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Face-memory and emotion: associations with major depression in children and adolescents

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Background: Studies in adults with major depressive disorder (MDD) document abnormalities in both memory and face-emotion processing. The current study used a novel face-memory task to test the hypothesis that adolescent MDD is associated with a deficit in memory for face-emotions. The study also examines the relationship between parental MDD and memory performance in offspring. **Methods:** Subjects were 152 offspring (ages 9–19) of adults with either MDD, anxiety disorders, both MDD and anxiety, or no disorder. Parents and offspring were assessed for mental disorders. Collection of face-memory data was blind to offspring and parent diagnosis. A computerized task was developed that required rating of facial photographs depicting 'happy,' 'fearful,' or 'angry' emotions followed by a memory recall test. Recall accuracy was examined as a function of face-emotion type. **Results:** Age and gender independently predicted memory, with better recall in older and female subjects. Controlling for age and gender, offspring with a history of MDD ($n = 19$) demonstrated significant deficits in memory selectively for fearful faces, but not happy or angry faces. Parental MDD was not associated with face-memory accuracy. **Discussion:** This study found an association between MDD in childhood or adolescence and perturbed encoding of fearful faces. MDD in young individuals may predispose to subtle anomalies in a neural circuit encompassing the amygdala, a brain region implicated in the processing of fearful facial expressions. These findings suggest that brain imaging studies using similar face-emotion paradigms should test whether deficits in processing of fearful faces relate to amygdala dysfunction in children and adolescents with MDD. **Keywords:** Face processing, adolescence, depression, cognitive neuroscience.

Memory dysfunction is one of the best-replicated neuropsychological abnormalities in adult major depressive disorder (MDD). Two findings are relatively consistent: an overall memory deficit and a tendency to selectively recall negative information, a finding known as abnormal 'emotional memory bias' (Bradley, Mogg, & Williams, 1995; Zakzanis, Leach, & Kaplan, 1998). These deficits are relatively specific to MDD, as they are not typically found in adult anxiety disorders (McNally, 1997). The fact that similar neural circuits are implicated in MDD and emotional memory (Phelps & Anderson, 1997; LeDoux, 1998; Drevets, 2000) has fostered particular interest in the relationship between MDD and memory for emotional information.

Questions arise concerning the stage in life during which relationships emerge between MDD and various memory deficits. Associations with *overall* memory deficits appear stronger in the elderly than in young adults or adolescents, suggesting that they may be consequences of chronic or recurrent MDD (Purcell, Maruff, Kyrios, & Pantelis, 1997; Neshat-Doost, Taghavi, Moradi, Yule, & Dalgleish, 1998; Purcell et al., 1998; Grant, Thase, & Sweeney, 2001). In contrast, abnormal *emotional memory bias* is found in both younger and older individuals with MDD, suggesting the association between emotional memory bias and MDD arises early in development (Blaney, 1986; Mathews & MacLeod, 1994; Bradley et al., 1995; Neshat-Doost et al., 1998).

Most studies of the relationships among memory, emotion, and MDD use words to convey emotional content (Mathews & MacLeod 1994; Bradley et al., 1995). However, these methods may be problematic, particularly in children and adolescents. The salience of verbal representations of emotional stimuli changes in adolescence, as does the capacity for verbal stimuli to generate emotion (Stattin, 1984). As a result, the level of emotion generated by words in children, adolescents, and adults might differ. Similarly, adolescent MDD may involve perturbations in language (Pine et al., 2000), possibly confounding associations between MDD and memory biases for words. Finally, some investigators consider memory bias for negative words in MDD to be an artifact of familiarity rather than a core emotional processing deficit. Memory performance is influenced by familiarity, and negative words are thought to be particularly familiar to individuals with MDD (Watkins & Teasdale 2001). Greater familiarity engendered by negative ideation could produce memory biases for negative words in individuals with MDD. Ideally, measures should be developed for studying emotion-related memory biases in child

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and adolescent MDD that place minimal emphasis on verbal material. In this regard, facial stimuli may provide unique advantages.

Facial photographs can depict a range of emotions in the same individual, allowing emotion to be manipulated while holding other stimulus features constant. Facial photographs have been used to study interactions between cognition and emotion in children, adolescents, and adults (McClure et al., 2000; Nelson et al., 2002). Deficits in face-emotion processing are thought to represent one component of social dysfunction in mood disorders. As a result, face-emotion processing tasks are thought to provide a means for documenting cognitive correlates of MDD in the laboratory, both among children and adults (Bouhuys, Geerts, & Gordijn, 1999; Gilboa-Schechtman, Erhard-Weiss, & Jeczemien, 2002; McClure, Pope, Hoberman, Pine, & Leibenluft, 2003). Moreover, several neuroimaging studies employ face-emotion photographs to investigate the role of specific brain regions in interactions between cognitive and emotional processes in healthy adults as well as adults with MDD (Drevets, 2001; Sheline et al., 2001; Haxby, Hoffman, & Gobbini, 2002).

