# Altered Emotional Processing in Pediatric Anxiety, Depression, and Comorbid Anxiety-Depression

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The goal of this study was to examine some of the mechanisms underlying emotion regulation in childhood affective disorders by examining the impact of distracting emotional information during performance on a working memory task ("Emotional *n*-back" or E-*n*-back). The sample included 75 children (38 girls and 37 boys) between 8 and 16 years of age meeting criteria for: Anxiety disorder (ANX, n = 17), Major depressive disorder (MDD, n = 16), Comorbid anxiety and depression (CAD, n = 24), or Low-risk normal control (LRNC, n = 18). Results showed that the MDD and CAD groups had significantly longer reaction times on negative emotional backgrounds compared to neutral backgrounds, whereas the LRNC group had significantly longer reaction times on positive backgrounds. These results suggest altered processing of emotional information particularly associated with depression. Because the E-*n*-back task engages higher-order cognitive processes, these results suggest that these alterations in processing emotional information also interfere with the cognitive processes that govern how attentional resources are allocated. Further, research is needed to replicate this study and delineate underlying neural mechanisms.

KEY WORDS: children; adolescents; anxiety; depression; emotional processing.

Pediatric anxiety and depression are highly comorbid disorders with significant lifetime morbidity and mortality (Axelson & Birmaher, 2001; Pine, Cohen, Gurley, Brook, & Ma, 1998). Although these emotional disorders are commonly thought to reflect some maladaptive changes in emotion regulation, there is currently little understanding of the mechanisms underlying these changes.

Information processing models have been proposed to explain these maladaptive changes of emotion regulation in affective disorders by focusing primarily on the cognitive aspects of emotional processing (Beck, 1967; Beck, Emery, & Greenberg, 1985; Mogg & Bradley, 1998; Williams, Watts, MacLeod, & Mathews, 1997). For example, research studies conducted in adults have demonstrated that anxiety and depression are associated with an attentional bias toward negative or threatening information (see Williams et al., 1997, for a review). These biases in processing of negative emotional information in affective disorders have been assessed through experimental studies examining the behavioral performance of subjects on tasks such as the visual dot-probe or the emotional stroop. In the emotional stroop task, for instance, subjects are asked to name the color of a word as quickly as possible and to ignore the content of the word. In this task, increased attention toward the negative emotional words is inferred by longer reaction times when naming the color of emotional words.

More recently, researchers have begun to address the question of emotional processing in pediatric affective disorders (see Vasey & MacLeod, 2001, for a review). Researchers found that, like adults, anxious children (i.e., generalized anxiety disorder, post-traumatic stress disorder, simple phobia) show a bias in processing threatrelated information (Dalgleish, Moradi, Taghavi, Neshat-Doost, & Yule, 2001; Kindt, Brosschot, & Everaerd, 1997;

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Vasey, Daleiden, Williams, & Brown, 1995; Taghavi, Neshat-Doost, Moradi, Yule, & Dalgleish, 1999). The results, however, related to depression are rather unclear. Some studies suggest that depression may be associated with a bias toward negative emotional information whereas others propose that this bias is specific to anxiety (Vasey & MacLeod, 2001). Recent studies in adults suggest that anxiety seems to be related to early attentional orienting toward threatening stimuli whereas depression seems to be related to sustained attention toward negative emotional information (Williams et al., 1997). Nevertheless, this tendency to focus attention toward negative or threatening information has been hypothesized by some to play a major role in the etiology and maintenance of these affective disorders (Beck, 1967; Bower, 1981; Bradley, Mogg, Falla, & Hamilton, 1998; Mathews & MacLeod, 1994; Williams et al., 1997; Vasey & MacLeod, 2001).

The nature of this attentional bias and to what extent it is similar in individuals with a comorbid condition remains unknown. Recent research has shown that anxiety and depression are related etiologically (Kendler, 1996; Neale & Kendler, 1995) showing correlated liabilities, that appear to be genetic in nature (Kendler, 1996). The fact that childhood anxiety tends frequently to precede the onset of depression (Kovacs, Gatsonis, Paulauskas, & Richards, 1989) would tend to support this etiological relationship. By including a group with co-morbid anxiety and depression, this should help us parse out to what extent altered processing of emotional information is specific to one of the disorders or to both.

Research studies suggest that attention is involved in processing emotional information (Vuilleumier & Armony, 2001) and that executive attention plays an important role in emotion regulation (Fernandez-Duque, Baird, & Posner, 2000; Posner & Rothbart, 2000). For instance, research conducted on infants indicates that the development of executive attentional or cognitive control abilities, such as the ability to shift attention away from negative stimuli or toward positive stimuli, are related to better regulation of distress and anger in young children (Posner & Rothbart, 2000). Furthermore, adults who reported being able to voluntarily shift and focus attention, reported having lower negative affect (Derryberry & Rothbart, 1988). Executive attention is thought of as a conscious control mechanism that facilitates the focus of attention on task- or goal-relevant information, while inhibiting task-irrelevant information (Casey, Durston, & Fossella, 2001; Miller & Cohen, 2002; Norman & Shallice, 1986) and is considered to be the result of the interplay between diverse frontal and subcortical neural systems (Gazzaniga, Ivry, & Mangun, 1998). Given that the prefrontal cortex is known to be involved in governing how attentional resources are allocated and in the modulation of emotional processing, the goal of this study was to develop a behavioral task that would involve processing emotional information while performing a cognitive task that required executive attention—in particular, the inhibition of processing task-irrelevant emotional information. In addition, because little is known about the neural circuitry involved in the development of attentional bias in children at risk or diagnosed with an affective disorder, the aim of this study was also to develop a task that could eventually be used in a neuroimaging environment.

Hence, we began with a cognitive task (the *n*-back working memory task) known to involve executive attention that had been used successfully in neuroimaging studies of both adults and children (Casey et al., 1995; Cohen et al., 1994), and then added an emotional component to it (Casey, Thomas, Welsh, Livnat, & Eccard, 2000). This affective version of the task is called the "Emotional n-back task" (E-n-back). It consists of superimposing the original *n*-back task onto photographs with images that had been rated as neutral, negative, or positive in affective content (Lang, Öhman, & Vaitl, 1988) and which were modified for use with children (McManis, Bradley, Berg, Cuthbert, & Lang, 2001). The task was designed to assess suppression of irrelevant emotional information while performing a nonemotional working memory task (Casey et al., 2000).

In this study, we compared the performance of children and adolescents assigned to one of four groups on the E-*n*-back task: Anxiety disorder (ANX), Major depression (MDD), Comorbid anxiety and depression (CAD), and Low-risk normal control (LRNC). Drawing on results from behavioral studies suggesting that both anxiety and depression are related to a tendency to process negative emotional information, we hypothesized that compared to the LRNC group, subjects in the ANX, MDD, and the CAD groups would have greater interference in performance when the letters were superimposed onto negative affective pictures. Interference was operationalized as a decrease in accuracy and an increase in reaction time.

