

# Impact of Perceived Stress on Brain Network Activation During Memory Retrieval in Adolescents

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## Introduction

- Adolescence is characterized by substantial structural and functional brain remodeling, particularly in memory-processing regions influenced by stress, including the frontal cortex and medial temporal lobe<sup>1-2</sup>
- Stress has been shown to impact these regions<sup>3</sup>, which may relate to emerging symptoms of depression, anxiety, and other mental health problems during the critical period of adolescent development<sup>4</sup>.
- Thus, this study investigated network activation in memory-processing regions during spatial memory assessed using a virtual analogue of the Morris water task (MWT)<sup>5</sup>. **Network activation** was examined relative to **memory performance and stressors** (perceived stress and rejection, and peer emotional abuse).

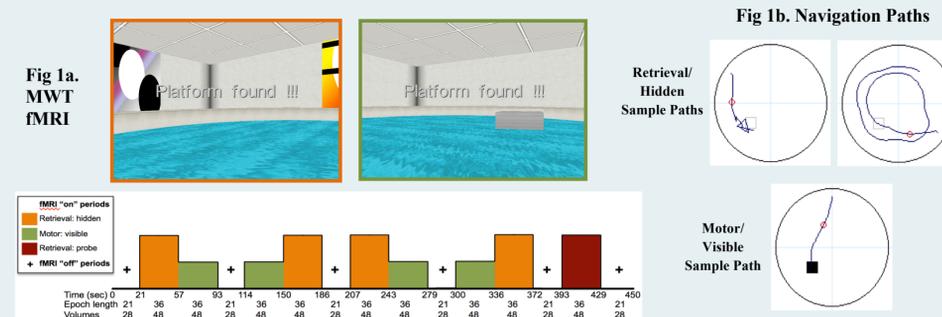
## Participants & Procedures

- Alcohol- and substance-naïve and psychiatrically healthy adolescents (aged 14.0 ± 0.6 years old, N=81) were recruited into a three-year longitudinal study. Data are presented from a subsample of N=58 who completed baseline visit. Sample was 59% female, 98% Non-Hispanic and 83% Caucasian.
- All participants provided assent and parents/guardians provided consent prior to study participation. The study protocol was approved by the Partners Healthcare Institutional Review Board of McLean Hospital.
- Adolescents completed the NIH Emotion Toolbox to measure **perceived stress and rejection** and the pediatric Maltreatment and Abuse Chronology of Exposure (MACE) to assess **peer emotional abuse**<sup>6</sup>.
- Participants completed structural, functional and spectroscopic imaging. Cognitive data on the MWT (offline learning and fMRI performance) (Table 2) and fMRI data are presented.

## Virtual Morris Water Task (MWT)

- Participants viewed a computer-generated environment from a first-person perspective and navigated using arrows keys (offline version) or MR-compatible fORP box. Participants completed blocks of learning/retrieval (orange: hidden) and motor (green: visible-no cues) trials, followed by a single probe trial (hidden environment with platform removed unbeknownst to participant) during BOLD fMRI (Fig 1a). Sample navigation paths are illustrated in Fig 1b.
- Whole brain multiband EPI 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)<sup>7</sup>.
- Behavioral task performance data, offline and during fMRI, were analyzed using SPSS 24.0 (SPSS, Chicago, IL).
- 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. Group analyses were conducted using cluster-based thresholding ( $z = 3.1$ ),  $p \leq 0.05$  corrected for multiple comparisons.
- Task-related activation of key brain networks also was explored using network template spatial maps<sup>8</sup> derived from Human Connectome Project data (<https://www.humanconnectome.org/study/hcp-young-adult>)<sup>9</sup>.

## Imaging Methods



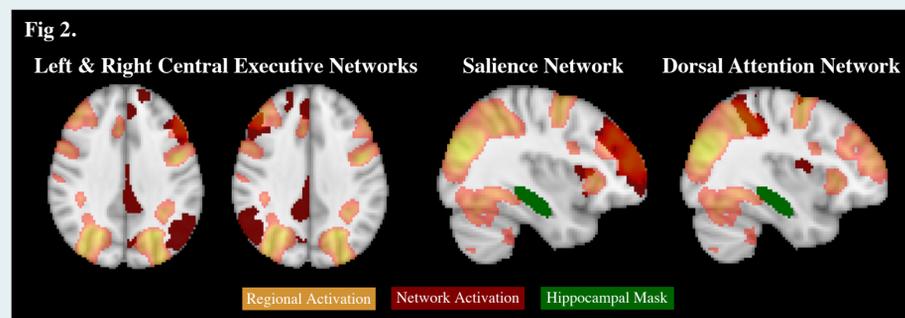
## MWT Memory Performance

- Greater levels of reported perceived stress and rejection, and peer emotional abuse were significantly associated with worse MWT performance during learning (probe trial, longer path to reach platform quadrant).

