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Intrinsic functional connectivity predicts individual differences in distractibility

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ABSTRACT

Distractor suppression, the ability to filter and ignore task-irrelevant information, is critical for efficient task performance. While successful distractor suppression relies on a balance of activity in neural networks responsible for attention maintenance (dorsal attention network; DAN), reorientation (ventral attention network; VAN), and internal thought (default mode network, DMN), the degree to which intrinsic connectivity within and between these networks contributes to individual differences in distractor suppression ability is not well-characterized. For the purposes of understanding these interactions, the current study collected resting-state fMRI data from 32 Veterans and, several months later (7 ± 5 months apart), performance on the additional singleton paradigm, a measure of distractor suppression. Using multivariate support vector regression models composed of resting state connectivity between regions of the DAN, VAN, and DMN, and a leave-one-subject-out cross-validation procedure, we were able to predict an individual's task performance, yielding a significant correlation between the actual and predicted distractor suppression ($r=0.48$, $p=0.0053$). Network-level analyses revealed that greater within-network DMN connectivity was predictive of *better* distractor suppression, while greater connectivity between the DMN and attention networks was predictive of *poorer* distractor suppression. The strongest connection hubs were determined to be the right frontal eye field and temporoparietal junction of the DAN and VAN, respectively, and medial (ventromedial prefrontal and posterior cingulate cortices) and bilateral prefrontal regions of the DMN. These results are amongst a small but growing number of studies demonstrating that resting state connectivity is related to stable individual differences in cognitive ability, and suggest that greater integrity and independence of the DMN is related to better attentional ability.

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1. Introduction

Attentional control requires the ability to suppress, filter, and disengage from task-irrelevant information (Clapp and Gazzaley, 2012; Leber, 2010; Theeuwes and Burger, 1998). This ability to minimize distraction is imperative to successfully navigate the demands of the world around us and is compromised in many psychiatric and neurologic populations (Bourel-Ponchel et al., 2011; DeGutis et al., 2015; Eglin et al., 1989; Esterman et al., 2013a; Mäki-Marttunen et al., 2015). Even within healthy populations studies have observed variation in distractor suppression ability (e.g., Esterman et al., 2014; Moser et al., 2012). More broadly, task-based neuroimaging studies have revealed that better distractor suppression and attentional control abilities are associated with

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optimal activation in numerous task-positive and task-negative brain regions both between-subjects (Bishop, 2009; Forstmann et al., 2008) and within-subject (Leber, 2010; Rosenberg et al., 2015). Considerably less work, however, has investigated whether intrinsic functioning of these networks reliably predicts individual differences in attention (Rosenberg et al., 2016; Visintin et al., 2015). Resting-state studies have proven highly useful in clinical applications (Fox and Greicius, 2010), particularly in diagnosis and outcome predictions, and can be used to predict normal variation in cognitive function. Intrinsic functional connectivity, for example, has been explored across several cognitive domains (Laird et al., 2011), including executive function (Reineberg et al., 2015), fluid intelligence (Finn et al., 2015), working memory (Sala-Llonch et al., 2012), and selective attention (Kelly et al., 2008; Visintin et al., 2015), but no studies to date have specifically addressed distractor suppression. Such findings would inform future characterization of pathological attentional dysfunction, as is found in normal aging, psychiatric, and neurological disorders (Esterman et al., 2013a; Moser et al., 2012).

Generally, attentional control is mediated by several brain regions primarily within two anatomically distinct networks — the dorsal and ventral attention networks (DAN and VAN, respectively). Task-based functional magnetic resonance imaging (fMRI) studies have characterized these networks as having separate, but complementary, functions in the control of attention (e.g., Vossel et al., 2014). Briefly, the DAN is thought to generate and maintain voluntary, goal-directed attention by biasing processing in relevant sensory regions via top-down control, while the VAN (or salience network) acts as a circuit-breaker to reorient attention toward new and salient information via bottom-up input (Corbetta et al., 2008). Current theories of distractor suppression point to the role of both top-down control/DAN-dependent processing (Connor et al., 2004) as well as bottom-up input/VAN-dependent processing (Theeuwes, 2004, 2010, 2013).

