#### ORIGINAL CONTRIBUTION

# Neutral face distractors differentiate performance between depressed and healthy adolescents during an emotional working memory task

Lucy R. Tavitian · Cecile D. Ladouceur · Ziad Nahas · Beatrice Khater · David A. Brent · Fadi T. Maalouf

Received: 29 May 2013/Accepted: 26 October 2013 © Springer-Verlag Berlin Heidelberg 2013

**Abstract** The aim of the present study is to examine the effect of neutral and emotional facial expressions on voluntary attentional control using a working memory (WM) task in adolescents with major depressive disorder (MDD). We administered the Emotional Face n-back (EFNBACK) task, a visual WM task with neutral, happy and angry faces as distractors to 22 adolescents with MDD (mean age 15.7 years) and 21 healthy controls (HC) (mean age 14.7 years). There was a significant group by distractor type interaction (p = 0.045) for mean percent accuracy rates. Group comparisons showed that MDD youth were less accurate on neutral trials than HC (p = 0.027). The two groups did not differ on angry, happy and blank trials

(p>0.05). Reaction time did not differ across groups. In addition, when comparing the differences between accuracies on neutral trials and each of the happy and angry trials, respectively [(HAP-NEUT) and (ANG-NEUT)], there was a group effect on (HAP-NEUT) where the difference was larger in MDD than HC (p=0.009) but not on ANG-NEUT (p>0.05). Findings were independent of memory load. Findings indicate that attentional control to neutral faces is impaired and negatively affected performance on a WM task in adolescents with MDD. Such an impact of neutral faces on attentional control in MDD may be at the core of the social-cognitive impairment observed in this population.

L. R. Tavitian

Department of Cross Cultural Psychology, Tilburg University, Tilburg, The Netherlands

C. D. Ladouceur · D. A. Brent · F. T. Maalouf Department of Psychiatry, The University of Pittsburgh, Pittsburgh, PA, USA

C. D. Ladouceur

Department of Psychology, The University of Pittsburgh, Pittsburgh, PA, USA

Z. Nahas

Department of Psychiatry, The American University of Beirut Medical Center, Beirut, Lebanon

B. Khater

Department of Family Medicine, The American University of Beirut Medical Center, Beirut, Lebanon

F. T. Maalouf (⊠)

Published online: 19 November 2013

Child and Adolescent Psychiatry Program, Department of Psychiatry at the American University of Beirut Medical Center, PO Box: 11–0236, Riad El Solh, 11072020 Beirut, Lebanon e-mail: fm38@aub.edu.lb **Keywords** Emotion processing · Depression · Adolescent · Attentional control · Emotional distracters

## Introduction

Major depressive disorder (MDD) in adolescence is a serious psychiatric condition with an estimated 5.3 % prevalence for a 12-month period [1]. MDD in adolescence is often associated with increased risk for substance use, educational impairments, suicide and non-suicidal self-injury which by itself also increases the risk for suicide attempts in this population [2–4]. While longitudinal studies of depressed adolescents report a fairly high 1-year remission rate (60–90 %) [5], follow-up studies indicate a 50–70 % recurrence of depressive episodes within a period of 5 years [6]. Considering the high recurrence rate and the associated morbidity and mortality, understanding the developmental pathophysiology of depression is crucial for planning appropriate treatment strategies.



There is mounting evidence demonstrating that emotion regulation and in particular attentional control are implicated in the pathophysiology of MDD. Two attentional control processes, a voluntary one and an automatic one play a major role in emotion regulation. Voluntary attentional control in the context of emotionally salient information involves the selective modulation of attention toward goal-relevant information while inhibiting emotionally salient distractors and automatic attentional control involves the more implicit direction of attention toward or away from emotional material [7].

Previous studies have investigated attentional control processes in the context of emotional stimuli using behavioral tasks. In a study using the Affective Go-No Go task, depressed adults were less accurate than matched controls, and slower on blocks of trials that required shifting from one emotional category to the other [8]. Another study using an emotional oddball task whereby participants respond to target stimuli, which are preceded by sad or yoked neutral pictures rated on a sadness/happiness Likert-type scale, showed that depressed adults were significantly slower than controls when responding to targets preceded by sad stimuli [9]. Depressed adults have also been shown to demonstrate reduced inhibition when processing negative material on the Negative Affective Priming task compared to controls; this effect was not observed among remitted depressed participants [10]. When using the Emotional and Face Go-No Go tasks to compare performance of depressed adolescents to that of healthy controls (HC), no significant differences in reaction times were detected. Here, depression severity was associated with greater reactivity to emotional stimuli [11]. In another study using the Affective Go-No Go, acutely depressed adolescents were slower shifting to negative targets than shifting to happy targets as compared to remitted and HC participants [12]. While the above studies assessed attentional control in the context of emotional distractors during tasks that involved lower order cognitive functions, to our knowledge no study has examined attentional control during a task that recruits higher-order cognitive functions such as working memory (WM), among depressed adolescents. Findings in the literature have not been consistent on the effect of distractors in lower vs higher-order cognitive tasks. According to Pessoa's dual competition model of information processing in the brain, stimuli compete for limited perceptual processing capacity and control of behavior [13]. Affective significance impacts the flow of this information and higher-order cognitive tasks would theoretically require more attentional resources and are more likely to be impacted by the interference of task-irrelevant emotional stimuli than lower order cognitive tasks.