	Pathlength to Reach the Platform Quadrant	
	r	p value
Perceived Stress	0.269	0.017
Perceived Rejection	0.318	0.004
Peer Emotional Abuse	0.727	<.001

## Regional and Network Activation during MWT Memory Retrieval

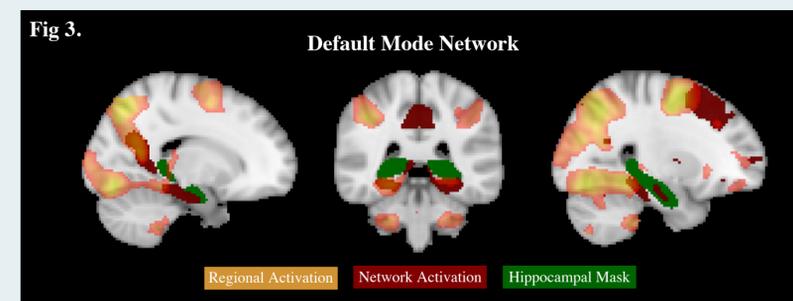
- Hippocampal and prefrontal cortex regions were significantly activated during task performance (retrieval > motor contrast, orange/yellow; hippocampal anatomy, green), as were networks (maroon), including central executive, salience, and dorsal attention networks (Fig 2).



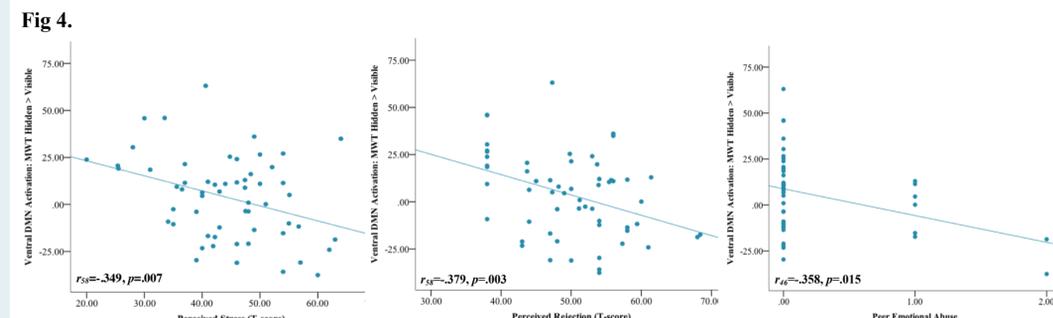
## Ventral Default Mode Network Activation

### Perceived Stress & Rejection, Peer Emotional Abuse

- Regional activation also overlapped with activation of the ventral DMN (MTL-DMN) network, the medial temporal lobe sub-network comprised of hippocampus, amygdala and prefrontal cortex (Fig 3).



- Extracted network strength from vDMN was significantly associated with higher perceived stress and perceived rejection, and greater peer emotional abuse (Fig 4).



## Discussion

- Regional brain activation during MWT performance overlapped with central executive, salience, dorsal attention and default mode networks, with extracted network strengths<sup>8</sup> from the latter network (MTL-DMN) being significantly associated with internalized stress, which also impacted on spatial memory performance.
- The extent to which an individual perceives daily social interactions as negative or distressing (e.g., how often people don't listen when they ask for help, or don't pay attention to them - perceived rejection) or perception about the nature of events and ability to cope (perceived stress) can impact daily life and psychological well-being<sup>3</sup>, perhaps via alteration of recruited neuronal networks.
- Modulation at the network level could reflect a biomarker of risk for early onset of mental health issues, which often emerge during adolescence<sup>4</sup>. Future work should aim to further elucidate relationships between neurobiology, cognition and psychological well-being, in order to identify potential factors that could protect against such vulnerabilities (e.g., connectedness with parental, school, and community).

## References

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**Table 1. Perceived Stress/Rejection, Peer Emotional Abuse**

Perceived Stress	44.4 ± 9.6
Perceived Rejection	49.9 ± 7.8
Peer Emotional Abuse	0.2 ± 0.5

Data represent mean ± standard deviation.

**Table 2. MWT Offline Learning/fMRI Task Performance**

<b>MWT – offline learning</b>	
Hidden path length	1.5 ± 0.7
Hidden percent time in quad	31.2 ± 10.7%
Visible path length	0.51 ± 0.2
<b>MWT – fMRI</b>	
Hidden trials completed	6.4 ± 3.5
Hidden path length	1.2 ± 0.6
Hidden percent time in quad	44.1 ± 14.7%
Visible trials completed	16.0 ± 2.1
Visible path length	0.48 ± 0.06

Data represent mean ± standard deviation.