While relatively consistent memory advantages for emotionally evocative vs. neutral scenes or stories have been demonstrated (Phelps & Anderson, 1997; Lang, Bradley, & Cuthbert, 1998), studies of memory biases for emotionally evocative facial photographs are less consistent (Lundh & Ost, 1996; Perez-Lopez & Woody, 2001; Gilboa-Schechtman et al., 2002). Investigators have shown that cueing subjects to attend specifically to emotional aspects of faces at encoding can enhance the detection of emotion-related memory bias (Perez-Lopez & Woody, 2001). Thus far, no study has used this approach in juveniles with psychiatric disorders.

Two theoretical perspectives predict different directions of memory biases in MDD for emotionally evocative faces. A cognitive model posits that MDD is associated with biased retention of negative material (Blaney, 1986; Bradley et al., 1995; McNally, 1997; Neshat-Doost et al., 1998). This model predicts that MDD is characterized by enhanced recall of negative and reduced recall of positive expressions (Clark, Beck, & Stewart, 1990). In terms of face-emotions, this model generates the prediction that MDD will be associated with reduced recall of happy faces and enhanced recall of either angry or sad faces (Gilboa-Schechtman et al., 2002).

Another model, generated from neuroscience, posits associations among MDD, amygdala dysfunction, and the processing specifically of fearful facial expressions. This model is based on the observation that MDD is characterized by amygdala dysfunction in brain imaging studies, manifest specifically as reduced activation during fearful-face viewing (Thomas et al., 2001; Drevets et al., 2002). Amygdala dysfunction, in turn, is associated with specific dysfunction in the ability to process fearful facial expressions, as opposed to other emotional expressions (Adolphs, 2002). These findings generate the specific hypothesis that MDD is associated with a specific deficit in memory for fearful faces. Given the dearth of studies on face-memory and MDD, neither of these two models can be seen as definitive when considering hypotheses on the relationship between face-memory performance and MDD.

The degree to which memory biases represent traits or relate to risk for MDD, as opposed to ongoing MDD, remains unclear. Studies using verbal stimuli generally detect memory biases in patients with ongoing MDD but not in patients with remitted MDD (Blaney, 1986; Bradley et al., 1995; Neshat-Doost et al., 1998). Studies of amygdala dysfunction, in contrast, suggest that associated deficits in face processing might occur in symptomatic as well as remitted patients (Drevets, 2000). However, no study has examined remitted MDD patients using a face-memory paradigm. Moreover, no study has used fearful faces to examine either symptomatic or remitted MDD patients, which is particularly important given findings relating amygdala dysfunction to ongoing and remitted MDD as well as to deficits in fearful face processing. In adolescents, no study has examined remitted MDD patients using any memory paradigm; and in no single age group has the relationship between memory and familial risk for MDD been examined. Some findings suggest that memory biases reflect risk for MDD (Hankin & Abramson, 2001), leading to the hypothesis that parental history of MDD predicts bias in face memory among offspring.

The current study examines the relationship between memory biases for specific face-emotion types and MDD in children and adolescents as well as their parents. To extend prior research in neuroscience, the current study probes memory for fear faces. Consistent with trait factors, biases in memory were predicted in juveniles with lifetime histories of MDD. In terms of directional hypotheses, theories from neuroscience suggest that MDD will be associated with a specific trait-related deficit in memory for fearful faces (Drevets, 2000). In addition, the influence of parental MDD history on memory bias in juvenile offspring is examined.

Methods

Subjects

One hundred and fifty-two offspring (ages 9–19) of parents with MDD, anxiety disorders (panic disorder or social phobia), or psychiatrically healthy parents were studied. A history of psychosis in either parent was an exclusion criterion. Exclusion criteria for offspring were: psychosis, mania, pervasive developmental disorder, use of psychotropic medication, IQ < 70, acute medical conditions, and residence outside the New York Metropolitan area. Chart reviews identified potential parents with MDD and/or anxiety disorders (proband

Table 1 Characteristics of depressed and non-depressed subjects

	MDD-positive	MDD-negative	Statistics
Number (*n*) studied	19	133	
Mean age	16.4 ± 2.4	14.8 ± 2.9	$t_{150} = 2.1$*
N (%) female	13 (68)	71 (53)	$X^2 = 1.2$
IQ†	101 ± 14	103 ± 11	$t_{150} = .5$
Social class rating	3.2 ± 1.0	2.7 ± .9	$t_{150} = 1.9$
ΨFace perception score	47.2 ± 3.5	45.0 ± 4.4	$t_{101} = 1.7$
Memory performance Percent correctly recalled			–
Angry faces	84 ± 20	78 ± 22	
Fearful faces	48 ± 14	55 ± 21	
Happy faces	64 ± 22	60 ± 21	–
Percent false alarms	5 ± 6	6 ± 7	

†Composite from verbal and design portion of Kaufman Brief Intelligence Test.
ΨScore on the Benton Test of Facial Recognition. Data only are available from a sub-set of the 152 subjects ($n = 103$) on this measure.
*$p < .05$.

