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Title: A review of cognitive biases in youth depression: attention, interpretation and memory

Running header: Cognitive biases in youth depression

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Abstract

Depression is one of the most common mental health problems in childhood and adolescence. Although data consistently show it is associated with self-reported negative cognitive styles, less is known about the mechanisms underlying this relationship. Cognitive biases in attention, interpretation and memory represent plausible mechanisms and are known to characterise adult depression. We provide the first structured review of studies investigating the nature and causal role of cognitive biases in youth depression. Key questions are i) do cognitive biases characterise youth depression? ii) are cognitive biases a vulnerability factor for youth depression? and iii) do cognitive biases play a causal role in youth depression? We find consistent evidence for positive associations between attention and interpretation biases and youth depression. Stronger biases in youth with an elevated risk of depression support cognitive-vulnerability models. Preliminary evidence from cognitive bias modification paradigms supports a causal role of attention and interpretation biases in youth depression but these paradigms require testing in clinical samples before they can be considered treatment tools. Studies of memory biases in youth samples have produced mixed findings and none have investigated the causal role of memory bias. We identify numerous areas for future research in this emerging field.

Key words: youth; depression; cognitive bias

Introduction

The risk of depression rises dramatically during childhood and adolescence. One-year point prevalence rates of major depressive disorder (MDD) are around 2-3% in early childhood (pre-adolescence) and increase to around 6% in adolescence (Costello, Erkanli, & Angold, 2006). By age 18 years the prevalence of MDD may be as high as 17%, a statistic which remains relatively unchanged at age 21 years (Hankin, et al., 1998). MDD in childhood and adolescence (hereafter referred to as youth depression) predicts poorer educational and psychosocial outcomes (Birmaher, et al., 1996; Fergusson & Woodward, 2002), long-term psychiatric problems (Knapp, McCrone, Fombonne, Beecham, & Wostear, 2002) and suicidal behaviour (Weissman, et al., 1999). Given these costs to the individual and to society (Wittchen, et al., 2011), identifying effective prevention and treatment is needed to reduce this disease burden. Adult models point to the role of cognitive biases at the level of attention, interpretation and memory in understanding the development and maintenance of depression. These cognitive biases, assessed using novel experimental paradigms, may represent mechanisms by which broader cognitive patterns, typically assessed using self-report measures, arise. Here we provide the first structured review of cognitive biases for negative information during childhood and adolescence – a developmentally sensitive juncture in life. Addressing biases in attention, interpretation and memory processes separately, we examine evidence i) of the presence of the biases in youth depression, ii) that the biases represent a vulnerability factor for youth depression, and iii) that the biases play a causal role in youth depression. Before turning to the child and adolescent literature we briefly outline the state of the adult literature and the contribution that cognitive bias research has made to extending previous cognitive models.

Current treatments for MDD (e.g. cognitive behavioural therapy) are based on cognitive-vulnerability models of depression. These models propose stable and internal cognitive vulnerability factors (e.g. attributional style, rumination) which in interaction with other vulnerability factors (e.g. genetic predisposition, personality) and when triggered by stressful events, can lead to the development of depression (Ingram, Miranda, & Segal, 1998). As such, individuals with dysfunctional attitudes (e.g. “I will never be respected at work”) are likely to respond more negatively to stressful events in life (e.g. a confrontation at work), than those who have a more adaptive cognitive

style (e.g. “my colleagues respect me”). These models are supported by empirical data from cross-sectional studies of clinical and community samples (Mathews & MacLeod, 2005). Prospective studies also suggest that these cognitive styles predict a later diagnosis of depression (Alloy, et al., 2000). Together, these studies - in which cognitive style is assessed using self-report measures - have been valuable in demonstrating the negative content that may characterise cognition in depressed adults. However, the precise mechanisms underlying the relationship between negative cognitive styles and depression are less well established.

Novel experimental paradigms which indirectly assess cognitive processes and minimise participant introspection may provide a more objective means for investigating underlying cognitive biases at various stages of information processing. Studies in depressed adults have revealed cognitive biases for negative information at the level of attention (e.g. speeded reaction times towards negative versus neutral stimuli), interpretation (e.g. resolution of ambiguous words in a negative ways) and memory (e.g. enhanced recall of negative words). For reviews of the presence of these biases in relation to adult depression see (Barry, Naus, & Rehm, 2004; De Raedt & Koster, 2010; Leppanen, 2006; Mathews, et al., 2005) and for a meta-analysis see (Matt, Vazquez, & Campbell, 1992; Peckham, McHugh, & Otto, 2010). Recent evidence supports a combined hypothesis model of cognitive biases in adult depression, in which attention biases for negative information are associated with more negative memories and in turn negative interpretations of novel ambiguous information (Everaert, Duyck, & Koster, 2014).

Experimental cognitive bias modification (CBM) tasks have been used to manipulate negative biases over repeated training sessions, with resultant effects on negative mood and depressive symptoms informing the causality of these biases. Adult CBM studies tentatively imply a causal role of attention and interpretation biases towards negative information in adult depression (Browning, Blackwell, & Holmes, 2013; MacLeod, 2012). Importantly, these cognitive deficits appear not only to play a role in the development of depression in the first place, but also to maintain a depressed mood state (Browning, et al., 2013). Nevertheless, there is a dearth of high quality randomised controlled trials of CBM paradigms in adult depression and meta-analyses of existing CBM paradigms for adult depression show relatively small effect sizes (Cristea, Kok, & Cuijpers, 2015; Hallion & Ruscio,

2011). Together these findings indicate the need for a more solid experimental evidence base on the precise role of cognitive biases in depression before these findings are translated into well-controlled CBM trials.

Can adult cognitive models be extended to youth depression (Lakdawalla, Hankin, & Mermelstein, 2007)? A large literature based on self-reported data demonstrates that youth depression is indeed characterised by negative cognitive styles (e.g. rumination) which in interaction with sources of stress, are longitudinally associated with depression (Abela & Hankin, 2008; Ingram, Nelson, Steidtmann, & Bistricky, 2007; Jacobs, Reinecke, Gollan, & Kane, 2008; Lakdawalla, et al., 2007). However, knowledge is currently lacking in relation to the mechanisms by which cognitive, biological and other vulnerability factors interact in youth depression and the advancement of such knowledge has been identified as a major research priority (e.g., Hankin, 2012). Although relatively under-investigated in youth depression, cognitive biases may prove to be helpful endophenotypes (biomarkers for a disorder which have a genetic component) in this endeavour. As a result of numerous social, cognitive and neurobiological developments which are ongoing during childhood and adolescence (Pfeifer & Blakemore, 2012), there is good reason to believe that the role of cognitive biases in depression may vary between youth and adults. However, predictions about the nature and direction of these effects are difficult to make. One possibility is that, compared to adulthood, cognitive biases play a relatively small role in youth depression, particularly in younger children and adolescents. Early developmental theories suggested that children only develop more stable cognitive styles in early adolescence, once their ability for abstract thinking and operational reasoning is more developed (Lakdawalla, et al., 2007)(see also (Shirk, 1988)). Before this age depressive symptoms may be the direct result of individual negative life experiences, whereas later in adolescence the effect of negative life experiences may be moderated by cognitive style (Cole, Turner, & Jackson, 1993). Based on this theory we might expect that younger children with depression show weaker cognitive biases. In contrast, older adolescents and adults with depression, who are likely to have developed more stable cognitive patterns of thinking, may show stronger cognitive biases (Dearing & Gotlib, 2009). An alternative possibility is that an innate bias towards negative information enables children to detect danger from a young age and that this bias gradually reduces

during development, only remaining present for children who are continually exposed to negative experiences and potentially contributing to their risk of psychopathology (Kindt & Van Den Hout, 2001). According to this theory, which is oriented towards youth anxiety but may have implications for youth depression, children and adolescents may show even stronger cognitive biases than in adults. Indeed, some studies have shown attention biases for negative information in children as young as five years (Kujawa, et al., 2011). These developmental theories highlight the need for more research into the role of cognitive biases in youth depression.