# METHOD

## **Participants**

Children and adolescents aged 8 years 0 months to 16 years 11 months who were participating in a larger project examining the psychobiological aspects of childhood depression were included in this study (Birmaher et al., 2000; Dahl et al., 2000). The mean age of the

overall sample (N = 75; 38 girls and 37 boys) was 12.69 (SD = 2.53) years. Children in the ANX group (n = 17;M age = 11.68; SD = 2.71; 7 girls and 10 boys), children in the MDD group (n = 16; M age = 14.78; SD = 1.25; 9 girls and 7 boys), and children in the CAD group (n = 24; M age = 12.57; SD = 2.43; 12 girls and 12 boys)were recruited from inpatient and outpatient clinics at the Western Psychiatric Institute and Clinic, Pittsburgh, PA. Children in the ANX group included children diagnosed with current anxiety disorder (Generalized Anxiety Disorder (GAD) (n = 12); Separation Anxiety Disorder (SAD) (n = 5); Social Phobia (SP) (n = 3); Specific Phobia (SpcP) (n = 2)), children in the MDD group included children in a current episode of major depressive disorder, while children in the CAD group included children diagnosed with a current anxiety disorder (listed above) and depression (MDD, Dysthymia, or Depression NOS). All clinical disorders were based on DSM-IV (American Psychiatric Association, 1994) criteria. Children in the clinical groups were asked to participate before commencing any type of medication treatment. Children in the LRNC group (n = 18; M age = 11.94; SD = 2.43;10 girls and 8 boys) were recruited through advertisement in the local newspaper.

Children in the LRNC group were required to be free of any lifetime psychopathology. In addition, they were required to have no first-degree relatives with a lifetime episode of any mood disorder or psychotic disorder, no more that 20% of second-degree relatives with a lifetime history of affective disorders, no more than one seconddegree relative with a lifetime single episode of MDD, no current substance abuse in either parent, no history of physical or sexual abuse. Exclusion criteria for all children included: IQ lower than 70, significant medical illness, use of psychotropic medications (other type of medication for medical illness), neurological disorder, or a DSM-IV developmental disorder. In addition, for the clinical groups, children with DSM-IV diagnosis of bipolar disorder, obsessive-compulsive disorder, schizoaffective disorder, disruptive disorder, eating disorders, or alcohol or drug abuse/dependence were excluded. Socio-economic status (SES) was measured with the Hollingshead Four-Factor Index (Hollingshead, 1975).

The majority of the sample was Caucasian (n = 62) with 5 children (3 ANX and 2 CAD) of African–American origin and eight children from other ethnic backgrounds. Overall Mean for SES was 42.63 (SD = 12.75). No between-group differences were found for gender, race, and SES. There was, however, a significant between-group age effect F(3, 74) = 6.11, p < 0.01. Post hoc t-tests with Bonferroni correction indicated that children in the MDD group were significantly older than children in the

ANX, CAD, and LRNC groups, p < 0.05. Age was thus included as a covariate.

The University of Pittsburgh Institutional Review Board approved the study. To participate, children and their parents were required to sign assent and informed consent forms, respectively.

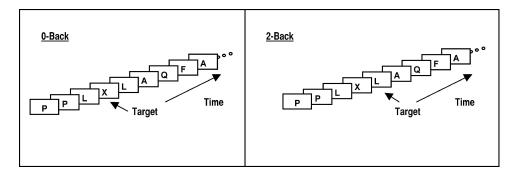
## Measures

*Diagnostic Interview.* The schedule for affective disorders and schizophrenia for school aged children present and lifetime version (K-SADS-PL) (Kaufman et al., 1997) was used to establish diagnosis. This interview provides assessments of present episode and lifetime history of psychiatric illness in children according to DSM-III-R and DSM-IV criteria.

*Self-reports*. Self-report measures were also used to establish a diagnosis. Participants and their parents or guardians were given the following self-report measures: a) the child behavior checklist—parent form (CBCL) (Achenbach & Edelbrock, 1983), b) the screen for child-hood anxiety and related disorders (SCARED) (Birmaher et al., 1999; Birmaher et al., 1997), c) the children's depression inventory (CDI) (Kovacs, 1985) (children, 8–12 years old, with the exception of 3 participants between the ages of 12 and 13 who completed the BDI), and the beck depression inventory (BDI) (Beck, Ward, Mendelson, Muck, & Erbaugh, 1961) (adolescents, 13–18 years old).

The Emotional n-back Task (E-n-back). The E-nback task (Casey et al., 2000) is a modified version of the *n*-back working-memory task described in Cohen et al. (1994) and in Casey et al. (1995). The original nback task consists of visually presenting a pseudorandom sequence of letters and asking subjects to respond to a pre-specified letter appearing on the computer screen. It includes memory conditions whereby the load on working memory varies as a function of the number of letters skipped for a target match. The *n*-back adapted for children includes two conditions: a no-memory condition (0-back) and memory condition (2-back) (Casey et al., 1995) (see Figure 1). In the 0-back condition, subjects monitor similar sequences of letters for any occurrence of a single, pre-specified letter (e.g., X). Thus, it does not involve any working memory load and serves as a control condition. The 2-back memory condition consists of subjects observing a sequence of letters and responding whenever the current letter is identical as the letter present two trials back (e.g., L-X-L).

The E-n-back task consisted of superimposing the original n-back task onto one of four backgrounds (i.e.,



**Fig. 1.** Illustration of the *n*-back task. The target in the 0-back control condition is any letter designated in the instructions (e.g., X) and the target in the 2-back memory-load condition is any repeat of a letter presented two trials back (e.g., L).

no picture (blank screen), negative picture, positive picture or, neutral picture) (see Figure 2) (Casey et al., 2000). The pictures were a subset of digitized slides from the International Affective Picture System Lang et al., 1988) determined to be appropriate for use with children (McManis et al., 2001). The no-background condition served to control for the probable interference related to the presence of a background and the positive background condition served to control for the probable interference related to the emotional valence (i.e., negative) of the pictures. The negative background condition included pictures such as: Shark, Angry face, Pit bull, Refugee, Deformed face, Boxer, whereas the positive background condition included pictures such as: Ice cream sundae, Bunnies, Smiling baby, Cat, Puppies, Smiling Face, and the neutral background condition included pictures such as: House, Fork, Car, Dishes, Book, Umbrella. There were eight blocked conditions comprising two memory-load conditions (i.e., 0-back and 2-back) by four background conditions (none, neutral, negative, positive). The blocked conditions included 16 trials each for a total of 128 trials.