parents) who were past or current outpatients at the New York State Psychiatric Institute, New York City, Long Island Jewish Medical Center, New Hyde Park, NY, or Freedom From Fear, Staten Island, NY, a clinic that treats individuals with anxiety and mood disorders. Comparison parents initially were identified from a pediatric dental clinic, or from the names of acquaintances of proband parents, using previously validated procedures (Mannuzza et al., 1992). About half of comparison parents were recruited from each source. Inclusion and exclusion criteria were the same for probands and comparisons, but comparison parents also could not have a lifetime history of a mood or anxiety disorder. Table 1 provides characteristics of the participants, in terms of age, gender, and social class. These characteristics are provided separately for subjects with and without MDD. Social class is measured with a standard five-point scale (Hollingshead & Redlich, 1958), where a rating of '1' indicates the highest and a rating of '5' indicates the lowest social class. As shown in Table 1, subjects in the sample included approximately 50% females, were from middle social strata, and were approximately 15 years old.

Mental status of proband and comparison parents was established by blind clinical interviews (described below). Proband and comparison parents were drawn from cohorts identified in earlier studies of children at high risk for MDD or anxiety disorders by virtue of having a parent with MDD or an anxiety disorder. The current data were collected as part of a two-hour assessment of emotional reactivity that ended with a carbon dioxide challenge procedure. Full disclosure was provided, and written informed consent was provided by parents and offspring age 18 or 19; assent was obtained for those aged 9–17.

From a total of 290 families with 497 children identified in previous studies, 255 children met criteria for study participation. Of these 255 children, 78 (31%) declined participation due to reservations about the CO_2 inhalation procedure. For an additional 25 children, data were not obtained due either to time constraints or technical problems. Therefore, this report is based on 97 families, with a total of 152 offspring (ages 9–19). Offspring who participated did not differ from offspring who did not participate in terms of age, gender, ethnicity, or rates of parental psychopathology, though there was a trend for participants to come from higher social classes than non-participants ($X^2 = 7.9$; $p = .095$).

Diagnostic assessment of parents

Parents were administered the Structured Clinical Interview for DSM (SCID: Spitzer, Williams, Gibbon, & First, 1992) by trained clinicians who were blind to all other information collected (offspring mental status, offspring test performance, etc.). Parents were interviewed individually. When one parent was unavailable, the other served as the informant. Satisfactory inter-rater and test–retest reliabilities have been reported for the disorders of interest (kappas = .50–.70) (Spitzer et al., 1992). Interviewers wrote clinical narrative summaries documenting the lifetime DSM-IV diagnoses formulated; these were blindly reviewed by an expert clinician for accuracy and completeness.

Diagnostic assessment of offspring

All offspring were administered a semi-structured clinical interview, the Parent As Respondent Informant Schedule (PARIS), by trained clinicians who were blind to all other information collected (parent mental status, offspring test performance, etc.). Additionally, parents were administered the PARIS about their offspring. Different interviewers conducted the direct and informant assessments. These interviews were used in our previous studies with juvenile patients and offspring of adult patients (Kentgen, Klein, Mannuzza, & Davies, 1997; Slattery et al., 2002). These interviews generate diagnoses for a child or adolescent both based on an interview with the parent about the child and based on a direct interview with the child. Fidelity of the procedures was monitored through audiotapes. Interviewers wrote clinical narrative summaries documenting DSM-IV diagnoses formulated; these were blindly reviewed by an expert clinician for accuracy. Final diagnosis of MDD was based on both direct and informant interviews, such that any subject who met criteria for MDD was considered affected, based either on the direct or the informant interview.

Face-memory task

Subjects completed the face-memory task as part of the two-hour home-based assessment, performed by a physician and technician blind to psychiatric status of parents and offspring. The face-memory task was designed to assess a subject's ability to form representations of individuals depicting high-valence emotions at encoding and then to recognize these individuals depicting neutral poses at recall. The face-memory task consisted of 48 different faces/actors presented as part of encoding and/or recall paradigms. For 24 of these faces/actors, presentation occurred both at encoding and recall; for the other 24, presentation occurred only at recall. Faces were presented on an IBM laptop

computer, with subjects seated approximately 24 inches from the monitor. The task was programmed in the e-prime psychological software package to ensure that presentation of face pictures was standardized and responses were recorded in a standard format. Prior to implementing the experimental face-emotion viewing paradigm, face identification ability was assessed with the Benton Test of Facial Recognition (Benton, Hamsher, Varney, & Spreen, 1983).

The face-memory task included two viewing paradigms separated by 30 minutes: an encoding paradigm and a recall paradigm. To compose the encoding paradigm, 24 different facial photographs of 24 different actors were randomly selected from two standard emotional expression data sets (Ekman, 1976) (www.uphs.upenn.edu/bbl/pubs/downloads/nptasks.shtml). Prior to selecting the photographs for the task, individual stimuli were inspected to insure that the photographs from the two data sets were matched for size of the face and background contrast. No subject had any exposure to any of the faces prior to testing. Thus, potential confounds from familiarity are minimized. Nevertheless, if one or another subject group had been exposed more frequently to one or another face-emotion type, this might potentially introduce a confound between subject characteristics and familiarity. For the encoding paradigm, the 24 different actors expressed 'happy', 'fearful', or 'angry' expressions (eight each), such that no actor depicted more than one emotion during encoding.