Developmental factors may also have implications for the value of CBM paradigms for youth depression. Since mid-late adolescence is a common period for the onset of depression, intervention during this period could be valuable for the prevention of depression. However, if cognitive biases play less of a role in depression during childhood and adolescence, interventions designed to modify them are likely to be ineffective. On the other hand, the plasticity of the adolescent brain may make this a prime time for targeting interventions designed to modify cognitive biases (Lau & Pile, 2015). A recent meta-analysis of CBM studies for youth mental health problems suggests that CBM can modify attention and interpretation biases, although effects on symptomology remain mixed (Cristea, Mogoase, David, & Cuijpers, 2015). Furthermore, both of these reviews have focussed on youth anxiety rather than depression. As is the case for the adult literature, more experimental evidence about the precise role of cognitive biases in youth depression would help to inform future CBM paradigms for this population.

In summary, the overarching goal of this review is to critique the evidence on cognitive biases in youth depression, arising from novel experimental studies of i) attention, ii) interpretation, and iii) memory biases. **Our first key question is: do cognitive biases characterise youth depression?** We include studies of depressed versus non-depressed children and adolescents. Since depression occurs on a continuous spectrum, and subclinical symptoms of depression predict later disorder (Fergusson, Horwood, Ridder, & Beautrais, 2005), we also include studies of the association between depressive symptoms and cognitive biases in community samples. Where available, we include studies of previously depressed (remitted) youth and their implications for the theory that an episode of depression may leave youth with a cognitive 'scar'. **Our second key question is: do these biases**

represent vulnerability factors for (rather than by-products of) youth depression? We therefore include studies of non-depressed youth with an elevated risk of depression (children of depressed parents). Where appropriate, we also highlight findings from studies of children at risk of developing depression due to other risk factors. **Our third key question is: do these cognitive biases play a causal role in youth depression?** To answer this question we include any study (clinical and unselected samples) targeting youth depression using an intervention (CBM) design in which attention, interpretation or memory biases are manipulated and effects on outcomes assessing youth depression (e.g. negative mood, stress reactivity, depressive symptoms) are measured. Of note, we identified some CBM studies which targeted youth anxiety, but which also included a secondary measure of depression or negative affect e.g. (Eldar, et al., 2012). These studies are not included in this review since they largely include clinically (or sub-clinically) anxious youth or anxiety-related stimuli.

In the interests of providing a timely summary of the breadth and nature of this new but rapidly developing field, and because studies of cognitive biases in youth depression use relatively heterogeneous methods (rendering meta-analytical statistical comparisons between studies meaningless), we elected for a structured rather than a systematic review. Our strategy for selecting papers was as follows. In March 2015 we searched the PubMed database for studies of relevance, using terms such as 'youth', 'child', 'childhood', 'adolescent' or 'adolescence', in combination with 'depression' and 'attention', 'interpretation', 'memory', 'cognitive bias', 'mood induction', 'ambiguous scenario' or 'dot-probe'. The reference lists of the identified studies were also searched. We then took a structured approach to extracting relevant data from the studies and critiquing the overall findings.

In the first three sections of this manuscript we summarise studies focussing on attention, interpretation and memory biases respectively. Within each section we briefly describe the methods used to assess the bias, before describing study findings as they relate to our three key questions. For each of the three sections a table of studies summarises the study characteristics and main findings. Since cognitive-vulnerability models posit that biases are activated during periods of low mood or under stress (Ingram, et al., 1998), the use of mood induction procedures is also documented in these

tables. In the fourth and final section we comment on the contribution these studies to existing cognitive models of youth depression, the limitations of the literature to date, and our recommendations for future research.

1. The role of attention bias in youth depression

Table 1 describes studies measuring attention biases in relation to youth depression.

(Table 1 about here)

Measures of attention bias. Early studies used an emotional version of the Stroop task to measure attention biases in youth depression. However, this measure might tap attention suppression rather than spatial orienting, as suggested by the poor correlation between Stroop task and more commonly used measures of attention bias such as the dot-probe task (Dalgleish, et al., 2003). In the **dot-probe task**, participants are exposed to a negative and a neutral stimulus (typically faces) presented simultaneously for around 500-1500ms (MacLeod, Mathews, & Tata, 1986). A probe subsequently appears in the location of either the negative stimulus (congruent trial) or neutral stimulus (incongruent trial) and participants' reaction times (RT) to identify a characteristic of the probe are measured. Attention biases towards negative stimuli are characterised by faster RTs to congruent trials and slower RTs to incongruent trials. Another measure is an emotional version of the **Go/No-Go task**, in which trials consist of a single presentation of a positive or negative word amongst non-target words for around 300ms (Hare, Tottenham, Davidson, Glover, & Casey, 2005). The target category (positive or negative) varies for each block of trials, with non-target category words acting as distractors. For each block, participants are required to indicate whether a given stimulus is a target and withhold responding if not. Attention bias is characterised by faster reaction times to negative (versus positive or neutral) target words. A more recently used task is the **Emotional Visual Search Task** (EVST)(De Voogd, Wiers, Prins, & Salemink, 2014). Although many variations of the task exist, in the version of the task used to assess attention bias in youth depression participants are presented with a 4 x 4 matrix of 15 distractor faces and one target. The matrix is displayed until the participant demonstrates their response. In one block, the target is a positive face and distractors are negative (fearful, angry or sad). In the other block, the target is a negative face and the distractors are positive. Negative attention bias

is characterised by faster reaction times to identify the negative compared to the positive target. In contrast to the previous tasks, Posner's **spatial cueing paradigm** presents one stimulus at a time and for a briefer duration than the former tasks (around 150ms) (Posner, 1980). In doing so, the task captures more covert, rather than overt, attentional processes (see (Weierich, Treat, & Hollingworth, 2008) for a comparison of attention bias measures). On each trial participants are required to detect a single (emotionally neutral) target, which appears either on the left or right of a fixation cross. A single cue (emotionally negative or neutral) precedes the target either on the same side (valid trial) or opposite side (invalid trial) as the target. Speeded reaction times to the valid trials when the cue is negative (compared to neutral) have been used to indicate a covert engagement bias for negative information. Slowed reaction times to the invalid trials when the cue is negative (compared to neutral) have been used to indicate a covert disengagement bias from negative information.

In addition to collecting behavioural (reaction time) data, eye-tracking has recently been employed to more dynamically (and with greater temporal resolution) investigate attention biases in youth depression (Harrison & Gibb, 2014).

Key question 1: does attention bias characterise youth depression?

Studies of depressed youth. Whilst early studies comparing a sample of clinically depressed youth aged 7-18 with healthy age-matched controls suggested no evidence of group differences in attention biases (Dalgleish, et al., 2003; Neshat-Doost, Moradi, Taghavi, Yule, & Dalgleish, 2000; Neshat-Doost, Taghavi, Moradi, Yule, & Dalgleish, 1997), these findings may be limited by the relatively small sample size studied, or because two of these studies used the emotional Stroop task (Dalgleish et al., 2003; Neshat-Doost et al., 1997), generally now accepted as a measure of inhibition of attention to negative stimuli rather than spatial orienting of visual attention. More recent studies have found evidence of attention biases towards negative stimuli in depressed (versus non-depressed) youth. For example, Hankin and colleagues delivered a dot-probe paradigm (1000ms stimulus exposure) to youth aged 7-19 years with a lifetime diagnosis of depression or anxiety and age-matched healthy controls (Hankin, Gibb, Abela, & Flory, 2010). Participants with depression (but no comorbidity with anxiety) showed an attention bias towards sad (versus neutral) faces. Salum et al. (2013) also used the dot-probe task (500 and 1250 ms exposure durations), finding that vigilance

towards threatening faces was associated with increased internalizing symptoms in children aged 6-12 years with a distress-related disorder (e.g. including depression) whereas in those with fear-related disorders (e.g., phobias), increased symptomology predicted avoidance of threat-related faces (Salum, et al., 2013). A third study investigated attention bias for sad faces in youth with a history of depression or anxiety (mean age 13 years) versus healthy controls with no psychiatric history. Across the whole sample, attention bias for sad faces was positively correlated with current symptoms of depression (Sylvester, Hudziak, Gaffrey, Barch, & Luby, 2015). Attention bias for sad faces was greater in youth with a lifetime diagnosis of depression or anxiety compared to healthy controls, although these effects appear to be driven by attentional avoidance of sad faces in the healthy control group. These effects were observed using the dot-probe task (500ms stimulus exposure) but not replicated using the spatial cueing paradigm (150ms stimulus exposure).