The present study aims to examine the extent to which emotional distractors influence voluntary attentional control processes during performance on a WM task in adolescents diagnosed with MDD as compared to HC. The task used in the current study includes high vs low WM demand which enables us to examine the extent to which emotional interference effects are present in high vs low order cognitive conditions.

It is known that emotionally salient stimuli can easily capture attention and interfere with ongoing cognitive processes [14, 15]. Working memory refers to the active maintenance and flexible updating of goal or task-relevant information. Such processes involve systematically revising items and resisting interference from irrelevant information [16]. Indeed, several studies have demonstrated that optimal WM function critically depends on interference filtering supported by attentional control processes [17– 19]. In addition, the interaction among attentional control, WM and their respective functional roles has been elaborated in conceptual and computational work [20-22]. In the present study, we are using the emotional face n-back (EFNBack) task. It involves the performance on a visual WM task while resisting interference from emotional distracters that could potentially impair the ability to maintain focus on task-relevant information to be stored in WM [23–25]. This task has previously been used in typically developing youth [24] as well as in individuals diagnosed with or at high risk for mood disorders [26, 27].

We hypothesized that adolescents with MDD compared to HC would exhibit greater difficulty resisting interference from the negative emotional distractors as evidenced by slower reaction times and reduced accuracy rates on trials with angry face distractors under the memory-load condition (2-back).

#### Methods

### **Participants**

The study protocol was approved by the Institutional Review Board. All participants and their parents were informed about study procedures and signed informed assent and consent forms, respectively. A total of 43 adolescents aged 12-18 participated in the study. These included 21 HC participants with no previous psychiatric history and 22 participants meeting criteria for MDD current (n = 19) or past (n = 3). MDD participants were recruited from an outpatient Child and Adolescent Psychiatry clinic at the American University of Beirut Medical Center and HC were recruited through advertisements placed in a Family Medicine clinic at the same institution. Participants who met eligibility criteria according to their treating clinicians and interested in the study were referred to the study team for further evaluation and consenting. One subject from the MDD group was excluded after



Table 1 Demographic and clinical data

	MDD $(n = 22)$	HC $(n = 21)$	Statistics
Sex (male/female)	6/16	11/10	$\chi^2(1) = 2.83,  p = 0.09$
Age in months, mean (SD)	188.68 (18.42)	176.57 (22.08)	t(41) = 1.96, p = 0.06
IQ, mean (SD)	91.45 (10.19)	102.62 (13.45)	t(41) = 3.08, p = 0.004, r = 0.19
BDI, mean (SD)	27 (8.34)	6.86 (9.38)	t(41) = 7.45, p = 0.000, r = 0.57
SDQ total, mean (SD)	17.09 (7.48)	9.48 (5.56)	t(41) = 3.77, p = 0.001, r = 0.26
SSI prior total, mean (SD)	8.71 (9.16)	0.05 (0.22)	t(40) = -4.34, p = 0.000, r = 0.32
SSI current total, mean (SD)	9.27 (11.79)	0.05 (0.22)	t(41) = -3.58, p = 0.001, r = 0.24
SDQ-emotional symptoms: mean(SD)	5.36 (2.82)	2.33 (2.78)	t(41) = 3.55, p = 0.001, r = 0.23
SDQ-conduct, mean (SD)	3.95 (1.59)	1.81 (1.25)	t(41) = 4.91, p = 0.000, r = 0.37
SDQ-anxiety score, mean (SD)	2.95 (1.67)	1.67 (1.88)	t(41) = -2.36, p = 0.023, r = 0.34
SDQ-hyperactivity score, mean (SD)	4.60 (1.70)	3.10 (2)	t(39) = 2.59, p = 0.01, r = 0.15