Two factors informed the specific choice of 'happy', 'fearful', and 'angry' face-emotion types, as opposed to other emotions. First, the encoding paradigm was designed to include eight replicates of each face-emotion type, since estimates of recall accuracy for a specific face-emotion are less reliable when they are based on relatively few replicates of each face-emotion type. While it would be desirable to include even more than eight replicates at encoding, pilot testing revealed that memory performance deteriorated when more than 24 different faces were presented at encoding. As a result, we designed the task to include only three specific face-emotion types, with eight replicates of each type. Second, we decided to include fear faces, based on the extensive neuroscience literature, and we decided to include happy faces so that we could consider the degree to which any perturbation in memory for face-emotions was specific to negative-valence emotions. For the third face-emotion type, we considered utilizing either angry or sad faces. Despite the obvious relevance of sad faces to the diagnosis of MDD, we ultimately chose to use angry instead of sad faces since considerably more data exist using angry relative to sad faces in research on neuroscience and on face-memory performance in psychopathology.

As noted above, the task was designed to test subjects' ability to recognize during a recall paradigm a neutral individual seen previously at encoding while expressing a high-valence emotion. Therefore, 24 individuals were seen at encoding while displaying an emotional expression. These same 24 individuals ('targets'), along with a set of 24 previously unseen novel individuals ('foils'), were seen during a recall epoch, all 48 of whom had displayed a neutral expression. Thus, no neutral faces were included at encoding and only neutral pictures were included at recall. With this design, all 48 pictures at recall represent novel pictures of neutral expressions, though 24 of these pictures depict previously viewed individuals who had expressed high-valence emotions at encoding.

Figure 1 illustrates the format for the encoding paradigm. Viewing conditions were standardized to facilitate encoding of particular aspects of each face, without explicitly cueing subjects to remember the faces. Subjects viewed each face three times for four seconds in three different encoding epochs and made one rating on a five-point scale during each viewing. The 72 face trials were divided into three 8-trial epochs. The three epochs were administered together as part of a single 'run', and a total of three, three-epoch runs were completed, resulting in 72 face trials (8 faces $\times$ 3 epochs $\times$ 3 runs). Order of face presentation, order of epoch, and pairings of faces to epochs were randomized, constrained by the requirement that each run include exactly one viewing of all 24 faces. Within a run, order of face presentation was free to vary across subjects and within epochs. Epochs were separated by fixation stimuli and by instructions cueing the participant to the particular rating set.

Prior to beginning the experimental paradigm, subjects were trained on the study procedures for the encoding paradigm until they could demonstrate appropriate performance. Subjects were specifically trained to rate one of three different aspects of faces during each of the three epochs when task instructions cued the subject to rate the specific aspect of the face. During one epoch, subjects rated the degree to which they felt afraid or anxious at the moment that they viewed a face. During a second epoch, subjects rated the degree to which a face appeared hostile. During a third epoch, subjects rated the degree to which the nose on each face appeared large or small, relative to other faces. Two of these three attention sets cued subjects to attend to negative aspects of faces. This was designed to facilitate encoding of negative emotion.

This encoding design has the advantage of facilitating recall accuracy, as subjects view each of the 24 faces three times, during which time they are cued to encode different features of each face. However, since each face is viewed in each of the three viewing conditions, one cannot examine the specific effect of task instructions on face-memory performance. This would be possible by using a stimulus set larger than 24 faces and only exposing a subset of each face-emotion type under one or another specific viewing condition. Unfortunately, pilot testing revealed that recall accuracy was poor with a stimulus set larger than 24. Alternatively, this would be possible by exposing a subset of the 24 faces under each of the three viewing conditions. This design would have the disadvantage of including very few replicates of each specific face-emotion type viewed under each specific cuing condition.

For the recall paradigm, subjects were given a 'surprise' memory test 30 minutes after the encoding paradigm. Subjects were told that a series of faces would be displayed, that all faces would depict 'neutral' emotions, and that the series would contain both photographs of previously viewed as well as novel actors. This series included a total of 48 photographs of neutral facial expressions from 48 different actors. This