While the DAN and VAN generally support attentional control, the default mode network (DMN) is thought to contribute to stimulus-independent tasks, internally directed attention and thought, and distraction (Buckner et al., 2008; Kucyi and Davis, 2014; Spreng and Grady, 2010). On the other hand, it has also been associated with more efficient attentional control (Esterman et al., 2013a). DMN engagement is typically suppressed during attentionally demanding cognitive tasks and is often characterized as relatively “anti-correlated” with the DAN during external goal-directed attention (Anticevic et al., 2012). Further, DMN connectivity to DAN contributes to individual differences in response time variability, such that greater positive correlation is associated with greater variability in task performance (Kelly et al., 2008). The DMN has a more nuanced relationship with the VAN. First, it can become positively connected with the VAN during internally directed goal-oriented tasks, which is related to better task performance (Vincent et al., 2008). In addition to this function, the VAN has more generally been proposed as biasing the co-activation of other networks such as DMN and DAN (Sridharan et al., 2008). In support of this theory, structural degradation of the VAN is associated with altered DMN activation (Bonnelle et al., 2012). Together, these findings suggest the DMN is relevant to attention both in its activation alone, as well as its potential coupling with the DAN and VAN.

It is within this context that we sought to investigate the association and predictive power of resting-state functional connectivity with distractor suppression using the well-validated additional singleton paradigm (Theeuwes, 1992). Within a cohort of Veterans, a population known to have a wide range of attentional abilities (Esterman et al., 2013a), we hypothesized that the intrinsic functional connectivity between and within the DAN, VAN, and DMN networks would, to some extent, reflect an individual's distractor suppression ability and predict performance outside of the MRI session. This hypothesis is consistent with previous studies. Namely, it is within these three networks that Visintin and colleagues (2015) identified regions as being correlated with the performance on the Attention Network Task, while Kelly et al. (2008) separately demonstrated that between-network interactions of the DMN and DAN as being related to individual differences in response variability. Thus, we further hypothesized that increased within-network communication in all networks would likely contribute to successful distractor suppression while between-network communication with the DMN would contribute to an increase in the susceptibility for distraction.

By way of support vector regression (SVR), we were able to predict distractor suppression behaviorally using a large number of intrinsic within- and between-network connections of the DAN, VAN and DMN. Further, we were able to assess the relative importance of these connections to classification, and their linear relationships with individual differences in behavioral performance.

2. Material and Methods

2.1. Participants

Thirty-one Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veterans and one pre-deployed service member (all male; M=31.8 years, SD=7.8) were recruited for this study from the VA Boston Translational Research Center for TBI and Stress Disorders (TRACTS) RR&D Center of Excellence (see Lippa et al., 2015 for a more in-depth description of the recruitment methods, demographics, and clinical description of this population). While no participants had a history of neurological conditions, physical impairments, or moderate-to-severe TBI, it should be noted that the Veteran population is characterized by common, overlapping conditions related to deployment (e.g., posttraumatic stress disorder, PTSD; depression) that can compromise aspects of cognition (Lippa et al., 2015). No participants, however, were excluded for low task accuracy (see below), which could have indicated either severe impairment or poor task compliance. This study was approved by the VA Boston IRB, written consent was obtained from all participants, and research was conducted in accordance with the Declaration of Helsinki.

2.2. Study design

As a part of the TRACTS study, participants underwent behavioral and clinical assessments and magnetic resonance imaging (MRI). In addition, a subset of individuals were given a follow-up evaluation, 7 ± 5 months post-MRI, that included the distractor suppression (attentional capture) task (Esterman et al., 2013a). Note that only a stable and robust relationship would remain after this length of time.

2.3. Psychological evaluation

Though not the focus of the current study, PTSD symptoms were assessed by administering the PTSD Checklist Civilian Version (PCL-C; Weathers et al., 1994) at each session. It is notable that greater PCL-C scores were previously shown to be associated with a larger attentional capture effect (see Esterman et al., 2013a). Participants' PCL-C assessments at the two visits were highly correlated ($r=0.84$, $p<0.0001$), suggesting that PTSD symptoms were generally consistent over this time.

2.4. MRI acquisition

Neuroimaging data were acquired using a 12-channel head coil on a 3T Siemens (Erlangen, Germany) TIM Trio scanner. Two T1-weighted anatomical MPRAGE (Magnetization Prepared Rapid Gradient Echo) scans (TR/TE: 2530/3.32 ms, flip angle: 7°, 1-mm isotropic) were acquired for surface reconstruction, inter-participant registration, and region of interest definition (per Yeo et al., 2011, see below). Resting-state functional data (gradient echo echo-planar imaging, TR/TE: 3000/30 ms, flip angle: 90°, $3.00 \times 3.00 \times 3.75$ mm^3, 38 slices) were also acquired in two 6-min runs, during which participants were given instruction to keep their eyes open and stay awake.

