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Review Article

What networks of attention are affected by depression? A meta-analysis of studies that used the attention network test

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ABSTRACT

Background: Depression is an all-too-common mood disorder that has been linked in various ways to the cognitive concept of attention. The Attention Network Test, based on the influential taxonomy of attention originally proposed by Posner, can be used to measure the efficacy of three components or networks of attention: Alerting, Orienting and Executive Control. Our focus here is to discover how depression might affect these networks.
Methods: Studies related to attention and depression were selected for this meta-analytic review using the online Attention Network Test (ANT) Database (Arora, Lawrence & Klein, 2020) resource. Based on the inclusion and exclusion criteria, 5 publications were analyzed with a Bayesian hierarchical model to compare participants with and without a diagnosis of depression.
Results: The posterior distribution of our model revealed no credible differences in the Alerting and Orienting networks but showed credible non-zero values for Executive Control. This suggests that Executive Control is less efficient in individuals suffering from depression.
Limitations: As literature using the ANT with depressed participants is limited, the methodological variability between studies in this meta-analysis should be considered when interpreting these results.
Conclusion: This meta-analysis review is the first quantitative review that aimed to address the ANT-depression literature. A consistent finding of no alerting and no orienting deficit but a deficit in the executive control suggests that some, but not all, components of attention are impaired in depression.

Introduction

Depression is a common mood disorder that afflicts over 250 million people from all ages and genders worldwide (Cooper, 2018). The World Health Organization (WHO, 2012) characterizes depression by emotional and behavioral symptoms of sadness, loss of interest/pleasure, feelings of guilt/low self-worth, poor sleep or appetite, increased tiredness, and poor concentration (MacDonald et al., 2000). As compared to typical mood fluctuations, which are short-lived emotional responses to a specific context and life challenges (e.g., not getting a good grade on a test), depression, persists for a longer period of time, varying between several weeks and months (sometimes even years).

Depending on the number, intensity, and severity of the symptoms, a depressive episode can be categorized as mild, moderate, or severe. An individual suffering from mild depression may exhibit certain difficulties in continuing with daily life activities, including work and social interactions, but would still somehow manage to function. However, individuals with severe depressive episodes are more likely to cease to function properly – both at the individual and interpersonal levels. That is why many individuals with recurrent depressive episodes also end up committing suicide (WHO, 2020). Depression, therefore, plays a key role in the quality of life and survival rate, accounting for more than 50 percent of psychiatric consultations and around 12 percent of all hospital admissions (Kuo, Tran, Shah and Matorin, 2015).

WHO (2019) reports the global and regional estimates of the prevalence of depression, and suggests that the prevalence varies from a low of 3.6 percent in the Western Pacific Region to 5.4 percent in the African region. Moreover, depressive symptoms are more common among females (5.1%) than males (3.6%). More than half of the people afflicted with depression live in the South-East Asia Region and Western Pacific Region (including India and China, for instance). Whereas the studies

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reporting the depression prevalence indicate that the collectivistic societies like Asian countries have more depression cases, the cross-cultural studies on symptomatology of mood disorder suggest otherwise. According to De Vaus et al. (2018) about 20% of Americans experience a major depressive disorder at some time in their lives, as compared to Chinese, where this is only about 2 percent (WHO, 2017).

Depression and cognition

Cognitive distortions and information processing biases are pivotal to the cognitive model of depression (Beck, 1976). The model assumes that an individual's dysfunctional attitude or belief influence information processing by orienting attention towards the negative aspect of the experiences. This leads to negative interpretations while inhibiting or blocking attention towards the positive events and memories (Beck, 2008), suggesting a mood-congruency effect (Bower, 1981). The mood congruency explanation limits the scope of Beck's cognitive model of depression to emotion-specific dysfunction and fails to explain the general cognitive dysfunction with non-affective stimuli (Ahern et al., 2019; Epp et al., 2012).