# Procedure

A semi-structured interview and self-report measures were used to establish diagnosis. The interview was administered independently with the child and one parent

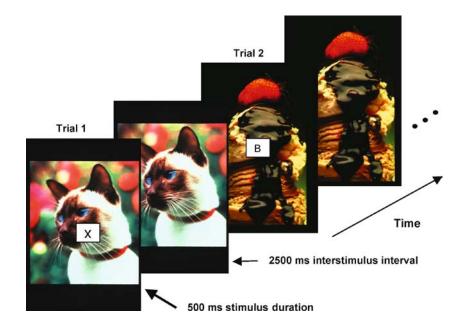


Fig. 2. Illustration of the Emotional *n*-back task (positive background/0-back condition).

about the child by clinically experienced interviewers. Reliability of clinical diagnoses was established through monthly reliability meetings which were conducted under the supervision of a child psychiatrist. The percentage of agreement between interviewers across the diagnoses covered in the K-SADS-PL ranged from 86% to 100%. Parent(s) or guardian(s) also completed self-report questionnaires at home and returned them by mail or on their next visit to the lab, which was approximately one week following the diagnostic interview. The interviewers compiled the scores on the self-report measures along with the details for each individual symptom and stated whether or not the symptom was present at a threshold or sub-threshold level. This information was presented at bi-weekly meetings attended by the clinical interviewers and two experienced child psychiatrists. Each case was discussed and a consensus diagnosis was determined based on DSM-IIIR and DSM-IV criteria. A best estimate procedure for diagnoses based upon all available information was employed to establish a diagnosis (Leckman, Sholomskas, Thompson, Belanger, & Weissman, 1982).

For the E-n-back task, stimuli presentation and response acquisition were controlled by a Macintosh computer and PsyScope software (Cohen, MacWhinney, Flatt, & Provost, 1993). Subjects were tested individually. They sat in front of the computer screen at a distance of approximately 24 inches in a quiet room to perform the task. Before starting the task, an experimenter gave subjects verbal instructions along with written examples to ensure comprehension. Subjects were told that they were going to see a series of letters that will be presented one at a time in front of pictures some of which will be pleasant (i.e., positive), somewhat pleasant (i.e., neutral), and not so pleasant (i.e., negative). Specific instructions were presented on the computer screen for each of the conditions. For the 0-back condition, subjects were asked to respond to a specific letter (e.g., X). For the 2-back condition, subjects were asked to respond to "skip one letter repeats"; that is, to respond to a letter if it skips one letter and repeats. The experimenter provided a written example of the "skip one letter repeats" (e.g., L-X-L) and asked open-ended questions to verify comprehension. Between each block, the instruction screen appeared for 6 s informing the subjects to either search for a specific letter (0-back condition) or to detect repeats of letters with one intervening letter (2-back condition). Each trial consisted of the simultaneous presentation of a letter and a blank screen or a picture. Letters and corresponding backgrounds appeared for 500 ms then disappeared leaving only the picture or blank screen visible for another 2500 ms. Trials were randomized within each block; pictures were randomized within each background condition and, letters were randomized across subjects. Subjects responded by pressing on a computer mouse to the target letters. The duration of the task was approximately 10 minutes.

# **Statistical Analyses**

Statistical analyses regarding self-reports included analyses of variance (ANOVAs) and analyses of covariance (ANCOVAS) whereas analyses regarding task performance included mixed-model multivariate analyses of covariance (MANCOVAS) with repeated measures (Tabachnick & Fidell, 1996). More specifically, in order to clarify differences between diagnostic groups with regard to symptomatology, post-hoc multiple comparison tests (Tukey HSD, p < 0.05) were conducted on either the total scores or the scaled-scores of the self-report measures. The CDI and the BDI were used in children and adolescents, respectively. In order to examine differences in depressive symptoms across the entire sample, standardized scale scores (z-scores) were used. Age was included as a covariate and gender as an independent variable in analyses performed on the SCARED-child, SCARED-parent, and the z-score CDI/BDI. Hypotheses concerning performance on the E-n-back task were tested by performing a 4 (Diagnosis: ANX, MDD, CAD, LRNC)  $\times$  2 (Memoryload: 0-back and 2-back)  $\times$  4 (Emotional Background: none, neutral, negative, positive) MANCOVA with diagnosis as a between-subject variable, memory-load and emotional background as within-subject variables, and age as a covariate on correct-trial reaction time and overall accuracy. The first two trials of each block were excluded from the analyses since in the 2-back condition, a target could not occur in the first two trials. In addition, reaction time data were filtered by removing all error trials. Outlying reaction time data points less than 100 ms or greater than 1000 ms were also filtered out; this comprised less than 1% of the trials. The mean correct-trial reaction time and accuracy score were then calculated for each of the participants as a function of each of the factors in the design. Age was used as a covariate to account for probable cognitive developmental effects and because children in the MDD group were significantly older than children in the ANX, CAD, and LRNC groups. Planned contrasts were performed to test the hypothesis that the ANX, MDD, and CAD groups would be slower and less accurate in the negative emotional background condition relative to the neutral condition. Preliminary analyses indicated that there were no main effects or interactions for gender or SES. Hence, these factors were not considered further in the analyses.

# RESULTS

# **Participant Characteristics**

Table I shows the means, standard deviations, and the number of participants included in the analyses separately for CBCL—externalizing subscale, CBCL—internalizing subscale, CBCL-total, SCARED-child, SCAREDparent, CDI/BDI z-score. Results indicated a significant group effect for the CBCL—internalizing, F(3, 66) =62.14, p < 0.001, CBCL—externalizing, F(3, 66) =14.81, p < 0.001, and CBCL—total, F(3, 66) = 36.06, p < 0.001. Analyses for the SCARED-child, SCAREDparent, and CDI/BDI z-score included age as a covariate and gender as an independent factor. Results did not yield any age, gender, or diagnostic group by gender effects. There were significant group effects for the SCAREDchild, F(3, 58) = 11.04, p < 0.001, SCARED-parent, F(3, 59) = 25.08, p < 0.001, and CDI/BDI z-score, F(3, 55) = 5.53, p < 0.01. Post hoc comparisons were performed using Tukey HSD on the means of each of the scales. Results indicated that compared to the LRNC group, the ANX, MDD, and CAD groups had significantly higher mean scores on CBCL-externalizing, CBCL—internalizing, and CBCL-total, p < 0.01. For the SCARED-child, the ANX and CAD groups had significantly higher mean scores compared to the LRNC group, p < 0.01, and the CAD group had significantly higher mean scores compared to the MDD group, p < 0.05. In addition, there were no significant differences in mean scores between the ANX and CAD groups. For the SCARED—parent, all three clinical groups had significantly higher mean scores compared to the LRNC group, p < 0.01. Furthermore, the ANX and CAD groups had significantly higher mean scores compared to the MDD group, p < 0.01. Similar to the SCARED-child, there were no significant differences in mean scores between the ANX and CAD groups. Regarding depression symptoms, the MDD and the CAD groups had significantly higher scores compared to the LRNC group, p < 0.01, on the CDI/BDI *z*-score. There were no significant differences between either the ANX and CAD groups or the AND groups. Moreover, there were no significant differences between either the ANX and CAD groups or the ANX and MDD groups.