Fairly consistent effects have been found with the Go/No-go task. Maalouf et al. (2012) found evidence of an attention bias towards sad words (300ms exposure) in currently depressed youth (mean age 15 years), but not in never-depressed youth. Similarly, compared to youth with no lifetime history of psychiatric disorder (and no family history of psychiatric disorder) a bias for sad faces (500ms stimulus exposure) was found in another study of clinically depressed youth aged 8-16 years (Ladouceur, et al., 2006). An attention bias for sad words (300ms stimulus exposure) was also found in a sample of youth with a recent episode of MDD (onset within the past year) versus youth with no lifetime history of MDD (Kyte, Goodyer, & Sahakian, 2005). However, another study utilising a Go/No-go task with a 300ms stimulus exposure duration found no evidence of a correlation between symptoms of depression and attention bias for negative words in a sample of adolescents and young adults (age range 14-21 years) with elevated symptoms of depression (score of 14 or above on the Beck Depression Inventory) (Micco, Henin, & Hirshfeld-Becker, 2014).

A final study using eye-tracking during a passive-viewing task (20 second stimulus duration) found that depressed versus non-depressed children aged 8-14 years spent less time attending to sad faces (and increased attention to positive faces) (Harrison, et al., 2014). The authors argued that the longer stimulus duration exposes an emotion regulation strategy (avoidance of sad faces) which is not observable at shorter stimulus durations. Indeed, a meta-analysis of eye-tracking studies during

extended passive viewing suggests that depressed adults also spend less time attending to sad stimuli than non-depressed adults (Armstrong & Olatunji, 2012).

Studies of previously depressed youth. Two studies have examined whether attention biases characterise youth with MDD who are in remission, with conflicting findings (Hankin, et al., 2010; Maalouf, et al., 2012). A dot-probe study (1000ms stimulus exposure) of children aged 9-17 years, found that previously- (versus never-) depressed youth showed an attention bias for sad faces (Hankin, et al., 2010). However, a study using the Go/No-Go task (300ms stimulus exposure) in adolescents (mean age 15 years) found no evidence of a group difference in attention bias for negative words (Maalouf, et al., 2012). One possibility is that attention biases in this group are less reliably seen when shorter stimulus exposure times are used, although comparison of these studies is limited due to the difference in paradigms and stimuli used.

Studies of community samples of youth. Of the four dot-probe studies of attention biases in community samples of youth, one demonstrates a correlation between attention bias towards negative faces (500ms stimulus exposure) and depressive symptoms in youth aged 13-17 years (Platt, Murphy, & Lau, 2015). A second study found attention bias towards negative words (1000ms stimulus exposure) to predict later depressive symptoms in a sample of students (mean age 17 years), for homozygous carriers of the short allele (S) of the 5HTTLPR genotype (Osinsky, Losch, Hennig, Alexander, & Macleod, 2012). A third study of 9-18 year-olds found a correlation between bias for negative words (1250ms stimulus exposure) and negative affectivity (an aspect of temperament thought to be a vulnerability factor for youth depression), but only in children with low effortful control (a trait marker of poor executive control ability) (Lonigan & Vasey, 2009). There was no relationship between attention bias and negative affect in children with higher levels of control. One possible explanation for these findings is that youth with a greater capacity for executive control are able to modify the potentially negative effect that attention towards threat has on their mood. A fourth study of youth aged 8-14 years found that an association between attention bias for negative words (1250ms stimulus exposure) and increased depressive symptoms was better explained by symptoms of anxiety (Reid, Salmon, & Lovibond, 2006). A final study using the EVST (infinite stimulus exposure)

in a sample of adolescents aged 13-16 years found no association between attention bias and depressive symptoms (De Voogd, et al., 2014).

In summary, studies of clinical and community samples suggest that attention biases for negative information do characterise youth depression.

Key question 2: does attention bias represent a vulnerability factor for youth depression?

Studies of children of depressed parents. Of the five studies of children of depressed parents (all mothers), just two studies included a mood induction procedure (Joormann, Talbot, & Gotlib, 2007; Kujawa, et al., 2011), an important methodological factor when testing cognitive-vulnerability models. Comparison of these five studies is made difficult by the fact that mothers in two of the studies did not meet criteria for a diagnosis of depression (Connell, Patton, Klostermann, & Hughes-Scalise, 2013), or had a diagnosis of either anxiety or depression (Waters, Forrest, Peters, Bradley, & Mogg, 2015). Furthermore, in two studies some of the children also showed elevated depressive symptoms (Connell, et al., 2013; Gibb, Benas, Grassia, & McGeary, 2009). Nevertheless, two dot-probe studies (both using stimulus durations of 1500ms) found that non-depressed children (aged 9-14 and 5-7 years respectively) of depressed (versus non-depressed) mothers show an attention bias towards sad faces (Joormann, et al., 2007; Kujawa, et al., 2011). Another two dot-probe studies (stimulus duration 1500ms and 1000ms respectively) found attentional *avoidance* of sad faces (Connell, et al., 2013; Gibb, et al., 2009) in the children (mostly non-depressed) of depressed mothers. Of note, findings in these studies were moderated by two vulnerability factors; the child's trait suppression (avoidance of expressing emotion) and genotype. Youth of depressed (versus non-depressed) mothers showed an attention bias towards sad faces if they reported low levels of suppression (Connell, et al., 2013). In contrast, youth of depressed mothers showed an attention bias away from sad faces if they reported high levels of suppression. Increased maternal symptoms of depression also predicted a greater attention bias away from threat in youths carrying the short (S or L_G) alleles versus those homozygous for the long (L_A) allele of the 5HTTLPR genotype (Gibb, et al., 2009). A final study using the dot-probe task with a shorter stimulus duration (500ms) found that the offspring (mean age 9 years) of mothers with either depression or anxiety displayed at attention bias towards negative stimuli if their mothers also lacked an attention bias towards positive stimuli (Waters, et al., 2015).

Other risk factors. We were able to find two studies of attention biases in children with an elevated risk of depression due to other risk factors; maltreated children aged 11-14 years (Romens & Pollak, 2012) and children aged 7-17 years with severe mood regulation disorder (SMD; a disorder characterised by severe and chronic irritability) (Hommer, et al., 2013). In the former study trait rumination (a risk factor for youth depression) was found to predict stronger attention biases towards sad faces (as measured by the dot-probe task; 1500ms facial stimulus exposure) (Romens, et al., 2012). In the latter study youth with SMD (a predictor of youth depression) showed a stronger bias for threatening faces than age-matched children with no current or past Axis 1 disorder (Hommer, et al., 2013).

In summary, evidence from studies of children of depressed parents suggests that attention biases do represent a cognitive vulnerability factor for youth depression.

Key question 3: does attention bias play a causal role in youth depression?

Current cognitive bias modification of attention (CBM-A) paradigms for youth depression have employed an EVST-based task to train attention towards positive facial stimuli and to encourage disengagement with negative stimuli (De Voogd, et al., 2014; Platt, et al., 2015). A two-session study using this paradigm in typically developing adolescents found that attention biases (as measured using the EVST) could be modified (De Voogd, et al., 2014), although there was no effect of bias change on negative mood. In order to see whether the attentional training effects transferred to another measures of attention bias (the dot-probe task), the same EVST-based CBM-A paradigm was used in another study (also typically developing adolescents) (Platt, et al., 2015). There was no evidence that attention biases had been modified using this task, although this may be because the study involved just a single-session of training.