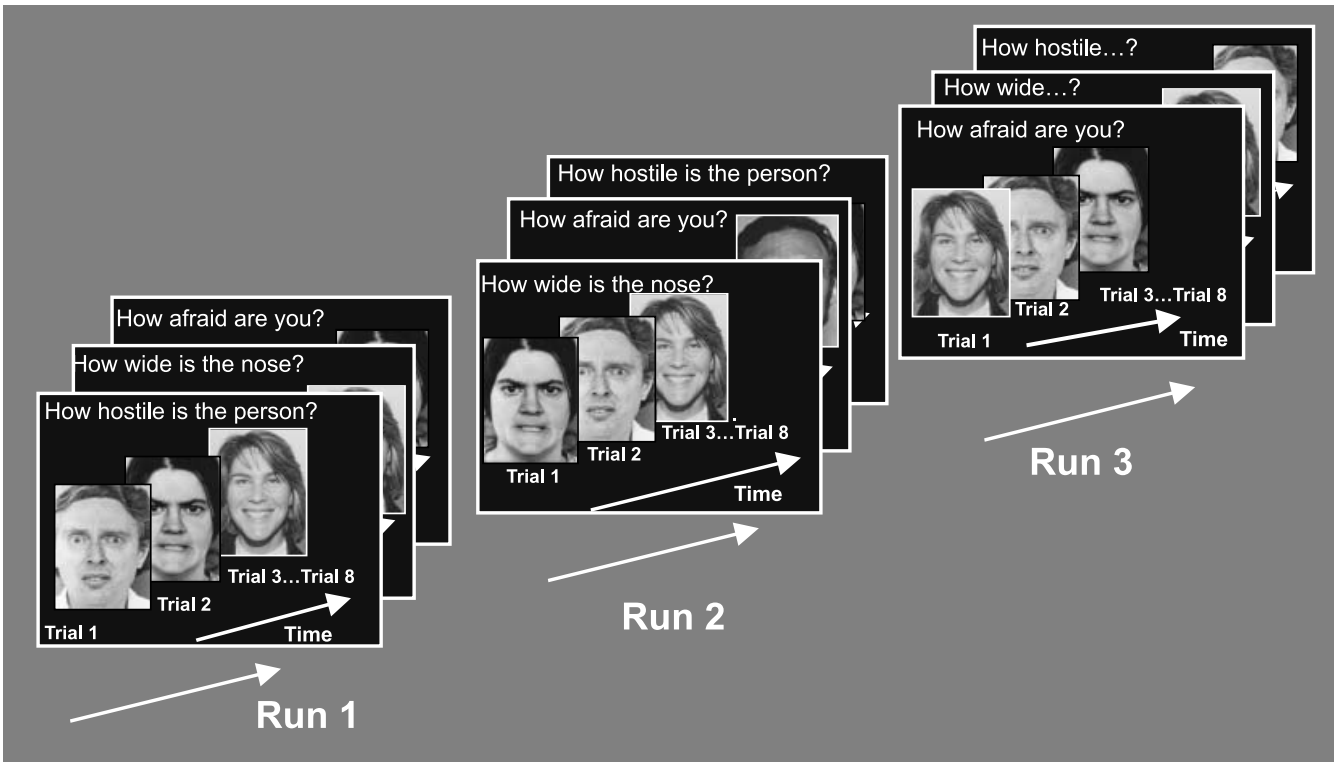

Figure 1 The experimental design for the encoding paradigm of the face-emotion viewing task. Each subject completes three runs during encoding. During each run, each of 24 faces is viewed one time under one of three instruction sets. These 24 faces comprise eight 'happy', eight 'fearful', and eight 'angry' face-types. Each of the 24 faces is rated once in each of the three different rating sets: levels of fear experienced by the subject, level of hostility depicted by the actor in the photograph, and size of a physical feature depicted in the face. Recall involves presentations of only neutral faces, including the 24 previously viewed actors and 24 novel actors

included 24 novel actors and 24 actors seen previously at encoding while depicting a high-valence emotion expression. Subjects were required to indicate by button press whether pictures were of previously viewed or novel actors.

The main dependent measure for the study was based on signal detection theory. Specifically, a measure of signal detection threshold (d') was calculated for each subject for each emotion by subtracting the *z*-score for hits for each emotion from the overall *z*-score for false alarms (Snodgrass & Corwin, 1988). This generated specific d' estimates for each face type: 'happy', 'fearful', and 'angry'. Conceptually, d' represents the degree to which a subject is capable of differentiating signals or 'true targets' from noise or 'foils/distractors'. A low d' indicates poor ability to correctly pick out a specific target type from among a series of distractors.

Beyond measures of signal detection threshold, we also considered generating a measure of response bias both for the entire task as well as for each emotion. Conceptually, measures of response bias, such as ß, estimate different characteristics of a subject's performance on memory paradigms than measures of signal detection threshold, such as d'. Measures of response bias represent the degree to which a subject is liberal or conservative in indicating that an item is a 'target'. A low ß indicates a high threshold for indicating that an item is a target as opposed to a foil. Typically, measures of response bias require an estimate of false alarm rates. An overall false alarm rate was generated with the current paradigm, but emotion-specific false alarms could not occur, since only neutral faces were presented at recall. As a result, we could not obtain estimates of emotion-specific response biases and their relationship to MDD.