#### Performance on the E-n-back Task

In order to examine whether overall performance was different across diagnostic groups, analyses of covariance with age as a covariate were performed comparing diagnostic groups on the percentage of total correct responses, errors of omission, and errors of commission. As shown in Table II, results indicated a significant age covariate for the correct responses, F(1, 70) = 15.25, p < 0.001, and for the errors of omission, F(1, 70) = 13.54, p < 0.001, indicating that the percentage of correct responses increased with age whereas the percentage of errors of

 Table I. Means and Standard Deviations of CBCL—externalizing, CBCL—internalizing, CBCL—total, SCARED—parent, SCARED—child, CDI total score, BDI total score, and CDI/BDI z-score

Participant characteristics	ANX $(n = 17)$		MDD $(n = 16)$		CAD $(n = 24)$		LRNC ( $n = 18$ )					
	М	SD	n	М	SD	n	М	SD	n	М	SD	n
CBCL—externalizing <sup>a</sup>	62.06	9.96	16	61.55	10.36	11	65.57	7.41	23	46.94	8.74	16
CBCL—internalizing <sup>a</sup>	69.50	7.26	16	67.63	6.45	11	71.04	5.55	23	43.63	7.77	16
CBCL—total <sup>a</sup>	68.31	9.07	16	68.36	8.77	11	70.17	7.36	23	44.44	8.49	16
SCARED—child <sup>b,c</sup>	30.31	15.19	16	23.42	15.32	12	36.72	14.84	23	11.77	9.98	16
SCARED—parent <sup>a,d</sup>	32.71	13.23	17	20.15	11.94	13	32.64	10.30	22	5.70	3.97	16
CDI total score	39.67	5.83	9	44.00	14.14	2	44.41	14.01	11	30.42	4.10	12
BDI total score	15.14	9.17	7	22.64	13.63	11	21.38	9.82	13	4.50	4.66	4
CDI/BDI z-score <sup>e</sup>	-0.03	0.67	15	0.39	1.14	11	0.35	1.08	24	-0.82	0.43	15

*Note.* ANX = Anxious disorder group; MDD = Major depression group; CAD = Comorbid anxiety and depression group; LRNC = Low-risk normal control group; CBCL—externalizing = Child behavior checklist—externalizing; CBCL—internalizing = Child behavior checklist—total; SCARED—child = The screen for childhood anxiety and related disorders—child form; SCARED—parent = The screen for childhood anxiety and related disorders—parent form; CDI = Children's depression inventory; BDI = Beck depression inventory; t-scores are presented for the CBCL measures whereas total scores are presented for the SCARED, and total scores and *z*-scores are presented for the CDI, and BDI; analyses were conducted on CDI/BDI *z*-scores only.

<sup>*a*</sup>LRNC < ANX, MDD, CAD, p < 0.01.

<sup>*b*</sup>LRNC < ANX, CAD, p < 0.01.

 $^{c}MDD < CAD, p < 0.05.$ 

 $^{d}$ MDD < ANX, CAD, p < 0.01.

<sup>*e*</sup>LRNC < MDD, CAD.

	Diagnostic group						
Performance	ANX $(n = 17)$	MDD ( $n = 16$ )	CAD $(n = 24)$	LRNC $(n = 18)$			
Correct responses Errors of omission Errors of commission	70.01 (3.44) 16.72 (2.00) 8.20 (1.94)	73.90 (3.78) 14.83 (2.19) 9.42 (2.13)	69.89 (2.83) 17.25 (1.65) 8.04 (1.60)	66.57 (3.31) 18.84 (1.93) 11.21 (1.87)			

*Note.* There were no significant diagnostic group differences for any of the above variables, p > 0.05.

omission decreased with age. Furthermore, results revealed that there were no significant differences across the diagnostic groups on any of these variables (correct responses: F(3, 70) = 0.67, p = 0.57; errors of omission: F(3, 70) = 0.62, p = 0.61; errors of commission: F(3, 70) = 0.66, p = 0.58).

Analysis of covariance was performed on overall accuracy scores (i.e., *number of correct responses* + *number of correct omissions/number of trials per block (16)*). Results showed a significant age effect, F(1, 70) = 16.14, p < 0.001, indicating that accuracy increased as a function of age. In addition, there was a significant memoryload main effect indicating that the level of accuracy was significantly lower in the 2-back compared to 0-back memory condition, F(1, 70) = 13.92, p < 0.001. However, accuracy level was not significantly different across diagnostic groups or emotional background conditions, and there were no significant interactions.

Analysis of covariance was also performed on correct-trial reaction time to examine the effects of diagnosis, memory-load, and emotional background on performance. Results showed a significant age covariate effect, F(1, 54) = 8.62, p < 0.01, indicating that reaction time tended to decrease as age increased. Results showed a significant overall emotional background effect (Wilk's Lambda: F(3, 52) = 6.00, p < 0.01). Post hoc pairwise comparisons using Shaffer's modification of the Bonferroni adjustments (Shaffer, 1995) indicated that reaction time for the no background condition was significantly faster compared to the neutral, negative, and positive background conditions, p < 0.001, that reaction time for the neutral background was significantly faster compared to the negative, p < 0.01, and that there was a trend for faster reaction time to the positive relative to the negative background, p = 0.025. There were no significant differences in reaction times between the neutral and positive backgrounds, p = 0.49.

Moreover, as shown in Table III and illustrated in Figure 3, results indicated a significant diagnosis by emotional background interaction effect (Wilk's Lambda: F(9, 127) = 2.28, p < 0.05). Planned contrast analyses

were performed comparing the neutral and negative background conditions for each of the diagnostic groups. Results indicated that the MDD and the CAD groups were significantly slower to respond to target stimuli in the negative condition relative to the neutral (MDD: F(1, 14) = 4.98, p < 0.05; CAD: F(1, 18) = 4.85, p < 0.05). There were no differences in reaction times for the ANX, F(1, 12) = 1.84, p = 0.20, or LRNC groups, F(1, 11) = 2.98, p = 0.11.

Simple contrast analyses were used to explore differences in reaction times between the neutral and the positive emotional backgrounds across diagnostic groups. Results revealed that reaction time was significantly longer in the positive condition relative to the neutral condition for the LRNC group, F(1, 11) = 10.02, p < 0.01, but not for the ANX, F(1, 12) = 4.15, *n.s.*, MDD, F(1, 14) = 0.20, *n.s.*, and CAD, F(1, 18) = 0.33, *n.s.*, groups. There were no significant diagnoses by memory-load by emotional background or memory-load by emotional background interaction effects.

## DISCUSSION

The goal of this study was to investigate alterations in emotional processing in children and adolescents diagnosed with anxiety, depression, and comorbid anxiety and depression as a way to better understand the causes underlying the maladaptive changes in emotion regulation associated with pediatric affective disorders. We were particularly interested in the role of executive attention processes in emotional processing. Thus, we developed the E-*n*-back task, which was designed to examine suppression of processing of irrelevant emotional information (Casey et al., 2000), and compared the performance of a group of children and adolescents diagnosed with an anxiety disorder, major depression, comorbid anxiety and depression, and at low-risk of developing an affective disorder.

Relative to the LRNC group, the MDD and the CAD groups had significantly longer reaction times in the

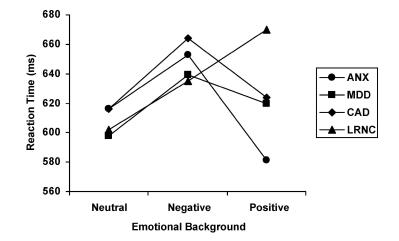


Fig. 3. Estimated marginal means of correct-trial reaction time as a function of diagnostic group and neutral, negative, and positive emotional backgrounds. ANX = Anxious disorder group; MDD = Major depression group; CAD = Comorbid anxiety and depression group; LRNC = Low-risk normal control group.

negative compared to the neutral background condition, which suggests that greater attentional resources were allocated to processing the emotional aspect of the stimuli than the target stimuli (i.e., letter) even though this information was irrelevant to the task (Massaro, 1988). Before considering the implication of these patterns of results, there are a number of methodological issues that merit discussion.