Individuals suffering from Major Depressive Disorder (MDD) have shown significant impairments in their non-affective cognitive functioning, which includes dysfunctions in attention, executive functions (EF), concentration, processing speed as well as learning and memory (APA, 2013; Zuckerman et al., 2018; Snyder, 2013). Poor attentional processes in depression, which impair psychosocial and occupational functioning, are also associated with poor clinical outcomes (Fehnel et al., 2016; Cotrena et al., 2016). Poor executive control has been associated with impairments in emotion regulation (Joormann and D'Avanzato, 2010; Joormann and Vanderlind, 2014; Snyder, 2013), and might contribute to the increased risk factor and maintenance of depressive symptoms. MDD patients have shown structural and functional abnormalities in prefrontal cortex (PFC), including dorsolateral prefrontal cortex (DLPFC), ventrolateral prefrontal cortex (VLPFC), and anterior cingulate cortex (ACC) corresponding to poor executive functions (Snyder, 2013). Studies have shown that poor attentional control is not only a prominent feature in depression, but it is also associated with vulnerability to develop affective disorders (DeJong et al., 2019; Ahern et al., 2019). However, the causal link between poor executive function, poor attention control, and depression is not established yet. The recent hot-cold cognitive model of depression (Ahern, Bockting and Semkovska, 2019) integrates the general cognitive dysfunction into emotional dysfunction and highlights the importance of examining the general cognitive functions in MDD patients. In a nutshell, understanding general cognitive dysfunction may have important implications for the onset, maintenance, and treatment of MDD.

Attention and depression

According to a recent review (Keller et al., 2019) attention dysfunction in depression encompasses different domains of the experiences of depressed individuals, including increased distractibility, increased sustained attention impairment, impairments in conflict resolution and monitoring of distractor and target stimuli. Because of the severity of depressive symptoms and attentional biases associated with depression, it is of high importance to enhance our understanding of the mechanisms behind attentional processes in depression. Depression, though categorized as a mood disorder, should be viewed in context with attentional features to understand the symptomatology in a better fashion. Although attentional impairments are often described as a prominent feature of depression, studies have typically used different attention tasks that explore uniquely different aspects of attention. For instance, some investigators have used the intermittent "oddball" stimuli (e.g., the continuous performance task) to examine sustained attention (Gyurak et al., 2016; Van Vugt et al., 2018; Lautenbacher et al., 2002); others have used tasks that require attending to both auditory and visual stimuli to examine divided attention (Kim et al., 2015); and some other studies have used neutral Stroop task to evaluate the deficits in attentional control in depression (Keller et al., 2019; Epp et al., 2012). This variety makes it difficult to draw conclusions about the effects of depression upon attention.

Following the influential work of Posner and his colleagues (Posner and Boies, 1971; Posner & Peterson, 1990) the term "attention" refers to isolable components: alerting, orienting and executive control. Building on this taxonomic work, Fan et al. (2002) developed the Attention Network Test (ANT), a simple to administer task that uses simple subtraction scores to provide measures of the efficacy of the three components of attention (cf, Klein, 2003). Later neuroimaging work confirmed that these attentional components are mediated by separate, but interacting brain networks (Fan et al., 2005). Subsequently, and for different reasons, many variants of the ANT have been developed (for a review, see Almeida et al., 2021). In this meta-analysis, we seek to understand the nature of attentional impairments in depression by focusing on studies that have used an ANT to measure the efficacy of the attention networks inspired by the work of Posner.

Attention network test

Designed by Fan and colleagues (Fan et al., 2002), the Attention Network Task (ANT) is an extension of Posner's cued reaction time task (Posner, 1980) and Eriksen's flanker interference task (Eriksen and Eriksen, 1974). This computerized task is designed to assess three attentional networks in children and adults, namely alerting, orienting, and executive control, where the participants are presented with a sequence of visual stimuli. During this cued reaction time conditions, one of four cue types is presented: no cue, a center cue, a double cue, or a spatial cue to inform the participants about the possible location of the target presentation. The subsequently presented target is a flanker condition, which comprises an array of arrows. Participants have to then respond to this array of stimuli, making a response by key press and suggesting the direction of the center arrow. The center arrow is surrounded by flankers, where the flankers are either congruent (the direction of the central arrow matching the direction of the surrounding arrows), incongruent (the direction of the central arrow not matching the direction of the surrounding arrows), or neutral (two horizontal lines on either side of the central arrow). Fig. 1 illustrates a typical visual sequence of ANT.