SD standard deviation, IQ intellectual quotient, BDI Beck depression inventory, SDQ strengths and difficulties questionnaire, SDQ-ESS strengths and difficulties questionnaire emotional symptoms score, SDQ-CON strengths and difficulties questionnaire conduct problems score, SDQ-HYP strengths and difficulties questionnaire hyperactivity score, PDS pubertal development scale, SSRI selective serotonin reuptake inhibitor, SSI scale of suicide ideation

screening due to not meeting intellectual quotient (IQ) cutoff criterion and one subject from HC group was moved to the MDD group after being found to have MDD. All MDD and HC adolescents were administered a structured clinical interview and completed self-report scales to assess for depression severity, suicidality, and other psychiatric symptoms. Current diagnoses were generated using the Arabic version of the development and well-being assessment (DAWBA), administered to adolescents alone [28, 29]. Exclusion criteria included a history of head injury, neurological disorder (epilepsy, developmental disorder, loss of consciousness for more than 10 min), premorbid IQ estimate <70, current psychotic symptoms, current (within the past month) history of alcohol and illicit substance abuse or dependence, and current history of untreated attention deficit hyperactivity disorder (ADHD). In addition, history of any psychiatric disorder was an exclusion criterion for HC. Participants' IQ score was derived using the matrices and spatial span subscales of the Wechsler nonverbal scale of intelligence. Eighteen participants from the MDD group were medication naïve at time of testing and only three participants were taking fluoxetine. Fourteen participants from the MDD group had one or more comorbid anxiety disorders, one had comorbid oppositional defiant disorder and one had comorbid treated ADHD (Table 1).

#### Materials

# Diagnostic interview

Diagnoses were generated using the computerized Arabic version of the DAWBA [28], which is a structured

interview used to formulate a psychiatric diagnosis of a child/adolescent based on DSM-IV-TR criteria. The Arabic version of the DAWBA was recently validated in a sample of adolescents seeking treatment at the same clinic with preliminary findings demonstrating its validity and reliability [29].

# Other measures

Depression severity was assessed using an Arabic version of the Beck depression inventory (BDI) [30]. The BDI is a 21-item self-report measure of cognitive, behavioral, affective, and somatic components of depression based on DSM-IV criteria. Items on the BDI are rated on a fourpoint Likert-type scale ranging from 0 to 3. (0-12 = notsignificant; 13-18 = mild; 19-28 = moderate; 29-63 = moderatesevere) [31]. Current and past suicide ideation was assessed using the 19-item Beck scale for suicide ideation (SSI) [32] which was translated to Arabic by the study team. The SSI evaluates intensity of suicidal thoughts, their characteristics and interviewee's attitude towards them. The SSI is scored by the clinician based on individuals' answers on a semistructured interview (cutoff = 6). The Arabic version of the strengths and difficulties questionnaire (SDQ) [33], which has been validated in the Arabic language [34] was administered as part of the DAWBA as a measure of emotional and behavioral difficulties. The SDQ yields five scores for difficulties—conduct problems (normal = 0-3, borderline = 4, abnormal = 5-10), inattention-hyperactivity (SDQ-HYP) (normal = 0-5, borderline = 6, abnormal = 7-10), emotional symptoms (normal = 0-5, borderline = 6, abnormal = 7-10), peer problems (normal = 0-3, borderline = 4-5, abnormal = 6-10), and



total difficulties score (normal = 0–15, borderline = 16–19, abnormal = 20–40)—and one score for strength/pro-social behavior (normal = 6–10, borderline = 5, abnormal = 0–4). We, in addition, have generated an SDQ-anxiety score (SDQ-ANX) using answers to the following statements specific to anxiety symptoms: I worry a lot, I am nervous in new situations. I easily lose confidence and I have many fears, I am easily scared.

The emotional faces n-back task

The EFNBACK task [24] is a modified version of a visual sequential letter WM n-back task. The visual n-back task consists of visually presenting a pseudorandom sequence of letters and asking participants to respond to a pre-specified letter appearing on the computer screen. The *n*-back includes two memory-load conditions: a no-memory load (0-back, press the button when you see the letter "M") and a memory load (2-back, press the button when the letter is identical to two letters back -N-L-N). The EFNBACK task consists of presenting the visual n-back task flanked by two identical pictures of an actor depicting either a neutral, fearful, or happy facial expression. Participants were informed that pairs of faces portraying three different emotions would flank either side of the letters and were instructed to attend to the letter while ignoring the faces. It includes eight blocks comprising two memory-load conditions by four distractor conditions] neutral, angry, happy or no distractors (i.e., letter alone)]. Each block includes 12 trials. Each trial consists of presenting a letter flanked with either no picture, or with a face distractor. The face stimuli consist of gray-scaled images 400 × 600 pixels of 20 individuals (10 males and 10 females) with neutral, angry, and happy expressions taken from the NimStim set that is available to the scientific community at (http://www. macbrain.org/resources.htm). All images were cropped using an oval shape and normalized for size and luminance. The modified pictures were then aligned according to the positioning of the eyes on each face to ensure that every face was positioned the same across every trial. Most participants completed three runs of eight blocks, with 12 trials in each block (total duration 21 min 12 s). Trial duration was 500 ms. The intertrial interval (ISI) consisted of a fixation cross (flanked with faces). The ISI was jittered, with a mean duration of 3,500 ms. Participants are instructed to respond to target letters by pressing number "2" on the keyboard with their index finger as quickly as possible while ignoring the faces that flanked the letters. Each block began with the 0-back no-face condition to ease participants into the task followed by different combinations of the distracter type by memory condition presented in a pseudorandom order. Brief instructions, informing participants about whether the block was a 0-back or 2-back condition, were presented on the screen at the beginning of each block. When projected on the screen, the size of each distractor picture was approximately  $5.5 \text{ cm} \times 8 \text{ cm}$ . Participants sat 50 cm from the screen, giving a visual angle of approximately  $3.5^{\circ}$  between the edges of the pictures (Fig. 1).