2.5. Distractor suppression task

To assess distractor suppression ability, participants were administered a version of the additional singleton paradigm (Theeuwes, 1992). This paradigm is regarded as a well-validated measure of distractibility from perceptually salient distractors. Each display consisted of an 8-item stimulus array with one unique shape where circles and triangles were randomly assigned as targets or distractors. Participants were instructed to search for a unique shape, and press one of two buttons on the keyboard to indicate whether the line inside this target shape was tilted left ("\") or tilted right ("/"). Participants were told to respond as quickly as possible without making errors and that they would receive feedback on their performance (after an error or 2 seconds of target display with no response, subjects heard a short beep). For 50% of trials, all items in the display were colored green (distractor-absent); for the other 50%, one of the non-unique shapes was colored red (distractor-present). Following 20 practice trials, participants performed 4 blocks of 75 trials. Reaction times (RTs) and accuracy were measured for each trial. The *attentional capture effect* was calculated as the difference in mean RT between distractor-present and distractor-absent trials (correct trial only) and served as the primary dependent measure of distraction.

2.6. Image processing

Neuroimaging data were processed using a combination of FreeSurfer (Fischl et al., 1999a), AFNI (Cox, 1996), and FSL (Jenkinson et al., 2012). FreeSurfer was used to reconstruct surface models as described previously (Lindemer et al., 2013; Robinson et al., 2015). FMRI scans were then processed using a standard stream (motion correction; time shifting; concatenation of scans; regression of motion, the global mean, white matter, and ventricles; band pass filtering between 0.01 and 0.1 Hz; and the censor of time points with framewise displacement > 0.5 mm). Data were resampled to and smoothed on the surface, and each brain was warped to a surface-based template (*fsaverage*) (Fischl et al., 1999b).

For subsequent analyses, the 17-network surface-based functional parcellations published by Yeo et al. (2011) were used to extract individual cluster time series associated with the core networks of the DAN (Network 6; 8 regions), VAN (Network 7; 7 regions), and DMN (Networks 15–17; 24 regions). The spatially averaged time series of these 39 regions were then correlated, which resulted in 741 total pairwise combinations.

2.7. Support Vector Regression (SVR)

These pairwise time series correlations were entered into a linear SVR model as features (without feature selection or exclusion) to predict attentional capture score (*libsvm*: http://www.csie.ntu.edu.tw/~cjlin/libsvm/, implemented in MATLAB [Mathworks, Natick, MA]). The classifier utilized a leave-one-subject-out (LOSO) cross-validation procedure (Esterman et al., 2010) resulting in 32 iterations, or folds. The model generated from any 31 subjects was used to predict the remaining participant's attentional capture (difference in RT between distractor present and distractor absent trials) based on their pattern of functional connectivity MRI (fcMRI). For each fold of the classifier, each feature was normalized based on the training set to a range of 0–1. The range transformation parameters were then applied to the test feature, thus test data were not used for range normalization.

The mean weights for each feature were averaged across all iterations of the classifier. Since the direct interpretation of classifier weights can be influenced by signal as well as noise, weights were transformed by multiplying the weight vector by the sample covariance matrix and corrected to reflect *activation* (see Haufe et al., 2014). Features (functional connections) with activations above zero indicated that greater connectivity predicted greater attentional capture, while negative activations indicated that greater connectivity predicted less attentional capture.

The 741 mean activations ("corrected" weights) were grouped by within- and between-network pairs (DAN-DAN, DAN-VAN, etc.) and one-sample *t*-tests were performed to determine whether such activations were significantly different than zero. To further determine if any of the 39 regions were significantly more "important" to the classifier than average (across all of its connections), the absolute value of the activations were averaged for each region (38 connections per region) and compared to the critical value calculated by a randomization test of 10,000 iterations of 38 random connections, with 2-tailed $\alpha = 0.025$ ($p < 0.05$). In other words, we determined whether the 38 connections with each ROI were significantly more important than any randomly selected 38 connections. Note that a lack of significance for any region does not indicate it is not important to the classifier, but rather the sum of its connections do not have greater importance than a random sample of any 38 connections.

