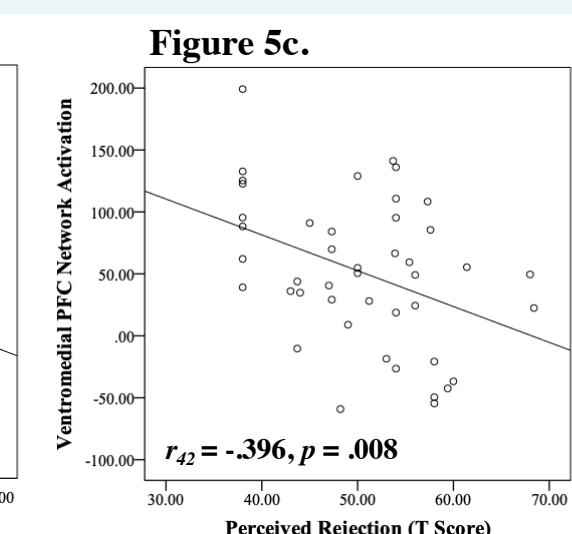

Figure 5a. Ventromedial Prefrontal DMN Sub-Network

Figure 5b.
$r_{42} = -.376, p = .01$

Figure 5c.
$r_{42} = -.396, p = .008$

- Weaker activation of the ventromedial PFC DMN sub-network (**Figure 5a**) was associated with greater perceived stress (**Figure 5b**) and perceived rejection (**Figure 5c**).

Discussion

- These findings suggest internalized stress may alter engagement of networks related to emotion regulation and social cognition during response inhibition during negative relative to neutral emotional distraction. Specifically, activity of DMN sub-networks associated with autobiographical recall (anterior & temporal lobe), theory of mind (anterior), and affective processing (ventromedial) was associated with perceived stress and rejection.

- Findings could reflect increased impulsivity and self-reflective processing, elicited by both negative and neutral stimuli that could serve as an early marker for later mental health problems, such as increased depression and anxiety symptoms.

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