Summary of the role of attention bias

Evidence from depressed (versus non-depressed) participants suggests that youth depression is characterised by attention biases towards negative (mostly sadness-related) stimuli. Studies from previously depressed youth, which test whether cognitive biases represent a cognitive 'scar' following depression, are less conclusive. Studies of community youth samples have found correlations between attention bias and depressive symptoms or negative affect, effects which are moderated by effortful

control and genotype. However, one study found no evidence of a correlation between attention bias and depressive symptoms and another found effects which may be better explained by anxiety (Reid, et al., 2006). Cognitive-vulnerability models of youth depression are supported by studies of children of depressed (versus non-depressed) parents, although these findings may also be moderated by genetic and personality factors, and by parental attention bias. Few studies have included mood- or stress-induction procedures, something which is important if cognitive-vulnerability models are to be tested.

To date, the visual-search paradigm is the only CBM-A paradigm to investigate the causal role of attention biases in youth depression. Preliminary data suggested that it is possible to modify attention to negative stimuli using this task, although multiple training sessions may be needed and it remains unclear whether training effects transfer to other measures of attention bias. Large-scale trials of the effectiveness of CBM-A in modifying symptoms of depression in youth are yet to be conducted.

2. The role of interpretation biases in youth depression

Table 2 describes the studies assessing interpretation biases in youth depression.

(Table 2 about here)

Measures of interpretation bias. Perhaps the most predominant measure of interpretation bias in youth depression is the ambiguous scenarios (AS) task (Mathews & Mackintosh, 2000). Participants read numerous ambiguous scenarios and are then presented with four possible interpretations, each of which they rate in terms of their own endorsement. One interpretation is positive, another negative, and the two remaining interpretations (also one positive and one negative) are foil interpretations (not related to the scenario). To ensure participants actively read the scenario, the last word of the scenario is always presented as a word fragment which participants must complete in order to see the possible interpretations. An alternative to the ambiguous scenarios task involves resolving ambiguous words (AW). In one version of the task participants listen to auditory stimuli which are blends of either positive-neutral or negative-neutral word pairs and are asked to identify which word they heard (Dearing, et al., 2009). In another version of the task participants are asked to generate a sentence from a given homophone (a word which has a negative as well as neutral/positive meaning e.g. leaves, hit,

hang). The resulting sentence is coded as negative or neutral depending on the meaning selected (e.g. "the boy hit him" versus "the song was a big hit") (Eley, et al., 2008).

Key question 1: does interpretation bias characterise youth depression?

Studies of depressed youth. The only study to date of interpretation biases in a clinical sample of youth used the AS task in adolescents (aged 14-21 years) with elevated depressive symptom scores (> 14 on the Beck Depression Inventory) (Micco, et al., 2014). Since the primary aim of the study was to evaluate the efficacy of a CBM training programme for depressed adolescents, there was no formal (non-depressed) control group. However, as part of a validation of the measure used to assess biases, the authors compared interpretation bias with a sample of adolescents with no psychopathology, finding significantly more negative interpretation biases in the depressed (versus non-depressed) group. Furthermore, within the depressed sample, interpretation bias showed a positive correlation with depressive symptom severity. As far as we are aware, no studies have investigated interpretation bias in previously depressed youth.

Studies of community samples of youth. Across all three studies using the AS task to measure the association between implicit interpretation bias and symptoms of depression in relatively large community samples of youth, increased depressive symptoms appear to be significantly associated with more negative interpretations (Dineen & Hadwin, 2004; Eley, et al., 2008; Reid, et al., 2006). These findings also appear to hold true when the AW task is used to measure interpretation biases (Eley, et al., 2008) and when free responses to the AS task are coded (Reid, et al., 2006). Studies of community samples have also examined the role of other factors, albeit with mixed findings. Whereas one large study of interpretation biases in twins suggests that the association between depression and interpretation biases (as measured by AW and AS) is independent of any association with anxiety (Eley, et al., 2008), another AS study suggests the opposite (Reid, et al., 2006). A sub-analysis by Dineen and colleagues compared interpretations (using the AS task) of self-judgements and other judgements (e.g. judgements about friends), finding that increased depressive symptoms were associated with more negative self-judgements specifically (Dineen, et al., 2004).

In summary, community studies suggest interpretation biases play a role in youth depression, findings which are supported in study of a clinically depressed population.

Key question 2: does interpretation bias represent a vulnerability factor for youth depression?

Studies of children of depressed parents. In the only study of children of depressed parents identified, never-depressed daughters of depressed mothers were found to draw significantly more negative interpretations (assessed using the AW and AS tasks), than never-depressed daughters of mothers with no psychiatric history (Dearing, et al., 2009).

Other risk factors. A study of young adults (mean age 18 years) used the scrambled sentences test to investigate interpretation biases in an unselected sample who reported on child abuse (a risk factor for depression) (Wells, Vanderlind, Selby, & Beevers, 2014). In the task participants are required to resolve a set of scrambled words into a sentence. Each set of words has two possible solutions (one negative and one positive (e.g. "the looks very future dismal bright"). Participants who had experienced child abuse and systematically resolved ambiguous sentences in a negative manner were most likely to experience depressive symptoms.

Key question 3: does interpretation bias play a causal role in youth depression?

Two studies have investigated the causal role of interpretation bias for negative information in relation to youth depression (Table 2). The first cognitive bias modification of interpretations (CBM-I) training study delivered a single session of positive versus negative interpretation bias (based on the AS task) to typically-developing adolescents (aged 13-17 years) and measured effects on interpretation bias (using the AS task) and mood (Lothmann, Holmes, Chan, & Lau, 2011). Both forms of training were effective in manipulating cognitive biases and mood (Lothmann, et al., 2011). A second CBM-I study of depressed youth (aged 14-21 years) found no effect of a single positive (versus neutral) training session on interpretation bias or symptom severity, although negative cognitions appeared to be improved and modest effects on interpretation bias were seen for patients who showed a bias at baseline (Micco, et al., 2014). A diagnosis of depression was not a prerequisite for inclusion in this study.

Summary of the role of interpretation bias

All three studies of community samples found evidence of a correlation between negative interpretation bias and increased depressive symptoms. A similar correlation was also found in a

sample of depressed adolescents. One study of the non-depressed daughters of depressed (versus non-depressed) mothers supports cognitive-vulnerability models of youth depression, tentatively suggesting that implicit interpretation biases may not simply be the by-product of depression. A study of a community sample of youth supports the causal role of interpretation bias in negative mood. However, neither this study, nor a study of depressed youth, found effects of CBM-I training on depressive symptoms.

3. The role of memory biases in youth depression

Table 3 describes studies of memory biases in youth depression. As far as we are aware, no studies have tested the causal role of memory biases using CBM paradigms therefore key question three cannot be addressed.

(Table 3 about here)

Measures of memory biases. The majority of studies have used free-recall tasks to assess the extent to which depression is associated with a tendency to recall negative (versus positive) stimuli from a previously encoded set of words (or stories), often using the self-referent encoding task (SRET) to encode stimuli (Hammen & Zupan, 1984). In this task participants are presented with positive and negative adjectives and are asked to rate how much they describe themselves. Participants are informed that a recall task will follow the SRET, in which they have one minute to recall as many words as possible. Memory bias is typically measured by the proportion of positive and negative words which the participant has endorsed as self-referent and is able to recall. Other researchers have tested free-recall of emotional (depression- or threat-related) words without the self-referent component to encoding or used recognition (rather than recall) tests of emotional (positive or negative) stories.

Key question 1: does memory bias characterise youth depression?