Data analysis

The study hypothesis was tested using mixed models for repeated measures in the PROC-MIXED module of SAS. The explanatory variables comprised both fixed effects (gender, age, diagnosis in parents or offspring, and face-emotion type) and random effects (family and subjects). The dependent measures comprised d'-values for each face-emotion type (angry, fearful, happy), treated as a repeated measure. These models tested the hypothesis that d' would differ between subjects with and without a history of MDD. Because prior studies find that age and gender influence face-memory performance (Nelson et al., 2002), models were fit to examine the relationship of face memory to both age and gender. To analyze associations with age, subjects were divided into three age groups, comprising 9–12-year-olds, 13–15-year-olds, and 16–19-year-olds. For diagnosis, indicator variables coded each subject for affected status (1 = affected; 0 = unaffected). For parent diagnoses, one index of parental MDD or anxiety was used, so that offspring born to either one or two affected parents were considered similarly affected. Thus, an offspring at risk for both anxiety and MDD might have one parent with both conditions or one

parent with MDD and another with anxiety. Analyses are presented for lifetime diagnoses but generate comparable results after excluding parents with current diagnoses. Two offspring had current MDD. Another 17 only had prior but not current MDD at the time of testing. Results were similar when the two offspring with current MDD were included or excluded. Therefore, results are presented using the 19 offspring subjects with lifetime MDD. The relationship of face-memory performance to age and gender was controlled in statistical models comparing face-memory performance in offspring with and without a personal or parental history of MDD. This adjusted results for the main analyses for any differences in gender ratios or age between subjects with and without MDD.

Repeated observations on the same individual across time as well as separate observations on individuals within the same family are not independent. Other studies of familial aggregation of psychiatric variables have used mixed statistical models (Verbeke & Molenberghs, 1997; Wolfinger, 1997; Rosenbaum et al., 2000; Slattery et al., 2002). This method was used in the current study, following the SAS mixed model procedures (Littell, Milliken, Stroup, & Wolfinger, 1996). Denominator degrees of freedom for the various fixed effects and their interaction terms were estimated by the SAS mixed model procedure (Littell, 1996).

Results

Lifetime diagnosis of MDD in offspring

Subjects with MDD (16.4 ± 2.4) were significantly older than those without MDD (14.8 ± 2.9) and included a non-significant excess of females (68 vs. 53%). To provide summary data on the overall level of memory performance in the sample, Table 1 provides data on the number of hits and false alarms on the face-memory task. Data on the relationship between face-memory performance and MDD were analyzed using d', as this is calculated on data from both hits and false alarms.

Results from the mixed repeated measures ANOVA for d' are shown in Table 2. Face-memory significantly varied as a function of emotion-type ($F[2,351] = 53$; $p < .001$). Memory for actors who depicted angry expressions at encoding was superior to memory for actors who had depicted happy or fearful expressions at encoding. This association is reflected by higher d' for angry faces. Older ($F[2,351] = 17$; $p < .001$) and female ($F[1,351] = 6.6$; $p < .01$) subjects also exhibited better memory for faces, as indicated by higher d' values. Interactions of face-type with either age or gender were non-significant, indicating that age- or gender-related memory advantages apply to each of the three face-emotion types.

Given the relationship between memory performance and both age as well as gender, analyses examining associations between memory performance and MDD co-varied for gender and age. As hypothesized, there was a significant interaction between MDD and face-emotion type as a predictor of memory performance ($F[2,351] = 3.3$; $p < .05$), controlling for age and gender. This interaction reflected the fact that memory for actors depicting fearful expressions was significantly ($F[1,51] = 8.2$; $p = .005$) reduced in subjects with a history of MDD, relative to non-MDD subjects (see Table 2). Face-memory performance for happy or angry faces did not differ significantly as a function of MDD.

In other analyses, we also examined the relationship between anxiety in the offspring and memory performance. These analyses entered anxiety disorder diagnosis in models shown in Table 2 and also entered anxiety disorder diagnosis alone, both with and without co-varying for age and gender. Anxiety

Table 2 Predictors of memory performance (d')

Dependent measure: †d' for each face-emotion type				*F* statistics	
Predictor variables	Happy faces	Fearful faces	Angry faces	Main effect	Interaction with face type
Age group				$F_{2,351} = 16.8$***	–
9–12 years old	1.4 ± 0.1	1.3 ± 0.1	1.9 ± 0.1		
13–16 years old	1.9 ± .1	1.7 ± 0.1	2.5 ± 0.1		
17–19 years old	2.0 ± 0.1	1.9 ± 0.1	2.7 ± 0.1		
Gender				$F_{1,351} = 6.6$**	–
Male	1.7 ± 0.1	1.6 ± 0.1	2.3 ± 0.1		
Female	1.9 ± 0.1	1.7 ± 0.1	2.5 ± 0.1		
Offspring diagnosis					
MDD				$F_{1,351} = 0.6$	$F_{2,351} = 3.3$*
Absent	1.9 ± 0.1	1.7 ± 0.1	2.4 ± 0.1		
Present	1.8 ± 0.2	1.4 ± 0.1	2.4 ± 0.2		
Parent diagnosis					
MDD				$F_{1,351} = 2.5$	–
Absent	1.9 ± 0.1	1.7 ± 0.1	2.4 ± 0.1		
Present	1.9 ± 0.2	1.6 ± 0.1	2.4 ± 0.2		

†Mean values for d', a measure of accuracy in memory performance, for each face type. Separate analyses examine associations with major depressive disorder (MDD) in offspring or in parents, each adjusted for age and gender. Values are presented as adjusted means ± standard error for estimate of adjusted mean.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

disorder diagnosis in offspring was not significantly associated with face-memory performance in any analysis, either as a main effect or as an interaction with face type (data not shown).