Data analyses

The IBM Statistical Package for Social Sciences version 19 was used to analyze the data. Mean differences in response accuracy (percent of accurate responses) and reaction time between MDD and HC were analyzed using two separate mixed multivariate analyses of variance with distractor type (neutral, angry, happy, blank) and memory condition (0-back, 2-back) entered as repeated measures variables and group as a between measures variable. The multivariate statistic reported was Wilk's Lambda. Main effects and interactions between groups were followed up with univariate analyses of variance and covariance (ANCOVA). Separate within subjects MANCOVAs were also conducted. In all analyses, participants' IQ, mean scores on SDQ-HYP, mean scores on SDQ-ANX and sex were entered as covariates. Bonferroni corrections were applied where necessary, and two-tailed tests were used. SDQ-HYP data were missing for two subjects in the MDD group and as such, when conducting MANCOVA and ANCOVA these missing values were replaced by the mean of the MDD group.

While most participants completed three runs of the EFNBACK task, three participants completed two runs. Correct trials with reaction times below 100 and above 3,000 were removed from the analysis. Mean reaction times per distractor type and memory condition for target trials were calculated for each participant. Accurate response was defined as responding to target stimuli (0 or 2 letters back) and not responding to non-target stimuli. Accuracy rates were converted to percentages from the total number of trials per participant to account for the differing number of total trials completed per participant. The data was free of missing values. Univariate and multivariate outliers were checked separately for each group. The data was normally distributed and was free of influential outliers.

#### Results

Demographic and clinical variables

The groups were not different in age [t(41) = -1.96, p > 0.05]. There were more females (72 %) in MDD than in HC (48 %); however, the groups were not different on



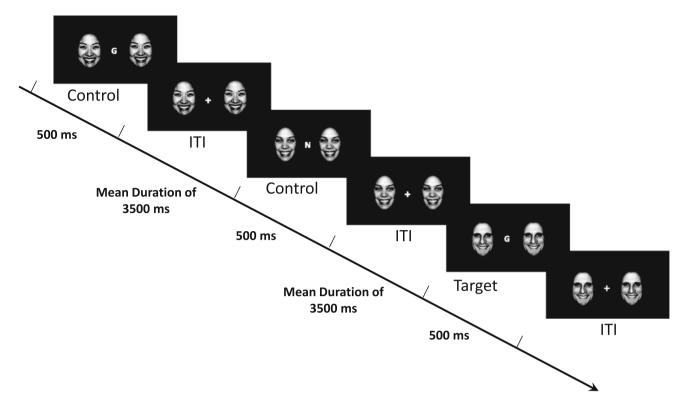


Fig. 1 Illustration of the emotional face n-back task (2-back happy face distracter condition). During the 0-back condition, participants must respond to the letter M. ITI intertrial stimulus interval. Copyright © 2009 by the American Psychological Association.

Reproduced with permission. The official citation that should be used in referencing this material is Ladouceur et al. [24]. The use of APA information does not imply endorsement by the APA

sex distribution [ $\chi^2(1) = 2.83$ , p = 0.09]. A significant difference between MDD and HC was found on IQ, [t(40) = 3, p = 0.004, r = 0.18) (Table 1).

The two groups differed on their respective SDQ total, SDQ emotional, conduct, hyperactivity and anxiety subscores in addition to SSI past and current and BDI scores (p < 0.05, for all) with effect sizes ranging from small (r = 0.15 on the SDQ-hyperactivity subscale) to large (r = 0.57 on the BDI). On these variables MDD scored significantly higher than HC (Table 1).

#### Response accuracy

#### Main analyses

In the mixed multivariate analysis of covariance (MAN-COVA), Mauchley's test indicated that the assumption of sphericity was not met for the main effect of valence and the interaction term of distracter type by memory  $[\chi^2(5) = 19.6, p < 0.05]$  and  $\chi^2(5) = 20.9, p < 0.05$ , respectively]. As such, the Greenhouse Geisser correction was used for the within subjects analyses.

The mixed MANCOVA indicated a significant group by distractor type interaction F(3,34) = 2.97, p = 0.045.

In addition, there was a significant main effect for memory [F(1,36) = 6.21, p = 0.017]. This indicates that regardless of distractor type and group belonging, participants' performance was different across the two memory conditions. As expected, participants were less accurate on the 2-back memory condition compared to the 0-back condition (p < 0.05). The group by distractor type interaction effect was followed up with analyses of covariance conducted on mean percent accuracies for each distractor type across both memory-load conditions while covarying for IQ, sex, SDQ-HYP and SDQ-ANX. MDD were less accurate on neutral trials than HC [F(1,36) = 5.35, p = 0.027] while the two groups were not different on any of the other distractor types (p > 0.05) (see Table 2).