As mentioned before, one of the components of the attentional network is alerting, which involves preparing for a stimulus by establishing and maintaining an alert and vigilant state (Kuo et al., 2015). The brain networks activated when involved in a task that requires alerting are frontal, parietal, and thalamic activity (Posner and Petersen, 1990). Likewise, alerting functions are also modulated by norepinephrine (Coull et al., 1996). In the ANT, alerting is calculated by subtracting the mean reaction time (RT) scores for the double cue condition from the mean RT scores of the no-cue condition. In short, alerting is measured as the difference between the conditions when the cue was present versus when the cue was absent before the presentation of the target stimuli.

Orienting involves the ability to voluntarily or involuntarily select and shift one's attention toward the direction of an incoming sensory event (Kuo et al., 2015). Orienting is associated with the activity in the superior and inferior parietal lobes, superior colliculus, reticular and pulvinar thalamic nuclei, and frontal eye fields (13). In addition, orienting functions are also modulated by acetylcholine (Corbetta and Shulman, 2002). In the ANT, the spatially informative cue condition informs the participants of an upcoming target's location. Therefore, orienting is calculated by subtracting the mean RTs following the spatially informative cue condition from the mean RT scores of the central cue condition.

Finally, executive control involves the detection and resolution of conflict and interference in mental operations as well as the manifestation of accurate behavioral responses (Kuo et al., 2015). Various brain

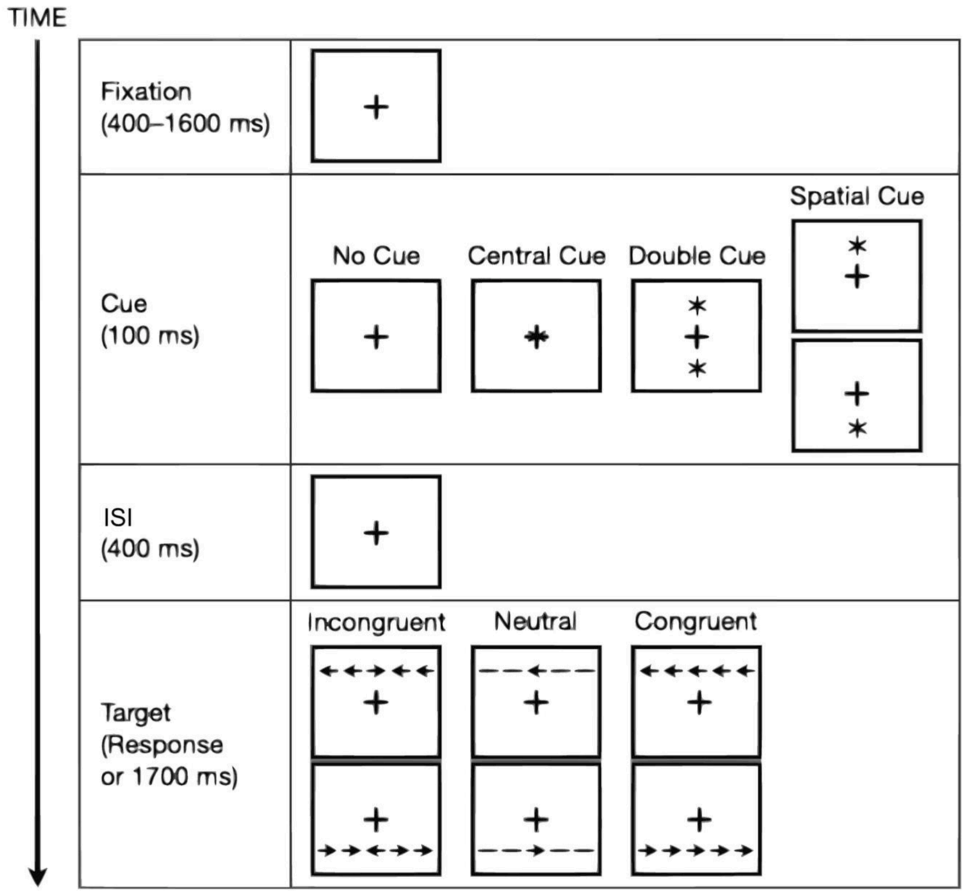

Fig. 1. An illustration of a typical ANT sequence alongside all possible stimuli associated with each event. Redrawn from MacLeod et al. (2010).

regions are involved in a task requiring executive attention because it requires online monitoring, detection, and resolution of presence or absence of distractor stimuli, as well as consequently producing an accurate behavioral response. The brain regions associated with executive control include the anterior cingulate cortex (ACC), lateral prefrontal cortex (LPFC), medial frontal cortex (MFC) (Coull et al., 1996; Davidson and Marrocco, 2000). In addition, the dopaminergic system also tends to modulate executive control functioning (Bush et al., 2000). In the ANT, executive control is measured by the participant's ability or inability to ignore distractor stimuli and identify the target arrow centered among the distractor arrows. Therefore, the executive control component of attention is calculated by subtracting the mean RT scores of all the congruent target trials from the mean RT scores of all the incongruent trials.