Table III. Estimated Marginal Means (Standard Errors) of Correct-Trial Reaction Time and Accuracy (Standard Errors) as a Function of Diagnostic
Group, Memory-load, and Emotional Background

	Diagnostic groups								
	ANX		MDI	)	CAI	)	LRNC		
Conditions	$\begin{array}{c} RT^{\dagger}\\ (n=13) \end{array}$	Accuracy* $(n = 17)$	$\begin{array}{c} \mathrm{RT}^{\dagger}\\ (n=15) \end{array}$	Accuracy* $(n = 16)$	$\begin{array}{c} \mathrm{RT}^{\dagger}\\ (n=19) \end{array}$	Accuracy* (n = 24)	$RT^{\dagger}$ $(n = 12)$	Accuracy* $(n = 18)$	
No background									
0-back	485.34 (18.36)	0.92 (0.02)	436.58 (18.03)	0.94 (0.03)	478.40 (14.86)	0.94 (0.02)	437.84 (18.79)	0.91 (0.02)	
2-back	519.92 (31.73)	0.84 (0.03)	489.53 (31.16)	0.86 (0.03)	561.37 (25.68)	0.85 (0.02)	505.73 (32.47)	0.83 (0.03)	
Total	502.63 (19.94)	0.88 (0.02)	463.05 (19.58)	0.90 (0.02)	519.89 (16.14)	0.90 (0.02)	471.79 (20.41)	0.87 (0.02)	
Neutral background									
0-back	589.08 (22.40)	0.91 (0.02)	587.59 (22.00)	0.95 (0.02)	571.65 (18.13)	0.92 (0.02)	578.64 (22.92)	0.94 (0.02)	
2-back	641.90 (34.47)	0.83 (0.03)	609.17 (33.85)	0.80 (0.03)	660.06 (27.90)	0.82 (0.03)	626.06 (35.27)	0.81 (0.03)	
Total	615.49 (22.68)	0.87 (0.02)	598.38 (22.27)	0.88 (0.03)	615.86 (18.36)	0.87 (0.02)	602.35 (23.21)	0.87 (0.02)	
Negative background									
0-back	629.64 (27.05)	0.91 (0.02)	646.76 (26.56)	0.93 (0.03)	699.35 (21.90)	0.91 (0.02)	640.69 (27.68)	0.88 (0.02)	
2-back	676.36 (33.64)	0.79 (0.03)	631.49 (33.03)	0.80 (0.03)	628.63 (27.23)	0.79 (0.03)	628.58 (34.42)	0.76 (0.03)	
Total	653.00 (26.70)	0.85 (0.02)	639.13 (26.22)	0.86 (0.02)	663.99 (21.61)	0.85 (0.02)	634.63 (27.33)	0.82 (0.02)	
Positive background									
0-back	586.23 (28.73)	0.94 (0.02)	598.19 (28.22)	0.93 (0.02)	590.91 (23.26)	0.92 (0.02)	643.95 (29.41)	0.89 (0.02)	
2-back	575.18 (38.35)	0.82 (0.03)	641.99 (37.66)	0.79 (0.03)	656.94 (31.04)	0.78 (0.02)	696.37 (39.25)	0.76 (0.03)	
Total	580.71 (28.63)	0.88 (0.02)	620.09 (28.12)	0.86 (0.02)	623.92 (23.18)	0.85 (0.02)	670.16 (29.30)	0.83 (0.02)	

*Note*. ANX = Anxious disorder group; MDD = Major depression group; CAD = Comorbid anxiety and depression group; LRNC = Low-risk normal control group.

\*Data are presented as mean overall accuracy scores which were calculated for each condition [number of correct responses + number of correct omissions/number of trials per block (16)]; all subjects were significantly more accurate in the 0-back than the 2-back condition.

<sup>†</sup>MANCOVA yielded a significant diagnosis × emotional background interaction (Wilk's Lambda:  $F_{9,127} = 2.28$ , p < 0.05); simple constrasts revealed (total) neutral < negative background conditions for the MDD and CAD groups but not the ANX and LRNC group whereas (total) neutral < positive background conditions for the LRNC but not the ANX, MDD, and CAD groups.

First, results presented in Table I suggest that for the most part the clinical groups were different on anxiety and depression measures and therefore differences in performance on the E-*n*-back are unlikely to be the consequence of overlapping symptomatology across diagnostic groups. For instance, the fact that the CAD did not differ from the ANX group on the anxiety measures and did not differ from the MDD group on the depression measure attests to the presence of comorbidity in that clinical group. The SCARED-parent provided evidence that the ANX and MDD groups were significantly different with regard to the presence of anxiety symptoms. Although the means were in the appropriate direction, the child selfreport measures (i.e., SCARED-child and CDI/BDI) did not yield significant group differences.

Secondly, although results did not yield a significant interference effect related to the negative pictures in the performance of the ANX group, Table III shows that this group did have longer reaction times in the negative  $(653 \pm 27.23 \text{ ms})$  compared to the neutral background  $(615.49 \pm 22.68 \text{ ms})$ . The lack of significant interference effect could possibly be attributed to the smaller n in that group. Another likely explanation however is that the type of cognitive processes that were being recruited in this task may explain why the emotional bias toward the negative emotional stimuli were not as strong in the anxious group compared to the depressed and comorbid groups. For instance, unlike the visual dot-probe task, which has shown consistent interference effects in anxious children and adults, this task does not tap into spatial attentional systems, which would appear to be more closely linked to anxiety (Luu, Tucker, & Derryberry, 1998). Alternatively, it is possible that the absence of significant differences in reaction times in the negative emotional background condition for the ANX group may reside in the high proportion of GAD diagnoses in that group (14 out of 17 participants). It would appear from a recent study that children with GAD show a larger bias toward threat-related stimuli (at least in comparison with children diagnosed with PTSD on a visual dot-probe task) (Dalgleish et al., 2003). Therefore, the lack of significant interference effect in the ANX group could be related to the fact that only some of the negative pictures were high in negative valence and high in arousal (considered as threat-related stimuli). However, because participants were not asked to rate the pictures a posteriori this hypothesis remains to be tested.

Thirdly, with regard to the nature of the negative stimuli and the extent to which they may have influenced the results, it is possible that the interference effects observed in the MDD and CAD groups could have been caused by a sub-group of pictures that were mainly high in negative valence (considered as depression-related stimuli). Although it would have been interesting to compare the influence of the nature of the negative pictures systematically (i.e., comparing threat-related versus depressogenic pictures) on the interference effect in the clinical groups, to our knowledge the IAPS pictures have not been systematically classified according to those characteristics making it difficult to test this hypothesis accurately. Furthermore, because this was not the goal of this study, the pictures were randomly selected according to predetermined valence and arousal dimensions (i.e., high in negative valence (depression related) and high in negative valence and high in arousal (anxiety related)). Finally, it is unlikely that differences in performance were related to differences in the perceptual characteristics of the pictures (e.g., color, contrast, or stimulus complexity) across the emotional background condition rather than the affective features of the pictures because of the presence of a diagnosis by emotional background interaction.