# Other analyses

To further explore the group by distractor type interaction effect, separate within subjects repeated analyses of variance and covariance were conducted for MDD and HC. No valence effect in either group was statistically significant (p > 0.05) but rather a memory effect was evidence in MDD (p = 0.009) but not HC (p > 0.05), suggesting that



 Table 2
 Mean percent

 accuracy per valence group

Distractor type	MDD $(n = 22)$	HC $(n = 21)$	Statistics
Neutral, mean (SD)	91.95 (9.71)	96.66 (3.84)	F(1,36) = 5.35, p = 0.027
Angry, mean (SD)	90.69 (13.78)	94.71 (5.83)	F(1,37) = 2.39, p > 0.05
Happy, mean (SD)	95.50 (6.38)	96.94 (3.79)	F(1,36) = 0.78, p > 0.05
Blank, mean (SD)	94.57 (4.49)	94.97 (5.62)	F(1,36) = 0.27, p > 0.05
HAPP-NEUT, mean (SD)	3.55 (5.35)	0.28 (3.01)	F(1,36) = 7.56, p = 0.009
ANG-NEUT, mean (SD)	-0.96 (6.19)	-1.95 (3.98)	F(1,36) = 0.004, p > 0.05

MDD's performance on the 2-back condition was worse than their performance on the 0-back condition.

To better understand the difference in the patterns of responding between both groups, we calculated the differences in percent accuracy on neutral trials and happy trials (HAP-NEUT) and neutral trials and angry trial (ANG-NEUT) in each group. Here, analyses of covariance after covarying for IQ, sex, SDQ-ANX and SDQ-HYP showed a group effect on HAP-NEUT (p=0.009) but not on ANG-NEUT (p>0.05). These findings highlight the fact that as compared to HC, MDD showed more interference by neutral faces relative to happy faces (Table 2).

#### Reaction time

In the mixed MANCOVA, Mauchley's test indicated that the assumption of sphericity was met for both the main effect of distracter type  $\chi^2(5) = .94$ , p > 0.05, but not the interaction term of distractor type by memory  $\chi^2(5) = 11.6$ , p = 0.04.

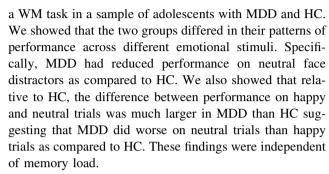
There was a significant main effect for memory condition on reaction times F(1,36) = 6.63, p = 0.014, Here, both MDD and HC showed slower reaction times for the 2-back compared to the 0-back condition. No other significant main effects or interactions were found.

#### Exploratory analyses

Both mixed MANCOVAs on accuracy and reaction time were repeated once excluding the three remitted MDD participants and once excluding participants with two enback runs. Results remained unchained in both repetitions. We then explored the possible effect of our clinical outcomes (SDQ total, SDQ-ESS, SDQ-CON, SDQ-HYP, SSI prior and current, and BDI) on reaction time and percent accuracy scores per group using Pearson's correlations in all four EFNBACK conditions. No significant correlations were found (p > 0.05).

# Discussion

The present study examined the effect of distracting emotional stimuli on attentional control during performance on



This pattern of responding among adolescents with MDD suggests that attentional control to neutral faces was impaired and negatively affected WM. To our knowledge, such difficulties in attentional control to neutral face distractors during a WM task have not been reported in adolescents with MDD. Our results are consistent with recent findings that brain activation to neutral faces in depressed participants has a different pattern than brain activation to neutral faces in HC [35]. They are also consistent with other behavioral findings in adults showing that depressed participants are slower responding to neutral faces as compared to other valences, an impairment that was still evident after remission [36]. Other work also reported that brain activity during the presentation of neutral faces accurately differentiated between youth at high risk for mood disorders and HC [37]. Findings similar to the ones presented here have been reported as well in a study of attentional control in generalized anxiety disorder using the Rapid Serial Visual Presentation task. Results indicated a significant decrease in percent accuracies for targets preceded by neutral and fearful distracter images; an effect not observed among controls. Moreover, this relationship was mediated by deficits in attentional control [38].

The interference effect of neutral faces in MDD sheds some light on how depressed youth process information in daily life. The capacity to control attention processes progresses gradually over the course of a child's development [39], and is considered a central cognitive function necessary in acquiring skills in other cognitive areas. Attentional control processes allow the allocation of attention to information-rich areas that are necessary for learning [40]. If attentional control is impaired in youth with MDD then the use of information in the environment in a way that promotes learning would be compromised.



Interestingly, both MDD and HC did not differ in their performance on angry trials and this may be due to the fact that accuracy on these trials was low in both groups. This may indicate a natural inclination towards alertness to negative stimuli in the environment which in evolutionary terms, is necessary for survival purposes [41].