Parental diagnosis

As shown in Table 3, there were 26 offspring of parents with no anxiety or MDD (non-ill parents); 53 offspring of parents with only MDD; 48 offspring of parents with both MDD and anxiety; and 25 offspring of parents with only anxiety disorders. Characteristics of each offspring group are presented in Table 3. There were no significant group differences in age, gender, IQ, or score on the Benton Face Perception test. Subjects born to parents with both anxiety and MDD had significantly lower social class (Hollingshead & Redlich, 1958), relative to subjects without MDD or anxiety. However, social class showed no relationship to face-memory performance (p-values all > .20). As a result, it was not considered in the analyses. Table 3 shows the raw values for d' for each face type in each parent-history group. Table 2 shows the results for the statistical analysis of the association between parental MDD and memory in offspring. Results were non-significant for associations between face-memory and parental history of MDD, irrespective of parental anxiety (main effect of diagnosis: $F[1,355] = .4$; diagnosis-by-face type interaction: $F[2,351] = .7$). A separate analysis examining associations between parental history of anxiety and memory also found no statistically significant relationship (main effect of diagnosis: $F[1,355] = .6$; diagnosis-by-face type interaction: $F[2,351] = .5$).

Discussion

The current study reports on 152 subjects born to parents with histories of MDD or anxiety disorders and comparisons. The study was designed to examine the relationship between MDD and biases in face memory in 9–19-year-olds. As predicted, a specific deficit in memory for fearful faces in youth with a history of MDD was obtained. However, face-memory performance was not related to parental history of MDD.

A novel face-memory task developed for this study successfully elicited biases in memory for specific face-emotion types. The task was designed with encoding instructions that cued subjects to attend to hostile or negative aspects of evocative faces. The task succeeded, as demonstrated by the finding that all types of subjects exhibited significantly better recall for angry faces than happy or fearful faces. Using this task, the study replicated previous reports of better face memory in older adolescents and in females (Nelson, Bloom et al., 2002). The consistency of these findings supports the validity of the task.

Most studies of emotional memory in MDD have relied on verbal memory tests to demonstrate a selective memory advantage for negative as opposed to neutral or positive words (Blaney, 1986; Mathews & MacLeod, 1994; Neshat-Doost et al., 1998). A recent study examined memory bias for faces in adults with MDD (Gilboa-Schechtman et al., 2002). This study found enhanced memory for angry faces and reduced memory for happy faces in adults with MDD, relative to adults with either anxiety or no disorder. These findings contrast with results from the current study but are consistent with cognitive theories of MDD (Clark et al., 1990). Results in the two studies, however, are not directly comparable, due to differences between the face-memory tasks and since the majority of subjects in the current study had a past history of MDD, whereas subjects in the study of adults had ongoing MDD. Most importantly, this prior study did not include fearful faces, for which subjects with MDD in the current study demonstrated a selective memory deficit.

Table 3 Characteristics and family history in sample

	No parental MDD or anxiety	Parental MDD only	Parental MDD & anxiety	Parental anxiety only
Number (n) studied	26	53	48	25
Mean age	15.5 ± 2.2	15.2 ± 3.1	14.8 ± 2.8	14.6 ± 3.2
N (%) female	12 (46)	31 (58)	26 (54)	14 (56)
IQ†	104 ± 10	102 ± 12	102 ± 10	104 ± 10
Social class rating	2.5 ± .7	2.7 ± 1.0	3.1 ± 1.1	2.6 ± .6
ΨFace perception score	44.4 ± 3.7	45.4 ± 5.1	45.8 ± 3.6	44.1 ± 4.7
*Major depression (n, %)	1 (4)	9 (17)	7 (15)	2 (8)
Face memory (d')‡				
Happy faces	2.0 ± .6	1.9 ± .8	1.9 ± .6	1.9 ± .6
Fearful faces	1.8 ± .6	1.8 ± .7	1.8 ± .6	1.6 ± .7
Angry faces	2.5 ± .6	2.4 ± .8	2.4 ± .8	2.3 ± 1.1

†Composite from verbal and design portion of Kaufman Brief Intelligence Test.
ΨScore on the Benton Test of Facial Recognition. Data only are available from a sub-set of the 152 subjects ($n = 103$) on this measure.
*Occurrence of at least one MDD episode at some point during lifetime.
‡Values expressed as mean ± standard deviation for d', a measure of accuracy in memory performance.