Given that the *n*-back task is known to engage higherorder cognitive processes (Shimamura, 2000), the results of this study using the E-n-back task stand out in contrast to the results of previous studies of emotional processing in childhood affective disorders as they are, to our knowledge, the first to show that the negative emotional saliency of the stimuli interfered with cognitive processes that are responsible for governing how attentional processes are allocated (Monk et al., 2003). The task was initially designed to assess the ability to suppress irrelevant emotion-related information (Casey et al., 2000). When examining the emotional background main effect, the increase in reaction time from no background to neutral background and from neutral background to positive and negative backgrounds speak to the influence of the emotional content on performance. Thus, one possible interpretation is that the negative content of the pictures was more salient for the MDD and CAD groups and as such, made it more difficult for them to inhibit processing the emotional information in these pictures leading to increased reaction time when responding to the target stimuli. If we consider recent research in affective neuroscience, this interference to the negative pictures could be interpreted as reflecting altered functioning of frontal-subcortical systems. Recent neuroimaging studies conducted in adults have shown that the prefrontal cortex, which supports higher-order cognition such as executive attention, plays an important role in emotional processing (Davidson, Pizzagalli, Nitschke, & Putnam, 2002; Gray, Braver, & Raichle, 2002; Lane, Fink, Chua, & Dolan, 1997) and that affective disorders, especially depression, may be related to altered functioning of these brain regions and their connections with subcortical limbic areas (Davidson et al., 2002; Drevets, 2001; Siegle, Granholm, Ingram, & Matt, 2002; Siegle, Steinhauer, Thase, Stenger, & Carter, 2002). For instance, a recent imaging study has shown that compared to controls, depressed adults will tend to continue processing negative emotional information for a longer period of time and that this sustained processing is related to increased activity in the amygdala and decreased activity in the dorsal lateral prefrontal cortex (Siegle et al., 2002). Given that the E-*n*-back task taps into cognitive processes supported by the prefrontal cortex, the increase in reaction time to the negative pictures in the MDD and CAD groups could reflect greater sustained attention to the negative content of the pictures thereby impeding efficient mobilizing of attentional resources to process the target in the *n*-back task.

Significant differences in reaction times to the positive emotional backgrounds relative to the neutral backgrounds were found in the LRNC group but not in the ANX, MDD, or CAD groups. Because the positive emotional backgrounds were used to control for the emotional content of the backgrounds in the negative background condition, the longer reaction times to the positive backgrounds in the LRNC group compared to the clinical groups were unexpected. Nevertheless, results suggest an interesting dissociation effect whereby children with affective disorders, in particular, depression or comorbid anxiety-depression in this study, appeared biased toward the negative emotional stimuli whereas controls appeared biased toward positive emotional stimuli. The LRNC group may have had a greater natural tendency to explore the pleasant pictures (e.g., ice cream cone, rabbits) compared to the ANX, MDD, and CAD groups and as such, attentional resources were pulled by the emotional saliency of the positive pictures. This tendency to explore positive or rewarding stimuli in controls and the absence thereof in affective disorders is consistent with recent research suggesting that depression in particular is associated with a lack of approach-related behavior (Davidson, 1994; Gray, 2001; Tomarken & Keener, 1998). Although few studies have used tasks that included an experimental condition with positive emotional stimuli, there is some evidence that compared to subjects diagnosed with an affective disorder, non-clinical control subjects tend to focus more on positive emotional information (Bradley et al., 1997; Gotlib, McLachlan, & Katz, 1988). Because all three clinical groups did not show longer reaction times to the positive stimuli, it is suggested that a common underlying feature of pediatric affective disorders such as anxiety and depression may be alterations associated with processing positive emotional information. This idea is consistent with the results of recent studies indicating that depressed adults have a bias away from labeling facial expressions such as happy (Surguladze et al., 2004) and show different activation patterns of the limbic system to happy v. sad facial expressions relative to normal controls (Phillips, Drevets, Rauch, & Lane, 2003). Little is known, however, about the processing of positive emotional information related to anxiety. Given the important role of shifting attention toward positive emotional stimuli when regulating negative emotional states, research is needed to elucidate further possible divergence in processing positive emotional information in anxious and depressed children and adolescents.

Analyses performed on accuracy indicated, as expected, that overall children were more accurate in the 0-back compared to the 2-back memory condition demonstrating that the 2-back condition was more demanding in terms of cognitive processing. However, the analyses did not yield any differences related to diagnosis or emotional background. Reaction time, rather than accuracy, may have been more sensitive to variation in performance because of the low probability of making errors on this task. Including extra trials in each of the blocks could help increase this probability and possibly enhance variance in performance. Another point to consider is the fact that reaction time appeared to be influenced by the valence of the emotional backgrounds but not by memory-load which suggests that the emotional content of the pictures had an effect on both lower and higher-order attentional processes. However, because there were only two levels in the *n*-back task, this interpretation of the results remains to be tested.

In sum, results of this study suggest that children and adolescents diagnosed with an affective disorder seem to process emotional information differently than children and adolescents from a normative sample, which is consistent with the results of previous studies of information processing (see Vasey & MacLeod, 2001). Separate groups of children diagnosed with an anxiety disorder, major depression, and comorbid anxiety and depression were included in an effort to shed some light on some of the distinguishing features of childhood anxiety and depression and to begin understanding processes associated with their high comorbidity (Axelson & Birmaher, 2001). Because the E-n-back engages higher-order cognitive processes, these results suggest that these alterations in emotional processing also involve cognitive processes that govern how attentional resources are allocated (Monk et al., 2003) and that altered processing of positive emotional information may represent a common underlying characteristic in pediatric emotional disorders.

Despite the emphasis on cognition and emotion interaction in cognitive-behavioral models of treatment of childhood anxiety and depression, the literature in this

area omits any references to alterations in emotional processing or how to incorporate these difficulties into standard cognitive-behavioral therapy (CBT) protocols. For instance, alterations in processing positive emotional information has important implications with regard to the ability to shift attention toward positive stimuli, engage in positive activities, or seek positive experiences. Future research is needed on how cognitive-emotional processes associated with childhood anxiety and depression may be included in the evaluation process (Garber & Kaminski, 2000; Vasey & Lonigan, 2000). This may lead to the development of refined clinical interventions that specifically target these disruptions in emotional information processing (e.g., teaching attention control strategies via games to enhance development of higher-order cognition in various emotional contexts or to focus attention on the positive aspects of situations). Finally, there have been very few investigations of cognitive emotional processes that have examined anxiety, depression, and comorbid anxiety and depression within the same study; therefore, the present study is helpful in contributing to this limited body of evidence.