2.7.1. Adjusting for PTSD

PTSD symptoms (as measured by PCL-C) at the time of each session were considered potential covariates in the analyses. To examine the influence of PTSD symptoms on the classifier's accuracy, we performed two control analyses. First, the covariates were included as additional features in the original classifier model. If the classifier performance improved, it would demonstrate that the covariates contributed above and beyond the functional connectivity in predicting attentional capture. Second, we computed "PTSD-corrected" capture scores from the residuals of a linear regression. If the classifier could still predict this corrected capture score, it would demonstrate that the functional connectivity predicts unique variance in attentional capture not yet explained by PTSD symptom severity.

3. Results

3.1. Clinical and behavioral assessments

We first sought to confirm that PTSD symptoms, which have shown to affect distractor suppression (e.g., Esterman et al., 2013a), were similar between the two sessions. Participants had a mean PCL-C score of 34.66 (SD = 14.90) during the first session and a mean of 35.72 (SD = 14.77) during the second and were highly correlated ($r = 0.84$, $p < 0.0001$). It should be noted that only six of the participants had a total PCL-C score above 50, indicative of clinical levels of PTSD, during at least one session (Forbes et al., 2001). Thus, the majority of the sample had sub-clinical levels of PTSD.

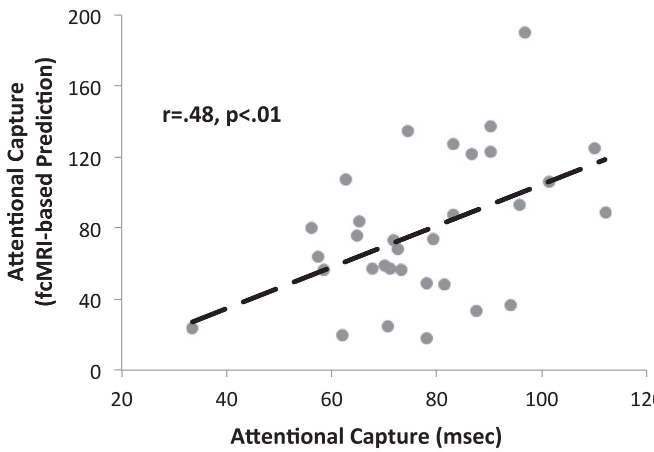

Fig. 1. The fcMRI-based classifier accuracy in predicting attentional capture (r=0.48, $p<0.01$).

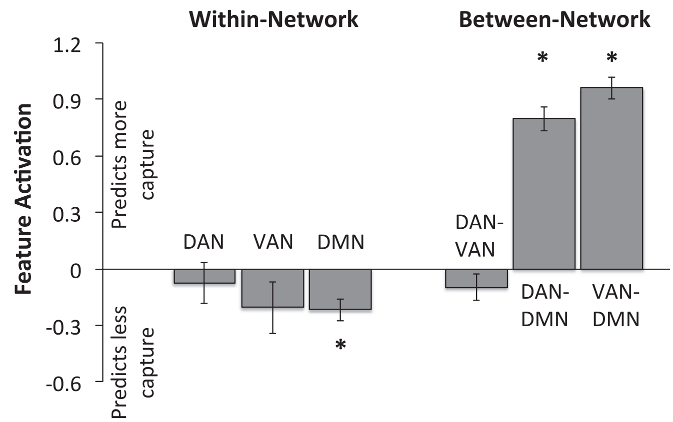

Fig. 2. The mean feature activations for each within- and between- network pair. Negative feature activations are those connections that predicted less attentional capture with greater strength, while those with positive activations predicted greater attentional capture.

Participants demonstrated a robust attentional capture effect (M=78.31 ms, SD=40.34, $p<0.001$), similar to what has been previously demonstrated (Esterman et al., 2013a). Mean accuracy was 93% (SD=6.7%) and was not different between distractor absent and present trials.

3.2. Classifier performance

The support vector regression model successfully predicted attentional capture above chance; classifier accuracy was confirmed as a significant correlation between the actual attentional capture scores and the functional connectivity-based predicted capture scores (r=0.48, $p=0.0053$; Fig. 1). This demonstrated that patterns of intrinsic functional connectivity within and between the DAN, VAN, and DMN were sufficient to predict 23% of the variance in attentional capture. Further, including PCL-C scores from both sessions as additional features (r=0.48, $p=0.0057$) or by way of residual scores (r=0.48, $p=0.005$), did not alter classifier prediction of attentional capture, suggesting PCL-C did not further explain unique variance. It is additionally noteworthy that there was no association ($p>0.4$) between distractibility and the quadratic mean of motion in the scanner.

When extended to other behavioral measures, the SVR model did not successfully classify mean RT, RT variability, or accuracy. Thus, the following results are exclusive to the capture effect.