Methods

Studies related to attention and depression were selected for this meta-analytic review through the use of the Attention Network Test (ANT) Database (Arora et al., 2020). The ANT Database is an online repository and of all studies that have used the ANT or an ANT variant. Using this database (now hosted at http://attentionnetwork.ca), we searched the keyword *depress** which generated a list of 20 publications associated with the term. Of these, we condensed the list to exclude non-relevant studies to the present research question (i.e. those that looked at attention network scores in children of depressed mothers vs. those taking medication, or those that did not have a control group). This selection process resulted in 11 publications (see Table 1).

Table 1
Studies that used the ANT or an ANT variant with depressive participants (DP) vs. healthy controls (HC).

Study	ANT-Version	# of HC	Mean age HC	# of DP	Mean age DP
Sommerfeldt et al. (2016).	ANT	62	16.60 ± 1.90	99	16.60 ± 1.90
Han et al. (2012).	ANT	30	17.46 ± 1.59	31	17.32 ± 1.59
Yang and Xiang (2019).	ANT	16	19.70 ± 0.90	17	20.10 ± 0.90
Bellaera and von Mühlenen (2017). (E2)	ANT-I	9	20.60 ± 1.20	10	20.60 ± 1.20
Tian et al. (2016).	ANT	30	34.20 ± 12.20	34	36.1 ± 13.30
Hasler et al. (2009).	ANT	17	39.00 ± 11.00	17	39.00 ± 11.00
Marchetti et al. (2018).	ANT	270	38.20 ± 15.10	90	39.10 ± 14.20
Lyche et al. (2011).	ANT	89	35.70 ± 12.00	33	44.20 ± 12.00
Gao et al. (2018).	ANT	74	28.90 ± 6.70	66	28.40 ± 7.70
Murphy and Alexopoulos (2006).	ANT	13	71.60 ± 5.40	13	71.50 ± 6.70
Togo et al. (2015).	ANT	29	44.00 ± 8.00	19	47.00 ± 8.00

Results

As can be seen in Table 1, a relatively wide range of ages has been tested across the studies that have used an ANT to explore whether any of the networks of attention are affected by depression. In Fig. 2 we present the results from the 10 studies that reported RT network scores,[1] plotted as a function of age. In this figure, the results from each study are represented by a particular symbol plotted in black for the depressed group and in grey for the control group. Although, in most cases, the two data points from a study are relatively close together in age, with Lyche et al. (2011), the average for these two groups was separated by about 8 years. Overall mean RT was not consistently reported across studies and therefore was not included in the present analysis, however the results from individual studies will be explored as appropriate below.

For the purpose of our meta-analysis, and for a variety of reasons, we did not include all experiments which reported network scores. We excluded those for which the participants were in remission (Hasler et al., 2009; Marchetti et al., 2018), were in experiments testing the efficacy of taking medication (Murphy and Alexopoulos, 2006), or reported comorbidity with other psychiatric disorders (Togo et al., 2015). One of these studies (Bellaera & von Mühelnen, 2017) employed the Attention Network Test - Interactions (ANT-I) which uses an auditory tone for the alerting cue and an uninformative visual cue to generate an orienting score (Callejas et al., 2005). Some network scores from this variant cannot be compared to those from studies that used the original ANT, but could be used to show relative differences between the clinical and control groups. As such, the subsequent analysis was conducted by including only the following five studies presented in Fig. 2 (Sommerfeldt et al., 2016; Han et al., 2012; Yang and Xiang, 2019; Tian et al., 2016; Lyche et al., 2011). The resulting age range was 16–45, with 214 participants in the depressed group and 227 in the control group.