## Limitations

An improved study would have included a larger number of subjects in each of the diagnostic groups and stratified age groups to address specific developmental questions more thoroughly such as the role of cognitive development and pubertal maturation. Although several studies have shown that the pictures taken from the International Affective Picture System (Lang et al., 1988) elicit emotional responses in adults (Lang, Bradley, Cuthbert, & Patrick, 1993) and children (McManis et al., 2001), it remains unclear whether the attentional resources of anxious, depressed, and anxious and depressed subjects were affected in a similar way. For instance, Williams et al. (1997) argued that anxiety is related to a shift of attention toward threat-related information whereas depression is related to a sustaining of attention toward negative information. Therefore, it is possible that that the mechanisms underpinning differences in reaction time relative to the LRNC group was divergent across diagnostic groups. Furthermore, given that the pictures were randomly selected to cover the range of negative valence and high negative arousal and that the participants did not subjectively rate the pictures at the end of the task, it is unclear whether a particular set of pictures was responsible for the results obtained in this study. This would be a hypothesis worth testing in a future study. Finally, future research including a group of children and adolescents at high-risk of developing an emotional

disorder could provide some insight to the question of etiology and maintenance of emotional disorders.

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# REFERENCES

- Achenbach, T., & Edelbrock, C. S. (1983). Manual for the child behavior checklist and revised child behavior profile. Burlington, VT: University of Vermont, Department of Psychiatry.
- American Psychiatric Association (1994). Diagnostic and statistical manual of mental disorders 4th edition. Washington, DC: Author.
- Axelson, D. A., & Birmaher, B. (2001). Relation between anxiety and depressive disorders in childhood and adolescence. *Depression and Anxiety*, 14, 67–78.
- Beck, A. T. (1967). *Depression: Clinical, experimental, and theoretical Aspects.* New York: Hoeber.
- Beck, A. T., Emery, G., & Greenberg, L. (1985). Anxiety disorders and phobias: A cognitive perspective. New York: Guilford Press.
- Beck, A. T., Ward, C., Mendelson, M., Muck, M., & Erbaugh, J. (1961). An inventory of measuring depression. Archives of General Psychiatry, 4, 561–571.
- Birmaher, B., Brent, D., Chiapetta, L., Bridge, J., Monga, S., & Baugher, M. (1999). Psychometric properties of the screen for child anxiety related emotional disorders scale (SCARED): A replication study. *Journal of the American Academy of Child & Adolescent Psychiatry*, 38, 1230–1236.
- Birmaher, B., Dahl, R. E., Williamson, D. E., Perel, J. M., Brent, D. A., Axelson, D. A., et al. (2000). Growth hormone secretion in children and adolescents at high risk for major depressive disorder. *Archives* of General Psychiatry, 57, 867–872.
- Birmaher, B., Khetarpal, S., Brent, D., Cully, M., Balach, L., Kaufman, J., et al. (1997). The screen for child anxiety related emotional disorders (SCARED): Scale construction and psychometric characteristics. *Journal of the American Academy of Child and Adolescent Psychiatry*, 36, 545–553.
- Bower, G. (1981). Mood and memory. *American Psychologist*, 36, 129–148.
- Bradley, B. P., Mogg, K., Falla, S. J., & Hamilton, L. R. (1998). Attentional bias for threatening facial expressions in anxiety: Manipulation of stimulus duration. *Cognition and Emotion*, 12, 737– 753.
- Bradley, B. P., Mogg, K., Millar, N., Bonham-Carter, C., Fergusson, E., Jenkins, J., et al. (1997). Attentional biases for emotional faces. *Cognition and Emotion*, 11, 25–42.
- Casey, B. J., Cohen, J. D., Jezzard, P., Turner, R., Noll, D. C., Trainor, R. J., et al. (1995). Activation of prefrontal cortex in children during a nonspatial working memory task with functional MRI. *NeuroIm*age, 2, 221–229.
- Casey, B. J., Durston, S., & Fossella, J. A. (2001). Evidence for a mechanistic model of cognitive control. *Clinical Neuroscience Research*, 1, 267–282.
- Casey, B. J., Thomas, K. M., Welsh, T. F., Livnat, R., & Eccard, C. H. (2000). Cognitive and behavioral probes of developmental landmarks for use in functional neuroimaging. In M. Ernst &

J. M. Rumsey (Eds.), *Functional Neuroimaging in Child Psychiatry* (pp. 155–168). New York: Cambridge University Press.

- Cohen, J. D., Forman, S. D., Braver, T. S., Casey, B. J., Servan-Schreiber, D., & Noll, D. C. (1994). Activation of the prefrontal cortex in a nonspatial working memory task with functional MRI. *Human Brain Mapping*, 1, 293–304.
- Cohen, J. D., MacWhinney, B., Flatt, M. R., & Provost, J. (1993). Psyscope: A new graphic interactive environment for designing psychology experiments. *Behavioral Research Methods, Instruments, and Computers*, 25, 257–271.
- Dahl, R. E., Birmaher, B., Williamson, D. E., Dorn, L., Perel, J., Kaufman, J., et al. (2000). Low growth hormone response to growth hormone-releasing hormone in child depression. *Biological Psychiatry*, 48, 981–988.
- Dalgleish, T., Moradi, A. R., Taghavi, M. R., Neshat-Doost, H. T., & Yule, W. (2001). An experimental investigation of hypervigilance for threat in children and adolescents with post-traumatic stress disorder. *Psychological Medicine*, *31*, 541–547.
- Dalgleish, T., Taghavi, M. R., Neshat-Doost, H. T., Moradi, A. R., Caterbury, R., & Yule, W. (2003). Patterns of processing bias for emotional information across clinical disorders: A comparison of attention, memory, and prospective cognition in children and adolescents with depression, generalized anxiety, and posttraumatic stress disorder. *Journal of Clinical Child and Adolescent Psychol*ogy, 32, 10–21.
- Davidson, R. J. (1994). Temperament, affective style, and frontal lobe asymmetry. In G. F. Dawson (Ed.), *Human Behavior and the Developing Brain* (pp. 518–536). New York: The Guilford Press.
- Davidson, R. J., Pizzagalli, D., Nitschke, J. B., & Putnam, K. (2002). Depression: Perspectives from affective neuroscience. *Annual Review of Psychology*, 53, 545–574.
- Derryberry, D., & Rothbart, M. K. (1988). Arousal, affect, and attention as components of temperament. *Journal of Personality and Social Psychology*, 55, 958–966.
- Drevets, W. C. (2001). Neuroimaging and neuropathological studies of depression: Implications for the cognitive-emotional features of mood disorders. *Current Opinion in Neurobiology*, 11, 240–249.
- Fernandez-Duque, D., Baird, J. A., & Posner, M. I. (2000). Executive attention and metacognitive regulation. *Consciousness and Cognition*, 9, 288–307.
- Garber, J., & Kaminski, K. M. (2000). Laboratory and performancebased measures of depression in children and adolescents. *Journal* of Clinical Child Psychology, 29, 509–525.
- Gazzaniga, M. S., Ivry, R. B., & Mangun, G. R. (1998). Cognitive neuroscience: The biology of the mind. New York: W.W. Norton.
- Gotlib, I. H., McLachlan, A. L., & Katz, A. N. (1988). Biases in visual attention in depressed and nondepressed individuals. *Cognition and Emotion*, 2, 185–200.
- Gray, J. R. (2001). Emotional modulation of cognitive control: Approach-withdrawal states double-dissociate spatial form from verbal two-back task performance. *Journal of Experimental Psychology: General*, 130, 436–452.
- Gray, J. R., Braver, T. S., & Raichle, M. E. (2002). Integration of emotion and cognition in the lateral prefrontal cortex. *Proceedings of the National Academy of Sciences of the United States of America*, 99, 4115–4120.
- Hollingshead, A. B. (1975). Four factor index of social status. New Haven, CT: Yale University Department of Sociology.
- Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., et al. (1997). Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. *Journal of the American Academy of Child & Adolescent Psychiatry*, 36, 980–988.
- Kendler, K. S. (1996). Major depression and generalised anxiety disorder same genes, (partly) different environments—revisited. *British Journal of Psychiatry*, 168, 68–75.
- Kindt, M., Brosschot, J. F., & Everaerd, W. (1997). Cognitive processing bias of children in a real life stress situation and a neutral situation. *Journal of Experimental Child Psychology*, 64, 79–97.