Recent neuroscience studies are consistent with the hypothesis that MDD is associated with a deficit in memory for fearful faces. This deficit is hypothesized to reflect the impact of neural anomalies on particular cognitive processes, based on two sets of findings (Drevets, 2001). First, brain imaging studies in adolescents and adults with MDD document abnormalities in amygdala function, including reduced activation to fear faces (Drevets, 2001; Thomas et al., 2001; Drevets et al., 2002). However, these studies have not examined memory biases during imaging. Therefore, evidence of the connection between amygdala function and reduced memory for fear faces in MDD remains indirect. Second, brain imaging studies in healthy subjects (Haxby et al., 2002) and cognitive studies in patients following brain injury (Adolphs, 2002) document an association between dysfunction in the amygdala and selective processing of fearful faces. Moreover, activation of the amygdala in healthy subjects has been shown to selectively predict enhanced memory for emotionally arousing stimuli (Phelps & Anderson, 1997). These findings provide further indirect evidence that cognitive abnormalities in MDD reflect dysfunction in underlying brain circuitry encompassing the amygdala and its connections with the hippocampus and ventral or medial prefrontal cortex. Few studies document cognitive abnormalities in MDD using tasks derived from neuroimaging paradigms, and virtually no studies examine this issue in adolescents. The current study provides such data by documenting reduced fear memory using stimuli previously shown to engage the amygdala.

The role of state vs. trait factors remains a key question relevant to studies of cognitive bias and amygdala dysfunction in MDD. A genetic polymorphism of the serotonergic transporter has been linked to personality traits associated with MDD and patterns of amygdala activation during the viewing of fearful faces (Hariri et al., 2002). Similarly, manipulations of the serotonergic nervous system that produce depressive symptoms in remitted patients selectively disrupt the processing of fearful facial expressions (Harmer et al., 2003). Like in these prior studies, the findings in the current study of fear memory deficits in juveniles with either ongoing or remitted MDD are consistent with hypotheses relating amygdala dysfunction, processing of fearful faces, and trait factors associated with MDD.

Recent studies implementing brain imaging procedures directly adapted from the paradigm used in the current study successfully document engagement of the amygdala during the viewing of fearful faces, though the nature of amygdala activation varies as a function of attention states, memory, and age (Monk et al., 2003; Nelson et al., 2003). Taken together, the current study and previous findings support the hypothesis that adolescent MDD is associated with perturbation in a specific neural circuit encompassing the amygdala and engaged by the processing of fearful faces. More precise conclusions on the nature of relationships among development, trait-aspects of MDD, amygdala activation, and emotional memory may be forthcoming, after imaging studies have directly compared brain activation patterns in depressed and healthy adolescents using face paradigms adapted from the current study.

The current findings should be considered in light of study limitations. Current findings are based in a relatively small sample of at-risk offspring recruited through parents who had sought treatment for MDD or an anxiety disorder. Similarly, comparisons were recruited from acquaintances or from other medical settings. Similar sampling strategies have been employed in many recent studies of familial risk or endophenotype classification (Weissman, Warner, Wickramaratne, Moreau, & Olfson, 1997; Merikangas, Avenevoli, Dierker, & Grillon, 1999), but they are vulnerable to referral biases. Due to the prohibitive costs of very large sampling, prior family studies have not randomly selected large samples of parents with severe MDD or anxiety disorders and their offspring from the community. It would be important to replicate the findings in such a community-based sample.

Given the small number of adolescents with MDD in the current study ($n = 19$), replication is needed in a larger sample, ideally from the community but even from a clinical setting. This issue appears all the more important, given that prior studies in neuroscience and cognitive psychology generate contradictory hypotheses concerning either reduced memory or enhanced memory for different face-emotion types. Similarly, the current study examined only a subset of offspring identified when their parents sought treatment for MDD or an anxiety disorder. Participants tended to differ from non-participants in terms of social class, though this difference was not significant. Regardless, the current findings may apply to a subset of subjects who are willing to participate in research on emotional reactivity. Finally, the current study should be viewed as an initial step towards mapping underlying brain circuits associated with MDD in adolescents. Prior studies have attempted to examine this issue through indirect measure of brain function, such as neuroendocrine challenge. Efforts to extend such prior results have been hindered by the lack of integration with research in neuroscience. This study examined associations with MDD using a paradigm previously shown to index functional aspects of a neural circuit implicated in MDD (Monk et al., 2003; Nelson et al., 2003). This sets the stage for studies that directly compare brain activation profiles in adolescents with and without MDD.

While the current study primarily addresses questions in cognitive neuroscience, the findings may also carry significant clinical implications. For example, considerable heterogeneity exists in

affective disorders among children and adolescents. Some individuals with affective disorders exhibit relatively few symptoms at long-term follow-up; others develop chronic unipolar depressive conditions; whereas still others develop bipolar disorder or non-affective syndromes. Clinical measures collected during initial presentation of an affective episode do not differentiate among children and adolescents who will exhibit one or another course (Costello et al., 2002). It may be possible to predict longitudinal course with more accuracy based on insights from research in cognitive neuroscience. Similarly, while some effective treatments exist for MDD, most adolescents exhibit residual MDD symptoms or high relapse rates even after being successfully treated (Emslie & Mayes, 2001; Clarke et al., 2002). As a result, there is a pressing need to develop novel treatments. Knowledge on core psychological correlates of MDD may provide clues in this respect. For example, if one or another form of memory deficit was shown to predict aspects of adolescent MDD, treatments might be developed based on their ability to alter this underlying memory deficit.

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