3.3. Classifier feature activations and importance

Fig. 2 illustrates the feature activations (“corrected” weights; see Methods) by network interaction of the original (non-adjusted) model. One sample *t*-tests of the mean activations revealed negative within-network DMN ($t(276)=-3.73$, $p<0.0001$) and positive between-network DMN-DAN ($t(192)=12.72$, $p<0.0001$) and DMN-VAN ($t(168)=16.52$, $p<0.0001$) associations with classifier prediction. This indicated that within-DMN connection strength predicted less attentional capture (better performance), while between-DMN connection strength predicted more attentional capture (worse performance). No significant associations were found at the group-level for DAN-DAN, VAN-VAN, and between-network DAN-VAN features.

To assess the relative importance of using the support vector regression algorithm, and considering, the added value of individual connections to a model, we utilized a two-step approach. First, we computed the mean correlations for each network pair (DAN-DAN, DAN-VAN, etc.), and then second, entered all six network averages into LOSO linear regression. We found that while the capture effect correlated with the mean DAN-DMN (r=0.35, $p<0.05$) and VAN-DMN (r=0.43, $p=0.014$) at the whole-group level, the six network summary statistics did not successfully predict the capture effect with linear regression and a leave-one-subject-out procedure (r=0.15, $p=0.402$). Closer examination revealed an outlier drove the overall (unweighted) DAN-DMN/VAN-DMN correlations. Without this observation, these overall pairwise network connectivity values were no longer correlated with the capture effect (r=0.21; $p=0.268$; r=0.23, $p=0.211$; respectively) and the LOSO linear regression was likewise non-significant. It should, however, be noted that the exclusion of this subject did not greatly impact the strength of the SVR LOSO classifier (r=0.41, $p=0.02$). These follow-up analyses reveal the importance of the SVR procedure to weight the unique contributions of numerous individual region-to-region connections to predict capture in a cross-validated manner.

Of the 39 regions, seven were identified as having overall average activation (for all 38 edges/connections) that were more important to the classifier than any random 38 connections (see Table 1 and Fig. 3): five within the DMN, one within DAN, and one within VAN. These included putatively core regions of these neworks, including the medial (ventromedial prefrontal and posterior cingulate cortices) and bilateral prefrontal regions of the DMN, as well as the right frontal eye field (FEF) of the DAN and temporoparietal junction (TPJ) of the VAN. It is important that these regions be considered as potential *hubs* in the relationship between functional connectivity (FC) and distractor suppression ability, rather than being the sole contributors to the classifier.

Table 1
Regions identified as having greatest importance to the classifier. RAI coordinates are reported for the volumetric centers of mass.

	Center of Mass (CM)			
Network	x	y	z	Anatomical location
DMN	7	−49	8	L Ventromedial Prefrontal Cortex (vmPFC)
	7	49	26	L Posterior Cingulate Cortex (PCC)
	22	−27	43	L Middle Superior Frontal Gyrus
	−23	−33	41	R Middle Superior Frontal Gyrus
	37	80	27	L Cuneus
DAN	−27	6	53	R Middle Frontal Gyrus / Frontal Eye Fields (FEF)
VAN	−59	27	23	R Temporoparietal Junction (TPJ)

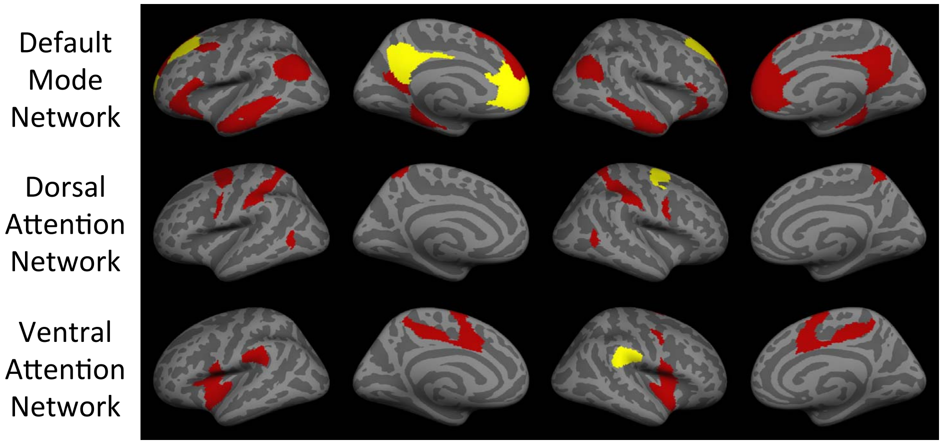

Fig. 3. All regions included in the classifier: the core default mode, dorsal and ventral attention network nodes of 17-network parcellation, as described in Yeo et al., 2011. Those identified as having overall greatest importance to the classifier are color-coded as yellow. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