Performance on enback measures voluntary attentional control processes which is one of two attentional control processes, the second one being automatic attentional control. Other tasks, including, for example, the emotional STROOP task have been employed to study automatic attentional control processes. Here, individuals attend to a nonemotional stimulus feature (for example, color of the stimulus) at the expense of the emotional content of the same stimulus. These two processes subserve different neural mechanisms [7]. Automatic attentional control processes appear to primarily implicate the medial prefrontal cortical system while voluntary attentional control processes appear to primarily implicate the lateral prefrontal cortical system [7]. Future studies should aim at comparing and contrasting both automatic and voluntary attentional control processes in this population.

Our findings also indicated that the impact of neutral facial expression on attentional control in MDD was independent of memory load suggesting that task difficulty did not affect attention allocation processes in our study. This finding is in line with previous research showing a decrease in emotion interference with increased task difficulty due to preferential allocation of attentional resources to the task at hand over task-irrelevant emotional stimuli. In some other studies, however, the interference effect was solely present during a higher memory load [27]. It would be advantageous that future studies employ tasks that manipulate cognitive load to gain a better understanding of the effect of this load on emotional interference in depression.

A possible limitation of our study is the fact that participants with comorbid diagnoses were not excluded from the present sample and as a consequence this may have affected the specificity of our findings with regard to MDD. For example, ADHD is highly comorbid with depressive disorders in adolescents [42] and is associated with executive dysfunctions [43]. Although not primarily an emotional disorder, ADHD has also been shown to be associated with emotional dysregulation [44]. A study that has looked at the effect of emotion processing on WM in children with ADHD as compared to children with bipolar disorder found that while the group with bipolar disorder had lower accuracy across emotions as compared to HC, the group with ADHD did not differ from HC [45]. It is expected that when examining attentional control in the context of emotional distractors in ADHD, deficits would be present across emotional valences rather than be specific to a certain valence since ADHD is primarily a disorder of executive control rather than emotion regulation. Nonetheless, to avoid the potential confounding effect of comorbid ADHD in the present study, we excluded subjects who have untreated ADHD and controlled for the presence of residual/subthreshold ADHD symptoms in our analyses. In addition and as it would be expected in this population, the prevalence of anxiety disorders was high in our sample. We also controlled for the presence of anxiety symptoms in our analyses in an effort to address this issue. Although future studies should aim at replicating our findings in a sample of adolescents with MDD and no comorbidities, this may not add to the generalizability of the findings to a clinical sample.

The lack of an emotion labeling task preceding the EFNBACK task administration is another limitation. Such a task would have provided some insight as to whether deficits in emotion labeling, if any, contributed to the present findings. Another limitation is the failure to include negative mood priming in the current study. Recognizing that according to the content-specific hypothesis, cognitive biases in information processing may be activated to a greater extent when depression-specific schema are activated [46], it was not clear how activation conditions would have affected performance of this novel task in youth with MDD.

In summary, this is the first study to demonstrate that distracting neutral faces impair attentional control during a WM task in adolescents with MDD as compared to HC. An interference effect of neutral faces with attentional control in adolescents with MDD suggests significant socio-cognitive impairment in this population. As such, there may be a need to develop treatment modalities focusing on cognitive training with emotional faces paradigms in this population. In addition, future studies are warranted to determine whether this interference effect is state or trait marker in adolescent MDD.

Acknowledgments The authors would like to acknowledge the grant support from the American Foundation for Suicide Prevention (PI: F. Maalouf) and the Medical Practice Plan-Faculty of Medicine at the American University of Beirut (PI: F. Maalouf). The authors would also like to acknowledge the contribution of the research team (Ms. Mia Atwi, Ms. Camelia Hatoum and Dr. Nayla Hariz) for their help in recruiting and conducting the clinical and neuropsychiatric assessments and would like to thank the participating adolescents and their families.

Conflict of interest Dr. Maalouf has received research funding from the American Foundation of Suicide Prevention. He has consulted Eli Lilly and is on the speaker bureau of Servier and Hikma pharmaceuticals. Dr. Brent works for the University of Pittsburgh School of Medicine and University of Pittsburgh Medical Center, Western Psychiatric Institute in Clinic. He also has research projects funded by the National Institute of Mental Health. Dr. Brent has received royalties from Guilford Press and eResearch Technology. He



is the editor of UpToDate Psychiatry and receives Honoraria from Oxford Press and Honoraria for presenting at Continuing Medical Education events. Ms. Tavitian, Dr. Ladouceur, Dr. Khater and Dr. Nahas declare no conflict of interest.