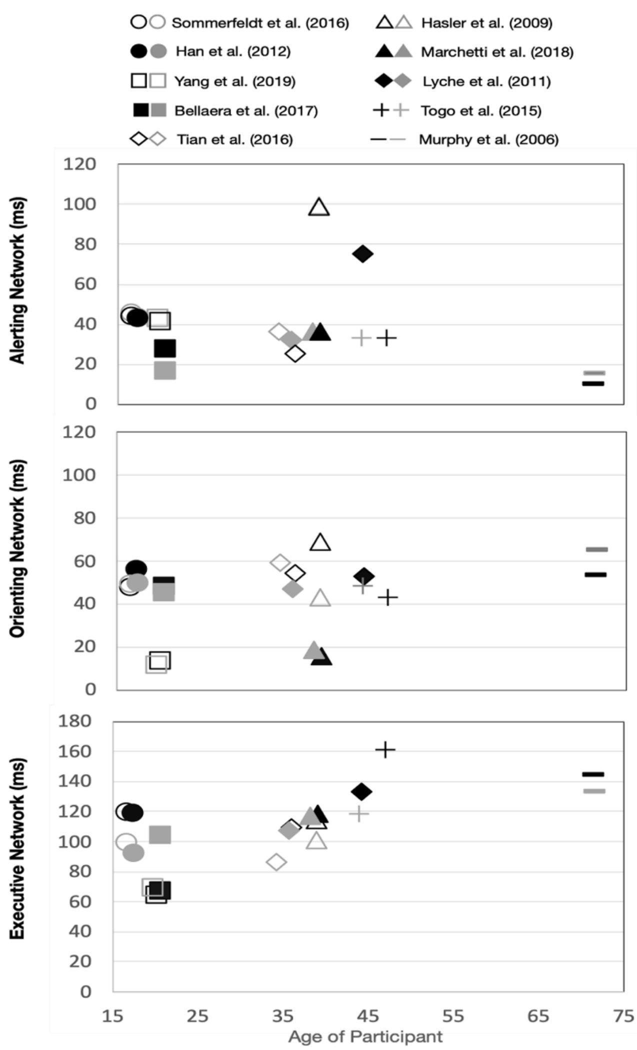

Fig. 2. ANT performance as a function of age in studies that reported network scores of participants with depression (DP) vs. healthy controls (HC). Data from DP are plotted in black, and HC are plotted in grey.

ANT data from these remaining 5 studies was analyzed in R studio using the Stan package (Carpenter et al., 2017). To compare the depressive and control participant groups, data was analyzed with a Bayesian hierarchical model using weakly informed priors and posterior samples generated across six independent chains. Each of these chains consisted of 10,000 warm-up and post-warm-up iterations and passed diagnostic tests from the rstan package (Stan Development Team, 2020).

Forest plots of the mean network scores and standard deviations for the control and DP groups are shown in the top panel of Fig. 3, and are presented in alphabetical order starting at the bottom of the graph. One study (Yang and Xiang, 2019) did not report variance of the network scores. Violin plots of the posterior distribution for between-group differences in each attention network (controls minus DP) are reported in the lower panel of Fig. 3. These were generated with a normally distributed random effects model using the standard errors from each study to calculate the corresponding measurement noise. Non-zero values were credible for between-group differences in executive control (median = −19 ms, 95% credibility interval [−31, −4]), whereas the credibility intervals for the alerting (−1 ms, [−13, 10]) and orienting (−1 ms, [−9,7]) networks included zero (were non-significant).

Discussion

Similar to past explorations of attention and depression, findings from our meta-analysis suggest differences in the executive network in participants with depression in comparison to healthy controls. Executive control facilitates higher level cognitive functioning in areas such as emotion regulation and concentration, which are areas in which depressive patients often have impairment (Perini et al., 2019). In fact, the most recent Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (APA, 2013) includes assessments for cognitive dysfunctions as part of a diagnosis for Major Depressive Disorder (MDD), which was the clinical subset in all but one study (Yang and Xiang, 2019) in our meta-analyses.