Studies of depressed youth. Findings from studies of depressed (versus non-depressed) youth provide mixed evidence of memory biases for negative information. One study of 8-16 year-olds found enhanced recall of negative versus positive self-referent adjectives in depressed versus non-depressed youth (Zupan, Hammen, & Jaenicke, 1987). These participants were recruited because their mothers

had either i) a history of depression or bipolar disorder, ii) a chronic medical illness, iii) or had no psychiatric or chronic medical history. Since maternal psychopathology was not taken into account in statistical analysis it is therefore difficult to determine the extent to which results reflect the child's current depressive symptoms versus maternal psychopathology. A memory bias in recall, but not recognition, of negative (versus positive) words did characterise a sample of non-clinically depressed versus non-depressed 10-17 year olds, with data suggesting that the association between negative memory bias and depression may increase with age (Neshat-Doost, Taghavi, Moradi, Yule, & Dalgleish, 1998). However, other studies have failed to replicate these findings. For example, an early study found differences between depressed and non-depressed children (aged 8-12 years) in their recall of self-referent words, although this may be because participants in the 'depressed' group showed elevated depressive symptoms rather than a diagnosis of depression (Hammen, et al., 1984). There was no evidence of a memory bias for negative words in sample of clinically depressed versus non-depressed youth aged 7-18 years (Dalgleish, et al., 2003). The most recent study investigated free-recall of self-referent words in currently-, previously-, and never-depressed youth (aged 8-18 years) following a mood induction procedure (Timbremont, Braet, Bosmans, & Van Vlierberghe, 2008). There was no evidence of a group difference in memory bias between currently- and previously-depressed youth, or between previously- and never-depressed youth. A final study assessed the role of memory bias in predicting depressive symptoms in a sample of youth psychiatric inpatients (aged 9-17) with a range of diagnoses (around 44% had a non-bipolar mood disorder) (Gencoz, Voelz, Gencoz, Pettit, & Joiner, 2001). Lower recall of positive adjectives (but not enhanced recall of negative adjectives) predicted increased symptoms of depression, although few patients in the sample had a diagnosis of depression alone.

Studies of community samples of youth. Two studies have used the self-referent encoding task (SRET) to measure memory bias for positive and negative words in community samples. In an early study of youth aged 8-14 years there was no evidence of an association between memory bias for negative words and depressive symptoms, although a variable combining symptoms of depression, fear, anxiety and aggression did positively predict negative memory bias (Reid, et al., 2006). In a more recent study of 6 year olds, reduced recall of positive words (but not enhanced recall of negative

words) predicted depressive symptoms at age 9 (Goldstein, Hayden, & Klein, 2014). The remaining two studies assessed memory bias for negative (versus positive) stories in community samples. The first study (children aged 5-11 years) found that those with more symptoms of depression were more likely to recall negative (versus positive) stories than those with fewer symptoms (Bishop, Dalgleish, & Yule, 2004). Although this study found no effect of age on the relationship between memory bias and depressive symptoms, this may be due to the relatively small age range of the sample. Contrary to expectations, the second study (youth aged 10-13 years) found that those with more depressive symptoms recalled *more* positive (and less negative) stories than those with fewer symptoms (Hughes, Worchel, Stanton, Stanton, & Hall, 1990). One possibility for these unusual findings is that encoded stimuli were not self-referent (see (Bishop, et al., 2004) for a discussion).

In summary, there is no consistent evidence from clinical or community samples for the role of memory biases in youth depression.

Key question 2: does memory bias represent a vulnerability factor for youth depression?

Studies of children of depressed parents. A study of the daughters (aged 10-14) of recently-depressed mothers found that genotype modified the effect of parental risk for depression on youth memory bias for self-referent words (Asarnow, Thompson, Joormann, & Gotlib, 2014). There was no difference in the recall of positive and negative adjectives between daughters of depressed versus non-depressed mothers. However, daughters of depressed mothers homozygous for the Val allele of the COMT Val158Met genotype recalled significantly more positive (but not negative) self-referent words than those homozygous for the Met allele, suggesting a protective role of the Val/Val genotype.

Summary of evidence for memory bias

The literature on negative memory biases in youth depression is relatively inconclusive. Although findings from two studies support a negative memory bias in depressed youth, one of these involved a clinically-heterogeneous sample and the other found evidence of a memory bias in recall but not recognition. A further three studies found no evidence of a memory bias in youth depression. Whereas two studies of community samples provide preliminary evidence to support the role of memory bias in youth depression, another found no effects and a third found depressive symptoms to be associated with memory bias for positive information. A study of daughters of depressed mothers tentatively

supports a cognitive-vulnerability model of memory bias in youth depression – finding that youth at familial risk of depression homozygous for the Met allele of the COMT genotype recalled less positive words that youth at-risk who possess the Val/Val genotype. There have been no studies investigating the causal role of memory biases for negative information in youth depression.

4. General discussion

This is the first review to assess the role of cognitive biases in youth depression, including the extent to which they represent a vulnerability factor and play a causal role in youth depression. We assessed the contribution of cognitive bias studies to models of youth depression across three key questions.

Our first key question was whether cognitive biases for negative information characterise youth depression. In line with the adult literature (Mathews, et al., 2005), we found relatively consistent evidence of an attention bias for negative (mostly sad) words and faces, in depressed versus non-depressed youth (Hankin, et al., 2010; Harrison, et al., 2014; Ladouceur, et al., 2006; Maalouf, et al., 2012; Salum, et al., 2013) as well as in community samples of youth (Lonigan, et al., 2009; Osinsky, et al., 2012; Platt, et al., 2015). Similar findings characterised studies of interpretation biases in community samples of youth (Dineen, et al., 2004; Eley, et al., 2008; Reid, et al., 2006), although to date no study has directly compared interpretation bias between depressed and non-depressed youth. Together, these findings implicate a role for cognitive biases towards negative information, at the level of attention and interpretation, in youth depression. They supplement existing cognitive models of youth depression by identifying the potential mechanisms that may underlie broader cognitive deficits. Of note, we found more mixed evidence for the role of memory biases for negative information in youth depression. This contrasts with the adult literature, where memory biases for negative information have been demonstrated consistently (Matt, et al., 1992) and perhaps even more so than attention biases (Williams, Watts, MacLeod, & Mathews, 1997). This discrepancy from the adult literature may be because relatively few studies have investigated the role of memory biases in youth depression. Findings concerning the presence of attention and memory biases in currently versus previously depressed youth are mixed, and no studies have investigated interpretation biases in these samples.

Our second key question was whether these cognitive biases represent cognitive vulnerability factors for youth depression. Support for the role of cognitive biases as a vulnerability factor for youth depression comes from studies of non-depressed youth who have an elevated risk of developing depression (e.g. the children of depressed parents). Compared to youth with a lower risk of depression, those with an elevated risk showed attention (Connell, et al., 2013; Gibb, et al., 2009; Hankin, et al., 2010; Joormann, et al., 2007; Kujawa, et al., 2011; Kyte, et al., 2005; Sylvester, et al., 2015; Waters, et al., 2015), interpretation (Dearing, et al., 2009), and memory (Asarnow, et al., 2014) biases towards negative information. In accord with major international research agendas (Hankin, 2012), these findings pave the way for investigating the mechanisms by which biological and environmental vulnerability factors interact in youth depression.

Our third key question was whether cognitive biases play a causal role in the development of youth depression. Building on the findings of cognitive bias modification studies of adult depression, we addressed this issue by reviewing evidence from CBM paradigms targeting youth depression. Preliminary evidence suggests that it is possible to modify attention (De Voogd et al., 2014) and interpretation (Lothmann, et al., 2011) biases using CBM-A and CBM-I tasks. Although there is some evidence that interpretation biases may play a causal role in negative mood in youth, no CBM-A paradigm has been able to modify negative mood and the effectiveness of CBM-A and CBM-I tasks in modifying symptoms of depression remains to be shown. CBM paradigms require further development before reliable changes in cognitive bias and mood can be measured and CBM paradigms also require testing in clinically depressed youth. With mixed evidence of the role of memory bias for negative information in youth depression, CBM paradigms aimed at modifying memory biases may be premature.