#### References

- Maalouf FT, Brent DA (2012) Child and adolescent depression intervention overview: what works, for whom and how well? Child Adolesc Psychiatr Clin N Am 21(2):299–312
- Thapar A, Collishaw S, Pine DS, Thapar AK (2012) Depression in adolescence. Lancet 379(9820):1056–1067
- Wilkinson P, Kelvin R, Roberts C, Dubicka B, Goodyer I (2011) Clinical and psychological predictors of suicide attempts and nonsuicidal self-injury in the adolescent depression antidepressants and psychotherapy trial (ADAPT). Am J Psychiatry 168(5):495–501
- Asarnow JR, Porta G, Spirito A, Emslie G, Clarke G, Wagner KD, Vitiello B, Keller M, Birmaher B, McCracken J (2011) Suicide attempts and nonsuicidal self-injury in the treatment of resistant depression in adolescents: findings from the TORDIA study. J Am Acad Child Adolesc Psychiatry 50(8):772–781
- Dunn V, Goodyer IM (2006) Longitudinal investigation into childhood-and adolescence-onset depression: psychiatric outcome in early adulthood. Br J Psychiatry 188(3):216–222
- Lewinsohn PM, Rohde P, Seeley JR, Klein DN, Gotlib IH (2000) Natural course of adolescent major depressive disorder in a community sample: predictors of recurrence in young adults. Am J Psychiatry 157(10):1584–1591
- Phillips ML, Ladouceur CD, Drevets WC (2008) A neural model of voluntary and automatic emotion regulation: implications for understanding the pathophysiology and neurodevelopment of bipolar disorder. Mol Psychiatry 13(9):833–857
- Murphy FC, Michael A, Sahakian BJ (2012) Emotion modulates cognitive flexibility in patients with major depression. Psychol Med 42(7):1373–1382. doi:10.1017/S0033291711002418
- Wang L, LaBar KS, Smoski M, Rosenthal MZ, Dolcos F, Lynch TR, Krishnan RR, McCarthy G (2008) Prefrontal mechanisms for executive control over emotional distraction are altered in major depression. Psychiatry Res 163(2):143–155. doi:10.1016/j. pscychresns.2007.10.004
- Joormann J, Gotlib IH (2010) Emotion regulation in depression: relation to cognitive inhibition. Cogn Emot 24(2):281–298. doi:10.1080/02699930903407948
- Han G, Klimes-Dougan B, Jepsen S, Ballard K, Nelson M, Houri A, Kumra S, Cullen K (2012) Selective neurocognitive impairments in adolescents with major depressive disorder. J Adolesc 35(1):11–20. doi:10.1016/j.adolescence.2011.06.009
- Maalouf FT, Clark L, Tavitian L, Sahakian BJ, Brent D, Phillips ML (2012) Bias to negative emotions: a depression statedependent marker in adolescent major depressive disorder. Psychiatry Res 198(1):28–33. doi:10.1016/j.psychres.2012.01.030
- Pessoa L (2009) How do emotion and motivation direct executive control? Trends Cogn Sci 13(4):160–166. doi:10.1016/j.tics. 2009.01.006
- Hodsoll S, Viding E, Lavie N (2011) Attentional capture by irrelevant emotional distracter faces. Emotion 11:346–353
- Pessoa L, Kastner S, Ungerleider LG (2002) Attentional control of the processing of neutral and emotional stimuli. Cogn Brain Res 15(1):31–45
- 16. Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A (2000) The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: a latent variable