Of these 5 studies, almost all reported preliminary differences in ANT performance on the executive network. However, there are often high rates of clinical comorbidities with depression diagnoses (Rohde et al., 1991). Han et al. (2012) reports a comorbidity of MDD and anxiety in almost 75% of their clinical subset, of which 48.4% reported generalized anxiety disorder (GAD). However, t-tests comparing MDD participants with and without GAD found no significant differences in performance in the alerting or executive networks, but orienting differences in the comorbid GAD group. Furthermore, when controlling for participant IQ, as MDD participants were lower than controls, the previously reported executive differences were no longer significant. Sommerfeldt and colleagues (2016) aimed to replicate this study and found similar differences in executive control compared to healthy controls, which in contrast to Han et al. (2012), were significant when controlling for IQ. When controlling for age, education level, and gender, Lyche and colleagues (2011) report no differences between MDD participants with and without comorbid anxiety. However, MDD participants showed significant differences compared to healthy controls in the alerting network, but not in the executive. All three studies found slower overall reaction times in MDD participants.

These three studies (Han et al. (2012); Sommerfeldt et al. (2016); Lyche et al. (2011)) reported demographic information pertaining to the

[1] Although Gao et al. (2018) did not report network scores we have written to the corresponding author to see if these can be provided to us for the purpose of our meta-analysis.