Limitations

A first limitation of the studies reviewed is that stimuli often vary between studies in terms of format (e.g. words versus faces), emotion (e.g. sad versus angry), and exposure duration (e.g., short and long durations), making collation and comparison of data difficult. The use of more standardised paradigms and stimulus sets would therefore be beneficial. A related limitation is that the mechanisms underlying the findings from current measures of attention bias need to be clarified. For example, whereas the

dot-probe task measures an overt engagement bias, the version of the EVST task used in studies of youth depression (which include trials where negative stimuli are distractors from a positive target) also contains an element of overt attentional disengagement. Although the spatial cueing paradigm attempts to distinguish the processes of attention engagement with and disengagement from negative stimuli, the short stimulus duration means that the task targets covert (rather than overt) attention processing (Weierich, et al., 2008). Furthermore, the measure of disengagement on invalid trials is confounded by the extent to which the participant initially engages with the cue (Grafton & MacLeod, 2014). In the search for paradigms which are able to tease apart overt and covert engagement versus disengagement, a novel modification of the dot-probe task, the "ARDPEI" task, may be helpful (Grafton, et al., 2014). Similarly, whereas most behavioural paradigms typically measure attention at a single point in time, eye-tracking may be more suited to capturing the dynamic nature of attention across time.

The third limitation of the studies reviewed is that although cognitive models of youth depression posit that cognitive biases are a vulnerability factor for depression – remaining latent in certain individuals and only eliciting depressive symptoms when activated by stress (Abela, et al., 2008) – few studies of cognitive biases in non-depressed samples have included a mood induction procedure, and just one has tested the effect of cognitive biases on stress reactivity.

A final limitation relates to the conduct of this review itself. A structured approach was chosen over a systematic review and/or meta-analysis, since the research field is emerging and includes relatively heterogeneous studies and just a few studies in some areas. Therefore, our aim was to provide a structured summary of this rapidly developing field that might stimulate further research. Nevertheless, it is possible that studies describing implicit cognitive biases using alternative terminology were inadvertently omitted from the review. As such, the comprehensiveness of the review, and ability of others to replicate our search strategy is compromised. Our hope is that the review stimulates and guides future research in this field such that a systematic review will be possible in the future.

Future research directions

In addition to addressing the methodological limitations of the existing literature, we identify some directions in which future studies of cognitive biases in youth depression could develop. Firstly, recent cognitive models of adult anxiety (Hirsch, Clark, & Mathews, 2006; Ouimet, Gawronski, & Dozois, 2009) and depression (Everaert, Koster, & Derakshan, 2012) emphasise the theoretical and clinical importance of studying the interplay between attention, interpretation and memory biases. Establishing the relationship between these biases could have important treatment implications. For example, modifying interpretation biases without addressing underlying attention biases may be ineffective in sustaining mood changes. Although this has been discussed in relation to youth depression (Reid, et al., 2006), it is yet to be empirically investigated.

Another important area of research would be to determine how the relationship between cognitive biases and depression changes developmentally throughout childhood and adolescence (Abela, et al., 2008). As previously discussed, if it is true that stable cognitions do not emerge until early adolescence (Cole, et al., 1993; Lakdawalla, et al., 2007), one might predict a weaker association between depression and cognitive biases for negative information in younger children (Dearing, et al., 2009). However, some studies reviewed here suggest that cognitive biases may be associated with depression as early as age 5 (Kujawa, et al., 2011), supporting the notion that cognitive biases do emerge from an early age (Kindt, et al., 2001). Future studies investigating biases across a wide developmental period would be helpful in establishing how and when these biases emerge.

Adult models of depression suggest that level of cognitive control may determine the impact of cognitive biases on vulnerability for depression. According to dual-process models, individuals who possess a cognitive bias towards negative stimuli are more vulnerable to depression if they are not able to control this automatic tendency through reflective (controlled and effortful) processing (Beevers, 2005). Two studies of youth also demonstrate that individuals who with less cognitive control show an increased (positive) association between markers of psychopathology (e.g. negative affect, symptoms of anxiety) and negative biases in attention (Lonigan, et al., 2009) and interpretation (Salemink & Wiers, 2012). Cognitive control may therefore be an important moderating factor to consider in future studies of the role of cognitive biases in youth depression.

In an effort to understand how cognitive biases emerge, another aspect worth considering in future research is the role of cognitive biases in the familial transmission of depression. Although cognitive biases are proposed as mechanisms by which the risk of depression is transferred from parent to child, astonishingly just one study has examined the association between child and parental cognitive biases (Waters, et al., 2015). No study has employed a similar design to investigate the transmission of interpretation bias from (depressed) parent to child and it remains unknown whether these biases are transmitted via genetic or learned pathways, or a combination of both.

With a greater understanding of the nature of cognitive biases in youth depression, an important next step in this field would be to develop more effective CBM paradigms for investigating the causal role of cognitive biases in youth depression. Single-session CBM studies for youth depression appear to be relatively unsuccessful in modifying cognitive biases and markers of depression. An ongoing study by De Voogd, Salemink and colleagues of multiple sessions of CBM-A and CBM-I training for symptoms of depression in youth is currently underway. Given that the literature reviewed suggests youth depression may be characterised by attention biases towards sad (as well as angry) faces, future CBM-A paradigms targeting these stimuli may also be worth investigating. The use of mental imagery techniques may improve the ability of CBM-I paradigms to modify biases and have an effect on symptoms. Although mental imagery appears to play an important role in the efficacy of CBM-I paradigms for adult depression (Lang, Blackwell, Harmer, Davison, & Holmes, 2012), existing CBM-I paradigms for youth have not yet included this element. Finally, although existing CBM-I studies have used the ambiguous scenarios test, our review suggests that equally strong biases can be found using ambiguous words, begging the question of whether even simpler, word-based, CBM paradigms would be effective. Robust CBM paradigms are necessary if the causal role of cognitive biases in predicting physiological responses to stress is to be studied in youth, as it has been in adults (Baert, Casier, & De Raedt, 2012).

A final note relates to the clinical application of CBM paradigms for youth depression. Although there is great excitement about the clinical potential of CBM paradigms, their application to the treatment of youth depression should perhaps progress cautiously, until there is robust experimental evidence of their ability to modify cognitive biases and symptoms of depression in youth

samples. This is particularly relevant since a recent review of the adult literature demonstrated that mixed findings in relation to CBM-A effects on symptoms of anxiety could be explained by the failure of CBM-A tasks to modify cognitive bias (Clarke, Notebaert, & MacLeod, 2014). Furthermore, once CBM tasks have shown to be effective in modifying cognitive biases and mood in large community samples, their ability to modify symptoms of depression should be tested in clinically depressed samples. We recommend that more resources be invested into understanding the precise nature of cognitive biases in youth depression, and using such knowledge to inform the development of effective CBM paradigms before CBM paradigms are considered therapeutic tools for the treatment of youth depression.

Conclusion

Contemporary models suggest that youth depression is associated with negative cognitive styles. An important next step is to establish the mechanisms by which a tendency for negative thinking leads to symptoms of depression. In this review we synthesised findings on attention, interpretation and memory biases for negative information in youth depression. We found reasonable evidence to support the role of attention and interpretation biases in youth depression but there was mixed evidence from studies of memory biases. Evidence of stronger biases in children at risk of depression suggests these biases may represent a cognitive vulnerability factor. Preliminary evidence supports a causal role of attention and interpretation biases in youth depression, although studies of larger, clinical samples are required, and CBM paradigms require further development before they can be recommended as treatment tools. Based on the review we have developed a number of suggestions for future research which we believe will inform the development of more effective treatment and prevention programmes for youth depression.

