Decreased sleep duration is associated with increased fMRI responses to emotional faces in children

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Abstract
In adults and children, sleep loss is associated with affective dysregulation and increased responsivity to negative stimuli. Adult functional neuroimaging (fMRI) studies have demonstrated associations between restricted sleep and neural alterations in the amygdala and reward circuitry when viewing emotional picture and face stimuli. Despite this, few studies have examined the associations between short sleep duration and emotional responsivity in typically developing children, and no studies have investigated this relationship using fMRI. The current study examined the relationship between sleep duration and fMRI activation to emotional facial expressions in 15 male children (ages 7–11 years). During fMRI scanning, subjects viewed and made perceptual judgments regarding negative, neutral, and positive emotional faces. Maternal reported child sleep duration was negatively associated with (a) activation in the bilateral amygdala, left insula, and left temporal pole activation when viewing negative (i.e., fearful, disgust) vs. neutral faces, (b) right orbitofrontal and bilateral prefrontal activation when viewing disgust vs. neutral faces, and (c) bilateral orbitofrontal, right anterior cingulate, and left amygdala activation when viewing happy vs. neutral faces. Consistent with our prediction, we also noted that emotion-dependent functional connectivity between the bilateral amygdala and prefrontal cortex, cingulate, fusiform, and occipital cortex was positively associated with sleep duration. Paralleling similar studies in adults, these findings collectively suggest that decreased sleep duration in school-aged children may contribute to enhanced reactivity of brain regions involved in emotion and reward processing, as well as decreased emotion-dependent functional connectivity between the amygdala and brain regions associated with emotion regulation.

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1. Introduction
A growing literature demonstrates the fundamental importance of sleep to human health, development, and wellbeing. Sleep problems have been linked to a variety of physical and mental health problems in adulthood (Benca et al., 1992; Buxton and Marcelli, 2010), as well as increased risk for emotional and behavioral problems in childhood (see Gregory and Sadeh, 2012; Reid et al., 2009; Tkachenko et al., 2014). Despite this, little is known about the physiological processes linking sleep disturbance to these adverse behavioral and psychological outcomes. Alterations in brain systems mediating emotional reactivity have been suggested as one potential mechanism underlying this relationship (Goldstein and Walker, 2014), as sleep disturbance has been associated with alterations in affective functioning across the lifespan (Gregory et al., 2005; Helm et al., 2010; Talbot et al., 2010; Walker and van der Helm, 2009).

In adults, much of the extant literature has focused on the emotional consequences of reduced or restricted sleep duration. Sleep deprivation has been linked to acute increases in emotional lability, emotional responsivity, and physiological arousal in response to positive and negative picture stimuli (Baglioni et al., 2010; Franzen et al., 2011; Walker and van der Helm, 2009; Zohar and Tschinsky, 2005). Adult functional neuroimaging (fMRI) studies have found that sleep deprivation is associated with increased amygdala activation in response to negative stimuli such as emotional pictures, as well as reduced functional connectivity between the amygdala and the medial prefrontal cortex, a brain region implicated in the top down regulation of emotional responses (Yoo et al., 2007). Gujar et al. (2011) also demonstrated that sleep deprived individuals exhibit increased responsivity to positive emotional stimuli in the insula, amygdala, and mesolimbic...
reward areas (ventral tegmental area and putamen), and show a positive bias in rating the valence of neutral and positive pictures relative to rested individuals. When taken together with recent work showing that self-reported sleep quality (which included measures of sleep duration and disturbance) actually moderates the association between amygdala response to fear and negative affect (Prather et al., 2013), these findings suggest that on a behavioral and neurobiological level, sleep deficits can influence individuals’ abilities to process and react to emotionally laden information.

Behavioral studies of sleep with children and adolescents have yielded similar findings. In adolescents, sleep problems such as night waking and poor sleep efficiency predict impaired emotional face processing (Soffer-Dudek et al., 2011). Sleep-restricted preadolescents also experience more intense self-reported feelings of anger, sadness, and fear after viewing negative emotional picture stimuli (Leotta et al., 1997). In school-aged children, sleep disturbance is associated with increased daytime affective dysregulation (Legenbauer et al., 2012). These correlational findings have been confirmed in experimental studies, suggesting that the effect of sleep on emotional responses may be causal in nature. For example, one recent laboratory study employing a nap restriction paradigm found that preschool children whose sleep was restricted were more likely to display negative affect in response to a challenging task (Berger et al., 2012). Another study experimentally manipulated sleep duration over a two week period and revealed that 8–12 year old children whose sleep duration was reduced by one hour per night expressed less positive affective responses to emotional stimuli and were less able to control their emotions, according to parental report (Vriend et al., 2013).