- analysis. Cogn Psychol 41(1):49–100. doi:10.1006/cogp.1999.
- 17. Engle RW, Kane MJ (2004) Executive attention, working memory capacity, and a two-factor theory of cognitive control. In: Ross B (ed) The psychology of learning and motivation, vol 44. Elsevier, New York, pp 145–199
- Kane MJ, Bleckley MK, Conway ARA, Engle RW (2001) A controlled-attention view of working memory capacity. J Exp Psychol Gen 130:169–183
- Fukuda K, Vogel EK (2009) Human variation in overriding attentional capture. J Neurosci 29:8726–8733
- De Pisapia N, Slomski JA, Braver TS (2007) Functional specializations in lateral prefrontal cortex associated with the integration and segregation of information in working memory. Cereb Cortex 17:993–1006
- O'Reilly RC, Frank MJ (2006) Making working memory work: a computational model of learning in the prefrontal cortex and basal ganglia. Neural Comput 18:283–328
- Cohen JD, Perlstein WM, Braver TS, Nystrom LE, Noll DC, Jonides J, Smith EE (1997) Temporal dynamics of brain activation during a working memory task. Nature 386(6625):604–608
- Erk S, Kleczar A, Walter H (2007) Valence-specific regulation effects in a working memory task with emotional context. Neuroimage 37:623–632
- Ladouceur CD, Silk JS, Dahl RE, Ostapenko L, Kronhaus D, Phillips ML (2009) Fearful faces influence attentional control processes in anxious youth and adults. Emotion 9(6):855–864
- Perlstein WM, Elbert T, Stenger VA (2002) Dissociation in human prefrontal cortex of affective influences on working memory-related activity. PNAS 99(3):1736–1741
- Bertocci MA, Bebko GM, Mullin BC, Langenecker SA, Ladouceur CD, Almeida JR, Phillips ML (2012) Abnormal anterior cingulate cortical activity during emotional *n*-back task performance distinguishes bipolar from unipolar depressed females. Psychol Med 42(7):1417–1428. doi:10.1017/S003329171100242X
- 27. Kerestes R, Ladouceur CD, Meda S, Nathan PJ, Blumberg HP, Maloney K, Ruf B, Saricicek A, Pearlson GD, Bhagwagar Z, Phillips ML (2012) Abnormal prefrontal activity subserving attentional control of emotion in remitted depressed patients during a working memory task with emotional distracters. Psychol Med 42(1):29–40. doi:10.1017/S0033291711001097
- Goodman R, Ford T, Richards H, Gatward R, Meltzer H (2000)
   The development and well-being assessment: description and initial validation of an integrated assessment of child and adolescent psychopathology. J Child Psychol Psychiatry 41(5):645–656. doi:10.1111/j.1469-7610.2000.tb02345.x
- Zeinoun P, Bawab S, Atwi M, Hariz N, Tavitian L, Khani M, Nahas Z, Maalouf FT (2013) Validation of an Arabic multi-informant psychiatric diagnostic interview for children and adolescents: development and well being assessment-Arabic (DAWBA-Arabic). Compr Psychiatry 54(7):1034–1041. doi:10.
- Farhood LF, Noureddine SN (2003) PTSD, depression, and health status in Lebanese civilians exposed to a church explosion. Int J Psychiatry Med 33(1):39–53. doi:10.2190/309d-7hqx-d4j4-t6tr
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J (1961) An inventory for measuring depression. Arch Gen Psychiatry 4:561–571. doi:10.1001/archpsyc.1961.01710120031004
- 32. Beck AT, Kovacs M, Weissman A (1979) Assessment of suicidal intention: the scale for suicide ideation. J Consult Clin Psychol 47(2):343–352. doi:10.1037/0022-006x.47.2.343
- Goodman R (1997) The strengths and difficulties questionnaire: a research note. J Child Psychol Psychiatry 38(5):581–586. doi:10. 1111/j.1469-7610.1997.tb01545.x



- Alyahri A, Goodman R (2008) The prevalence of DSM-IV psychiatric disorders among 7–10 year old Yemeni schoolchildren. Soc Psychiatry Psychiatr Epidemiol 43(3):224–230. doi:10.1007/ s00127-007-0293-x
- Oliveira L, Ladouceur CD, Phillips ML, Brammer M, Mourao-Miranda J (2013) What does brain response to neutral faces tell is about major depression? Evidence from machine learning and fMRI. PLoS One 8(4):e60121. doi:10.1371
- Leppanen JM, Milders M, Bells JS, Terriere E, Hietanen JK (2004) Depression biases the recognition of emotionally neutral faces. Psychiatry Res 128(2):123–133
- Mourão-Miranda J, Oliveira L, Ladouceur CD, Marquand A, Brammer M, Birmaher B, Axelson D, Phillips ML (2012) Pattern recognition and functional neuroimaging help to discriminate healthy adolescents at risk for mood disorders from low risk adolescents. PLoS One 7(2):e29482. doi:10.1371/journal.pone. 0029482
- Olatunji BO, Ciesielski BG, Armstrong T, Zhao M, Zald DH (2011) Making something out of nothing: neutral content modulates attention in generalized anxiety disorder. Depress Anxiety 28(5):427–434
- Davidson MC, Amso D, Anderson LC, Diamond A (2006)
   Development of cognitive control and executive functions from 4

- to 13 years: evidence from manipulations of memory, inhibition, and task switching. Neuropsychologia 44(11):2037
- 40. Wass S, Scerif G, Johnson M (2012) Training attentional control and working memory–Is younger, better? Develop Rev
- Pratto F, John OP (1991) Automatic vigilance: the attentiongrabbing power of negative social information. J Pers Soc Psychol 61(3):380–391
- Daviss WB (2008) A review of co-morbid depression in pediatric ADHD: etiologies, phenomenology, and treatment. J Child Adolesc Psychopharmacol 18(6):565–571
- Seidman LJ (2006) Neuropsychological functioning in people with ADHD across the lifespan. Clin Psychol Rev 26(4):466–485
- 44. Barkley RA (2010) Differential diagnosis of adults with ADHD: the role of executive function and self-regulation. J Clin Psychiatry 71(7):e17
- Passarotti AM, Sweeney JA, Pavuluri MN (2010) Emotion processing influences working memory circuits in pediatric disorder and attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 49(10):1064–1080
- Bistricky SL, Ingram RE, Atchley RA (2011) Facial affect processing and depression susceptibility: cognitive biases and cognitive neuroscience. Psychol Bull 137(6):998–1028. doi:10.1037/ a0025348