Table 1: Studies of attention biases in youth depression

Study	Sample description	Measure of bias	Stimuli valence	Use of mood induction procedure	Analysis	Results
	Depressed youth					
(Dalgleish, et al., 2003)	N=93 youth aged 7-18 with MDD (N=19), PTSD (N=24), anxiety (N=24) or no lifetime psychiatric disorder (N=26)	Dot-probe (words; 1500ms) and Stroop	Threat; depression-related (e.g. sad); neutral	No	Between-groups	Depressed adolescents showed no evidence of an attention bias for threat- or depression-related words on the dot-probe or Stroop task.
(Hankin, et al., 2010)	N=161 youth aged 9-17 with a lifetime psychiatric diagnosis (N=29 MDD; N=14 MDD + anxiety; N=21 anxiety) or no lifetime psychiatric disorder (N=97)	Dot-probe (faces; 1000ms)	Sad; happy; angry, neutral	No	Between-groups	Attention biases to sad faces characterised youth with a lifetime diagnosis of depression compared to anxious youth and healthy controls. Findings characterised both currently and previously depressed adolescents (compared to anxious youth and healthy controls).
					Symptom x bias correlation	No correlation between symptoms of depression and attention bias.

(Harrison, et al., 2014)	N=40 youth aged 8-14 with MDD (N=19) or no lifetime psychiatric disorder (N=21)	Passive-viewing task (faces; 20 s)	Happy; sad; angry; neutral	No	Between-groups	Children with depression, compared to children with no history of depression, spent less time looking at sad faces and more time looking at happy faces.
(Kyte, et al., 2005)	N=79 youth (mean age=15 years) with a recent episode of MDD (N=30) or no history of MDD (N=49)	Go/No-go (words; 300ms)	Positive (happy); negative (sad)	No	Between-groups	Recently depressed adolescents (versus control group) made more errors on happy versus sad trials. There were no group differences in omissions.
					Symptom x bias correlation	No correlation between symptoms of depression and attention bias.
(Ladouceur, et al., 2006)	N=68 youth aged 8-16 with current MDD (N=19) or anxiety (N=23), or no lifetime psychiatric disorder and no familial risk of psychopathology (N=26)	Go/No-Go (faces; 500ms)	Angry; fearful; sad; happy; neutral	No	Between-groups	Depressed versus control youth responded more quickly towards sad (Go) trials embedded in neutral (No-Go) trials.
(Maalouf, et al., 2012)	N=57 youth (mean age 15 years) with a current (N=20) vs. past (N=20) vs. no (N=17) MDD	Go/No-go (words; 300ms)	Positive (happy); Negative (sad)	No	Between-groups	Currently depressed adolescents were faster on the shift to negative stimuli than previously- and never-depressed adolescents.
					Symptom x	No correlation between symptoms of depression and attention

					bias correlation	bias.
(Micco, et al., 2014)	N=45 youth aged 14-21 with a BDI score ≥14	Go/No-go (words; 300ms)	Positive; negative	No	Symptom x bias correlation	No correlation between symptoms of depression and attention bias.
(Neshat-Doost, et al., 1997)	N=64 youth aged 9-18 with MDD (N=19), MDD + anxiety (N=19) or no lifetime psychiatric disorder (N=26)	Stroop (words)	Depression-related; threat; trauma; happy; neutral	No	Between-groups	No group difference in attention bias.
					Symptom x bias correlation	No correlation between symptoms of depression and attention bias.
(Neshat-Doost, et al., 2000)	N=45 youth aged 9-17 with MDD (N=19) or no history of emotional disorder (N=26)	Dot-probe (words; 1500ms)	Physical threat; social threat; depression-related	No	Between-groups	No group difference in attention bias.
(Salum, et al., 2013)	N=1774 youth aged 6-12 with a distress-related disorder (N=66), a fear-related disorder (N=86), a behavioural disorder	Dot-probe (faces; 500 and 1250ms)	Angry; happy; neutral	No	Between-groups	Interaction between group, stimulus valence, and internalizing symptom severity. A bias for threatening faces was found for those with no disorder or a distress-related disorder (but not those with a fear-related disorder or behavioural disorder) who also showed high (versus low) internalising symptom severity. In those

	(N=211) or no psychiatric disorder (N=1411)					with fear-related disorders, high (versus low) internalising symptom severity predicted avoidance of threat-related faces.
(Sylvester, et al., 2015)	N=73 youth (mean age 13) with a history of MDD or anxiety (N=40) or no history of psychiatric disorder (N=33)	Spatial cueing paradigm (faces; 150ms)	Angry; sad; neutral	No	Between-groups	No between group differences in bias towards sad faces.
					Symptom x bias correlation	No correlation between symptoms of depression and attention bias.
		Dot-probe task (faces; 500ms)	Angry; sad; neutral	No	Between-groups	Youth with a history of depression showed a greater bias towards sad faces compared to youth with no history.
					Symptom x bias correlation	Attention bias towards sad faces correlated positively with current symptoms of depression.
	Community samples					
(De Voogd, et al., 2014)	N=32 unselected youth aged 13-16	EVST (faces; infinite presentation)	Positive (happy); negative (sad, angry, fearful)	No	Symptom x bias correlation	No correlation between symptoms of depression and attention bias.
					2 sessions of EVST-based	Training was more effective than placebo-control training in modifying biases but did not change mood or self-esteem.

					CBM-A training	
(Lonigan, et al., 2009)	N=104 youth aged 9.6-18.5 selected based on scores in the upper or lower quartile for negative affect and effortful control	Dot-probe (words; 1250ms)	Threat; neutral	No	Between-groups	Children high in negative affect and low in effortful control demonstrate attention bias towards threat.
(Osinsky, et al., 2012)	N=120 students (mean age=17.7)	Dot-probe (words; 1000ms)	Negative; neutral	No	Regression	Attention bias towards negative words predicted increased symptoms of depression across a semester. This effect was moderated by serotonin transporter (5HTTLPR) genotype, with the relationship only present in homozygous carriers of the short (S) allele.
(Platt, et al., 2015)	N=105 unselected youth aged 13-17	Dot-probe (faces; 500ms)	Threat; neutral	No	Symptom x bias correlation	Correlation between negative attention bias and increased depressive symptoms.
					1 session of CBM (visual-search)	No effect of training on attention bias or mood.

					training	
(Reid, et al., 2006)	N=133 unselected youth aged 8-14	Dot-probe (words; 1250ms)	Threat; neutral	No	Symptom x bias correlation (regression)	Attention bias towards threat was correlated with increased depressive symptoms but overall anxiety explained these effects.
	Children of depressed parents					
(Connell, et al., 2013)	N=59 youth aged 11-17 with parents who had 'concerns about symptoms of depression'. Some of the children had CDI scores above the clinical cut-off of 12	Dot-probe (faces; 1500ms)	Sad; happy; neutral	No	Regression	Increased depressive symptoms predicted bias *away* from sad faces. Increased depressive symptoms and high suppression was associated with a bias *towards* sad faces, whereas depressive symptoms and low suppression were associated with a bias *away* from sad faces.
(Gibb, et al., 2009)	N=74 youth aged 8-12 of mothers with MDD during the child's lifetime (N=40) or no psychiatric history (N=34). Ten children had MDD	Dot-probe (faces; 1000ms)	Sad; happy; angry; neutral	No	Between-groups	Children of depressed mothers showed attentional avoidance of sad faces (compared to controls). Effects remained when controlling for current symptoms in the child and mother. Some evidence that attention bias in children of depressed mothers was stronger for those carrying the short allele (S or L_G) of the serotonin transporter (5HTTLPR) genotype

					Symptom x bias correlation	Higher child depression scores were associated with greater avoidance of sad faces.
(Joormann, et al., 2007)	N=41 non-depressed girls aged 9-14 of mothers with a history of MDD (N=20) or no history of MDD (N=21)	Dot-probe (faces; 1500ms)	Happy; sad; neutral	Yes	Between-groups	At-risk children showed bias towards negative faces but no bias towards positive faces. Control participants showed opposite pattern of effects.
(Kujawa, et al., 2011)	N=99 non-depressed youth aged 5-7 of mothers with (N=36) or without (N=63) a lifetime history of MDD	Dot-probe (faces; 1,500ms)	Happy; sad; neutral	Yes	Between-groups	Daughters of depressed mothers showed a bias towards sad faces, whereas daughters of non-depressed mothers, and sons in both groups, showed no attentional bias.
					Symptom x bias correlation	No correlation between symptoms of depression and attention bias.
(Waters, et al., 2015)	N=67 youth (mean age 9 years) of mothers with an emotional disorder (MDD or anxiety; N=38) or mothers with no psychiatric history (N=29)	Dot-probe (faces; 500ms)	Angry; happy; neutral	No	Between-groups	No main effect of maternal psychopathology on child attention bias, but child attention bias did correlate with maternal attention bias. Children of mothers with an emotional disorder showed an attention bias if their mother had an attention bias away from positive information.
					Symptom x	No correlation between symptoms of depression and attention

					bias correlation	bias.