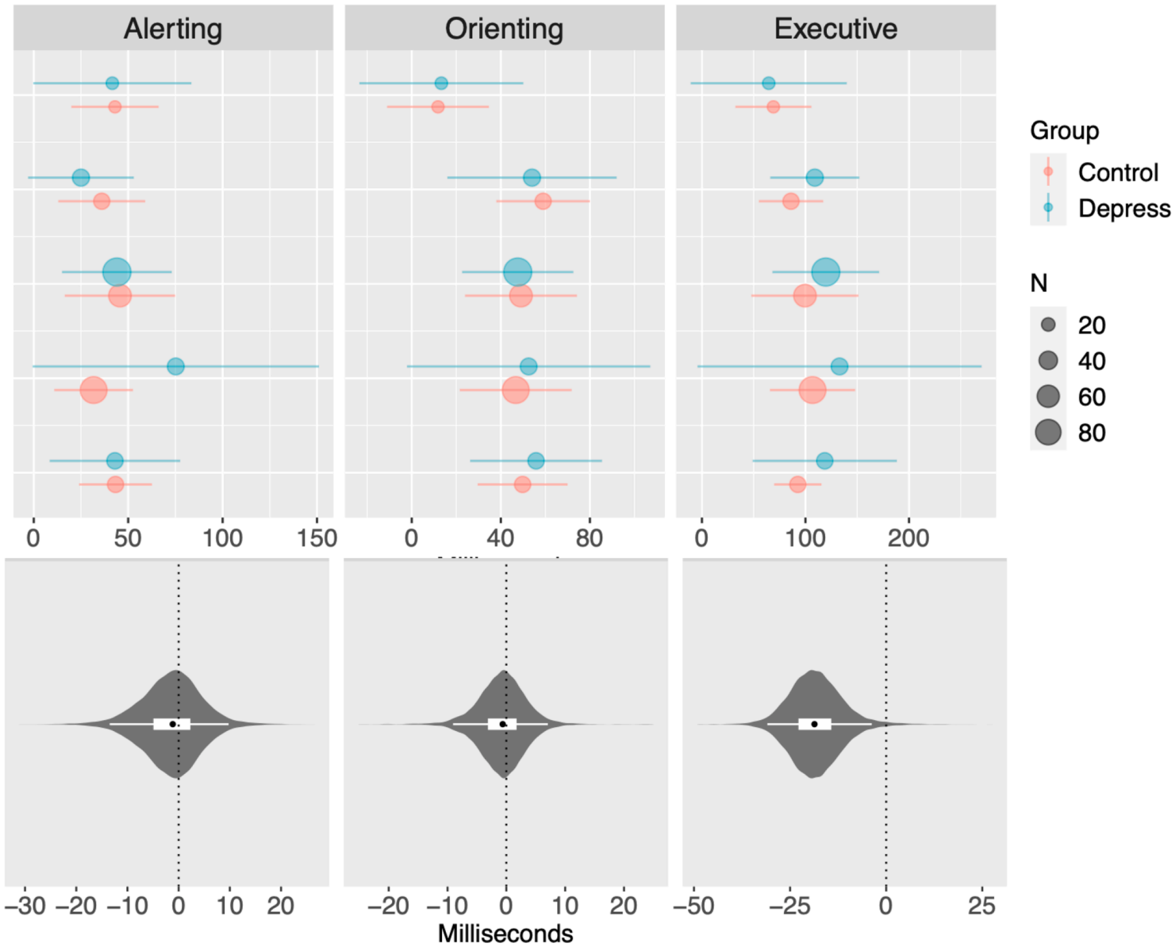

Fig. 3. Forest plots of network scores for the depressive and control participants are presented in the top panel. Data points represent the mean network score, and the relative size corresponds to the number of participants in the study. Error bars are ± 1SD. The lower panel presents violin plots of the posterior distribution of differences between groups (control minus DP). Black dots correspond to the posterior median, thick and thin white bands represent the 50% credibility interval and 95% credibility interval respectively.

use of medication within their clinical subsets. Roughly 35–39% of the MDD participants were taking medication at the time of the experiment (though in Lyche (2011) was not administered the morning of participation). These first two studies either did not report effects of medication treatment or did not find any significant differences. Whereas Sommerfeldt et al. (2016) analyzed between group ANT performance as pairwise comparisons for medicated and unmedicated MDD participants and found differences in the executive network were no longer significant. This could suggest that deficits in executive functioning facilitated by depressive episodes may be ameliorated by pharmacological intervention (McIntyre et al., 2015). However, conclusive inferences cannot be made as other research (Herrera-Guzman et al., 2010; Lam et al., 2010) report such interventions do not improve cognitive impairments associated with depression.

Encouraged, perhaps, by Beck's (1976) influential ideas, some have suggested that depressed individuals have attentional "radar" for negative information in their environment that causes such information to capture attention more powerfully than such information would in non-depressed individuals (for one review, see Bellaera, and von Mühlenen, 2017). In contrast to this view, we believe that the description made by Mineka & Sutton in their 1992 review still applies: "Anxiety, but not depression, appears to be associated with an attentional bias for threatening material. Depression, but not anxiety, appears to be associated with a memory bias for negative mood-congruent material." (Mineka and Sutton, 1992, p. 65). But, once negative information is attended by a depressed individual, they may have greater difficulty disengaging from it (see Clasen et al., 2013 and Mathews and MacLeod, 2005, for support for this possibility) than would a non-depressed individual. Such a difficulty would be more closely related to executive control than to orienting. Because the ANT was specifically designed to be neutral emotionally, any findings from it (such as the executive control deficit and absence of orienting and alerting deficits we have found) are specifically not about the emotional contents that might enter into or remain in awareness either because they were perceived in the environment or retrieved from memory.

Strengths and limitations

This meta-analysis offers various strengths as well as certain limitations. One of the primary and significant strengths comes from the fact that it is the first meta-analytical review that attempts to provide an insight into the depression-related ANT literature. A second strength derives from the methodological homogeneity rooted in the fact that the analyzed studies all used the same task to measure attention.

Despite these aforementioned strengths, this meta-analysis also carries certain limitations. To begin with, the existing literature on depression-related attentional functions using the ANT is relatively sparse. Moreover, despite their similar use of the ANT, the studies analyzed differ in many other ways – particularly how their depressed samples were defined and recruited. It is thus recommended that more research be conducted using the ANT to explore attentional impairments in depression.

Future directions

The present meta-analysis reveals a severe lacuna in the application of ANT in measuring attention impairments in depression. Given that a relatively small number of studies were identified, this review also rightly highlights that the present line of attention research in depression is majorly confined to measuring mood and emotion congruency effects in attentional biases. Tasks such as Stroop, dot-probe, or emotion priming only assess one component of attention and thereby ignoring the rest, which could be potentially problematic for bridging the gap in attentional biases studies. Future depression research, therefore, should attempt to capture general attentional mechanisms to facilitate a better insight into the underlying mechanisms of attentional biases in mood disorders. Such an approach that includes measuring the attention network may also further help develop newer frameworks and models of depression to replace or extend the existing models.

Conclusion

This meta-analysis review is the first quantitative review that aimed to address the ANT-depression literature. Despite the small number of studies that have used the ANT in depression, the consistent findings of no alerting and no orienting deficit seem likely to be true. In contrast, our analysis of executive control suggests that depressed individuals may have a deficit, at least as assessed by the flanker compatibility effect.

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