Few neuroimaging studies have examined the relationship between sleep and the neural mechanisms that underlie emotional responsivity in children. In fact, of the four studies to examine youth sleep and brain function, all examined adolescents and focused on reward-based or cognitive control paradigms rather than responsivity to emotional face stimuli more generally (Beebe et al., 2009; Hasler et al., 2012; Holm et al., 2009; Telzer et al., 2013). Thus, despite growing evidence of sleep’s impact on emotional functioning in childhood, relatively little is known about the relationship between sleep disturbance and children’s neural responses to positive and negative emotional stimuli.

The current study addresses this gap in the literature by examining associations between youth sleep and neural responsivity to negative and positive emotional faces in a sample of school-aged children. Given that relevant neuroimaging studies in adults have largely focused on the effects of reduced sleep duration on emotional responsivity, we examined associations between maternal reports of the number of hours children slept the night before testing, as well as the number of hours children typically slept, and fMRI activation when children viewed negative (fear, disgust, anger) and positive (happy) emotional faces.

Guided by findings in the adult literature demonstrating that sleep loss is associated with decreased prefrontal regulation of emotion generation, we hypothesized that youth sleep duration would be negatively correlated with greater activation to emotional stimuli in regions closely linked to emotion generation, including the amygdala and insula. Because different emotions typically elicit different patterns of regional brain activation, we further hypothesized that these correlations with sleep duration would reflect the regions most commonly associated with each emotion, such as the insula for disgust faces and reward-associated regions such as the orbitofrontal cortex for happy faces (Hamann, 2012; Lindquist et al., 2012; Vytal and Hamann, 2010). In line with previous work that has found associations between functional connectivity and sleep duration in adults (Gujar et al., 2011; Yoo et al., 2007), we also predicted that emotion-dependent functional connectivity between the amygdala and regulatory regions such as the prefrontal and cingulate cortex would be positively associated with sleep duration, as this would be consistent with the prediction that sufficient sleep is associated with more effective emotion regulation.

2. Methods

2.1. Participants

Participants in this study were recruited from a larger sample (N=88, 100% male) of children and parents who had recently completed a study on fear processing and child behavior problems (Sylvers et al., 2011). Families in the larger study responded to flyers that targeted pre-adolescent children who were considered by their parents to be “a handful”. Exclusion criteria included mother-reported autism spectrum disorders and intellectual disability. Mothers in the larger study completed the Achenbach Child Behavior Checklist (CBCL; Achenbach, 1991) and children completed a series of laboratory tasks. A subsample of these children (N=18) then participated in the current study several months later. Inclusion criteria for the current study included: right-handedness, no contraindications for MRI, and English as primary language. Children prescribed psychotropic medications other than stimulants were excluded. Children who were prescribed stimulant medications (n=4) refrained from taking them 24 h prior to scanning. Participants underwent a mock scanner training session approximately one week before their scans. Parents provided written consent and children provided written assent prior to the study.

Of the 18 participants who were scanned, 15 provided usable fMRI data for analyses (2 were dropped due to excessive motion artifact, and one was dropped due to experimenter/technical error). Demographic and other descriptive information for the sample as a whole and those included in the final analyses are presented in Table 1.

2.2. Measures

2.2.1. Sleep

Mothers completed a brief health questionnaire on the day of their child’s scan. This questionnaire contained two items relevant to child sleep duration: (1) how many hours did your child sleep last night? (M=9.27, SD=1.22, Range 7–12), and (2) how many hours does your child typically sleep? (M=9.00, SD=1.24, Range=6–10.5). These two maternal reported sleep duration measures were not significantly associated (r=.26, p=.35), and were conceptualized as capturing two distinct features of potential sleep deprivation—chronic and acute. The linear combination of these measures was also included in subsequent analyses and was

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Sample characteristics.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In original sample (n=73)</td>
</tr>
<tr>
<td>Child age in years</td>
<td>8.92 (.97)</td>
</tr>
<tr>
<td>Child ethnicity: %white</td>
<td>46.6</td>
</tr>
<tr>
<td>% African American</td>
<td>42.5</td>
</tr>
<tr>
<td>% Asian</td>
<td>6.8</td>
</tr>
<tr>
<td>% Hispanic</td>
<td>4.1</td>
</tr>
<tr>
<td>CBCL Internalizing T score</td>
<td>55.49 (12.21)</td>
</tr>
<tr>
<td>CBCL Externalizing T score</td>
<td>61.35 (10.08)</td>
</tr>
<tr>
<td>CBCL “Trouble Sleeping” Item</td>
<td>0.29 (0.57)</td>
</tr>
</tbody>
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