BDI=Beck Depression Inventory; CDI=Children's Depression Inventory; CBM=Cognitive Bias Modification; MDD=Major Depressive Disorder; EVST = Emotional Visual Search Task: PTSD=Post-traumatic Stress Disorder

Table 2: Studies of interpretation biases in youth depression

Study	Population	Measure	Stimuli valence	Use of mood induction procedure	Analysis	Results
	Depressed youth					
(Micco, et al., 2014)	N=45 youth aged 14-21 defined as depressed based on a BDI score ≥14	AS	Positive; negative	No	Between-groups (informal comparison with a sample of 24 healthy participants)	Depressed participants had more negative biases at baseline than healthy controls.
					Symptom x bias correlation	Interpretation bias correlated with depressive symptoms.
					Single-	Of those with a bias for negative information at baseline, the

					session CBM (AS-based) Positive versus neutral training	intervention group showed greater improvement in interpretation bias at mid- and post-treatment. The intervention group overall had greater improvements in self-reported negative cognitions than the control group at post-intervention and two-week follow-up. No differences between groups in symptom change.
	Community samples					
(Dineen, et al., 2004)	N=29 unselected youth aged 6-10	AS (second person)	Negative; neutral	No	Regression	Increased depressive symptoms were associated with more negative interpretations.
(Eley, et al., 2008)	N=300 eight-year-old twin pairs with high or low trait anxiety	AS; AW	Threatening: neutral	No	Symptom x bias correlation	Depressive symptoms correlated with both measures of interpretation bias (remained when anxiety was controlled for). Genetic and environmental factors contributed to the association between depression and AS interpretations.
(Lothmann , et al., 2011)	N=82 unselected youth aged 13-17	AS	Negative; positive	No	Single-session CBM (AS-based).	Both forms of training were successful in manipulating interpretation bias. For male (but not female) participants, positive training reduced negative mood and negative training reduced positive mood.

					Positive versus negative training.	
(Reid, et al., 2006)	N=133 unselected youth aged 8-14	AS (free responses coded)	Negative; or positive; neutral (social situations with peers)	No	Symptom x bias correlation	Depressive symptoms correlated with interpretation bias (although a regression model including depression was not significant).
	Children of depressed parents					
(Dearing, et al., 2009)	N=39 non-depressed daughters of mothers with a history of MDD during the child's lifetime (N=16) or mothers with no current or previous Axis-1 diagnosis (N=23)	AW, AS	AW: Positive (e.g. joy); depression-related (e.g. sad); social-threat-related (e.g. hated); neutral AS: Positive; negative; neutral	Yes	Between-groups	Daughters of depressed mothers interpreted ambiguous words more negatively and less positively, and ambiguous stories more negatively, than did daughters of never-disordered mothers.

BDI=Beck Depression Inventory; AW=Ambiguous Words task; AS=Ambiguous Stories task

Table 3: Studies of memory biases in youth depression

Study	Population	Measure	Stimuli valence	Use of mood induction procedure	Analysis	Results
	Depressed youth					
(Dalgleish, et al., 2003)	N=93 youth aged 7-18 with MDD (N=19), PTSD (N=24), anxiety (N=24), or no psychiatric diagnosis (N=26).	Free recall (words)	Threat; depression-related; happy neutral	No	Between-groups	There was no interaction between group and word type (threat, depression, neutral) on recall.
(Gencoz, et al., 2001)	N=58 youth aged 9-17 admitted to a psychiatric hospital (around 44% had a non-bipolar mood disorder)	Free recall following SRET (words)	Positive; negative	No	Regression analysis	Lower recall of positive adjectives (but not enhanced recall of negative adjectives) predicted increased symptoms of depression.
(Hammen, et al., 1984)	N=26 youth aged 7-12 who scored high on the CDI (CDI ≥10) and low on a measure of self-esteem (N=14) or low	Free recall following SRET (words)	Positive; negative	No	Between-groups	Whereas the non-depressed children showed a bias towards positive (versus negative) words, depressed children showed no bias either way.

	on the CDI (CDI ≤4) and high on self-esteem (N=12)					
(Neshat-Doost, et al., 1998)	N=38 youth aged 10-17 with MDD (N=19) or no current or previous episode of MDD (N=19)	Free recall and recognition (words)	Positive; negative; neutral	No	Between-groups	Enhanced recall of negative adjectives in depressed versus non-depressed youth (stronger in older participants). No evidence of group difference in memory bias in the recognition task.
					Symptom x bias correlation	Strength of the bias for negative words was correlated with symptoms of depression across the whole sample.
(Timbremont, et al., 2008)	N=73 youth aged 8-18 who had current (N=18), previous (N=16) or no (N=39) MDD	Free recall following SRET (words)	Positive; negative	Yes	Between-groups	There was no interaction between group and word valence on recall.
(Zupan, et al., 1987)	N=41 youth aged 8-16 with MDD (N=20) or no MDD (N=21)	Free recall following SRET (words)	Positive; negative	No	Between-groups	Enhanced recall of negative adjectives in the depressed versus non-depressed group.
	Community samples					
(Bishop, et al., 2004)	N=113 youth aged 5-11 with high (DSRS≥9; N=59) or	Recall (stories)	Positive; negative; neutral	No	Between-groups	Depressed children showed enhanced recall performance for negative stories (versus positive stories) which did not

	low (DSRS≤8; N=54) depressive symptoms					characterise non-depressed children.
(Goldstein, et al., 2014)	N=434 unselected youth aged 6 followed up at age 9	Free recall following SRET (words)	Positive; negative	No	Between-groups	Poor recall of positive words (but not increased recall of negative words) predicted depressive symptoms at age 9.
(Hughes, et al., 1990)	N=322 youth aged 10-13 with high or low scores on the CDI	Free recall and recognition (stories)	Positive; negative	No	Between-groups	There was an interaction between group and stimulus valence on recognition memory such that more depressed participants recalled more positive and less negative stories than less depressed participants. There was no interaction between group and valence on recall.
(Reid, et al., 2006)	N=133 unselected youth aged 8-14	Free recall following SRET (words)	Positive; negative	No	Symptom x bias correlation	Participants showed a significant bias for negative (self-referent) words which was accounted for by a combination of anxiety, fear, depression and aggression, but not depression alone.
	Children of depressed parents					
(Asarnow, et al., 2014)	N=151 girls aged 10-14 with a recently-depressed mother (N=60) and a never-	Free recall following SRET	Positive; negative	Yes	Between-groups	There was no main effect of group (high or low risk) on the recall of positive or negative self-referent words. However, high-risk girls with the COMT Val158Met Val/Val

	depressed mother (N=91)	(words)				polymorphism recalled more positive (but not negative) words than did high-risk girls who were homozygous for the Met allele. COMT was not associated with recall of words in low-risk girls.

CDI=Children's Depression Inventory; DSRS=Depression self-rating scale for children; PTSD=Post-traumatic Stress Disorder; SRET=Self-referent Encoding Task

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