- Kovacs, M. (1985). The children's depression inventory. Psychopharmacology Bulletin, 21, 995–998.
- Kovacs, M., Gatsonis, C., Paulauskas, S. L., & Richards, C. (1989). Depressive disorders in childhood IV. A longitudinal study of comorbidity with and without risk for anxiety disorders. Archives of General Psychiatry, 46, 776–782.
- Lane, R. D., Fink, G. R., Chua, P. M.-L., & Dolan, R. J. (1997). Neural activation during selective attention to subjective emotional responses. *Neuroreport*, 8, 3969–3972.
- Lang, P. J., Bradley, B. P., Cuthbert, B. N., & Patrick, C. J. (1993). Emotion and psychopathology: A startle probe analysis. *Progress in Experimental Personality & Psychopathology Research*, 16, 163–199.
- Lang, P. J., Öhman, A., & Vaitl, D. (1988). The international affective picture system [photographic slides]. Gainesville, Florida: The Center for Research in Psychophysiology, University of Florida.
- Leckman, J. F., Sholomskas, D., Thompson, W. D., Belanger, A., & Weissman, M. M. (1982). Best estimate of lifetime psychiatric diagnosis: A methodological study. *Archives of General Psychiatry*, 39, 879–883.
- Luu, P., Tucker, D. M., & Derryberry, D. (1998). Anxiety and the motivational basis of working memory. *Cognitive Therapy and Research*, 22, 577–594.
- Massaro, D. W. (1988). Ambiguity in perception and experimentation. Journal of Experimental Psychology: General, 117, 417–421.
- Mathews, A., & MacLeod, C. (1994). Cognitive approaches to emotion and emotional disorders. Annual Review of Psychology, 45, 25–50.
- McManis, M. H., Bradley, M. M., Berg, W. K., Cuthbert, B. N., & Lang, P. J. (2001). Emotional reactions in children: Verbal, physiological, and behavioral responses to affective pictures. *Psychophysiology*, 38, 222–231.
- Miller, E. K., & Cohen, J. D. (2002). An integrative theory of prefrontal cortex activation. *Annual Review of Neuroscience*, 24, 167–202.
- Mogg, K., & Bradley, B. P. (1998). A cognitive-motivational analysis of anxiety. *Behaviour Research and Therapy*, 36, 809–848.
- Monk, C. S., McClure, E. B., Nelson, E. E., Zarahn, E., Bilder, R. M., Leibenluft, E., et al. (2003). Adolescent immaturity in attention-related brain engagement to emotional facial expressions. *NeuroImage*, 20, 420–428.
- Neale, M., & Kendler, K. (1995). Models of comorbidity for multifactorial disorders. American Journal of Human Genetics, 57, 935–953.
- Norman, D. A., & Shallice, T. (1986). Attention to action: Willed and automatic control of behavior. In R. J. Davidson, C. E. Schwartz & D. Shapiro (Eds.), *Consciousness and self-regulation: Advances in research and theory* (Vol. 4, pp. 1–18). New York: Plenum Press.
- Phillips, M. L., Drevets, W. C., Rauch, S. L., & Lane, R. (2003). Neurobiology of emotion perception I: The neural basis of normal emotion perception. *Biological Psychiatry*, 54, 504–514.
- Pine, D. S., Cohen, P., Gurley, D., Brook, J., & Ma, Y. (1998). The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Archives of General Psychiatry*, 55, 56–64.
- Posner, M. I., & Rothbart, M. K. (2000). Developing mechanisms of self-regulation. *Development and Psychopathology*, 12, 427–441.
- Shaffer, J. P. (1995). Multiple hypothesis testing. Annual Review of Psychology, 46, 561–584.
- Shimamura, A. P. (2000). Toward a cognitive neuroscience of metacognition. Consciousness and Cognition, 9, 313–323.
- Siegle, G. J., Granholm, E., Ingram, R. E., & Matt, G. E. (2002). Pupillary and reaction time measures of sustained processing of negative information in depression. *Biological Psychiatry*, 49, 624–636.
- Siegle, G. J., Steinhauer, S. R., Thase, M. E., Stenger, V. A., & Carter, C. S. (2002). Can't shake that feeling: Event-related FMRI assessment of sustained amygdala activity in response to emotional information in depressed individuals. *Biological Psychiatry*, 51, 693–707.
- Surguladze, S. A., Young, A. D., Senior, C., Brebion, G., Travis, M. J., & Phillips, M. L. (2004). Recognition accuracy and response bias to happy and sad facial expressions in patients with major depression. *Neuropsychology*, 18, 212–218.

- Tabachnick, B. G., & Fidell, L. S. (1996). Using multivariate statistics, 3/E. New York: Harper Collins College Publishers.
- Taghavi, M. R., Neshat-Doost, H. T., Moradi, A. R., Yule, W., & Dalgleish, T. (1999). Biases in visual attention in children and adolescents with clinical anxiety and mixed anxietydepression. *Journal of Abnormal Child Psychology*, 27, 215– 223.
- Tomarken, A. J., & Keener, A. D. (1998). Frontal brain asymmetry and depression: A self-regulatory perspective. *Cognition and Emotion*, 12, 387–420.
- Vasey, M. W., Daleiden, E. L., Williams, L. L., & Brown, L. M. (1995). Biased attention in childhood anxiety disorders: A preliminary study. *Journal of Abnormal Child Psychology*, 23, 267– 279.
- Vasey, M. W., & Lonigan, C. J. (2000). Considering the clinical utility of performance-based measures of childhood anxiety. *Journal of Clinical Child Psychology*, 29, 493–508.
- Vasey, M. W., & MacLeod, C. (2001). Information-processing factors in childhood anxiety: A review and developmental perspective. In M. W. Vasey & M. R. Dadds (Eds.), *The developmental psychopathology of anxiety* (pp. 253–277). Oxford, England: Oxford University Press.
- Vuilleumier, P., & Armony, J. L. (2001). Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. *Neuron*, 30, 829–841.
- Williams, J. M. G., Watts, F. N., MacLeod, C., & Mathews, A. (Eds.). (1997). Cognitive psychology and emotional disorders. (2nd ed.). Chichester, England: Wiley.