4. Discussion

The current study demonstrates that distractor suppression ability is related to resting, intrinsic functional connectivity in attention-related brain networks, in line with recent work relating fcMRI with individual differences in cognition (Kelly et al., 2008; Reineberg et al., 2015; Visintin et al., 2015; Rosenberg et al., 2016). Rather than simply demonstrating this relationship, we found that multivariate patterns of FC were able to predict individual variation in distractor suppression with moderate accuracy ($r=0.48$). Further, support vector regression revealed within-network DMN connectivity, as well as DMN coupling with attention networks (DMN-VAN and DMN-DAN), to be the strongest predictors of attentional capture. These findings suggest that both the internal coherence of the DMN, as well as its distinctiveness from attention networks, are important for optimal distractor suppression ability. This study corroborates existing task-based fMRI literature on the roles of these three networks and further highlights the importance of the DMN functioning for attentional control.

Our findings reveal that stronger internal DMN integrity supports better distractor suppression. This is consistent with a wealth of literature that associates the loss of internal DMN integrity with a number of clinical disorders that impact attentional control. For example, weakened within-DMN communication has been reported in adult ADHD (Castellanos et al., 2008; Uddin et al., 2008), pre-clinical pathological and normal aging (Andrews-Hanna et al., 2007; Sheline et al., 2010), Alzheimer's disease (Balthazar et al., 2014), and PTSD (Sripada et al., 2012). Greater internal integrity of DMN may be associated with *less* task-evoked activation of DMN, and less DMN activation typically coincides with better attentional performance. Along these lines, Mennes et al. (2010) found decreased within-DMN connectivity during rest was associated with increased task-evoked activation of DMN. Such increased DMN activity during tasks has been shown in other studies to negatively impact the ability to maintain goal-directed attention (Christoff et al., 2009; Esterman et al., 2013b; Kucyi and Davis, 2014; Weissman et al., 2006).

In addition to internal integrity of the DMN, our findings also reveal that DMN hyperconnectivity with task-related networks (DAN and VAN) is associated with poorer distractor suppression ability. This is consistent with evidence showing that weakened anti-correlations between the DMN and attention networks are associated with worse cognitive performance and clinical status. Weaker anticorrelations with task-positive networks, for example, have been associated with greater behavioral variability in ADHD (Kelly et al., 2008), lower general fluid intelligence (Cole et al., 2012), sleep deprivation (De Havas et al., 2012), and psychosis (Wotruba et al., 2014) and could suggest an increasing shift from the external to the internal focus of attention. Taken together, our findings support the idea that disruption of within-network DMN connectivity as well as increased (or less anti-correlated) communication with the other networks contribute to DMN over-activation, and ultimately failures during task performance.

Somewhat surprisingly, the internal integrity of DAN and VAN themselves were not as a whole, significantly important to the classifier, although this does not preclude the possibility that only specific within-network connections were indeed critical. Along those lines, two regions of the DAN and VAN were found to have greatest overall importance to the classifier (Fig. 3). In the DAN, the right FEF was revealed to have particularly important connections and likely serves as a locus of interaction between the DMN and other task-positive regions. Beyond the control of eye movements, the right FEF has been shown to be involved in covert target selection and the top-down control of attention (Buschman and Miller, 2007; Schall and Hanes, 1993). Disruption to the area from TMS, for example, has contributed to increased distractor interference (Hung et al., 2011) and poorer sustained attention (Esterman et al., 2015). In the VAN, the right TPJ was also highly significant to the classifier. This area is thought to be a circuit-breaker for shifts in attention and is important for target detection (Corbetta and Shulman, 2002). Reduced neural activity in this region, paired with reduced deactivation of the DMN, has been shown to underlie transient lapses in attention and slower response times (Weissman et al., 2006).

Within the context of attentional ability, the current study is among the first to successfully classify behavior using resting-state functional connectivity. With moderate accuracy, this model, comprised of only three functional networks externally-defined by Yeo et al., (2011), implies consistent relationships between task-positive/task-negative regions and distractor suppression. Similarly, a recent study by Rosenberg et al., (2016) also demonstrated that resting functional connectivity could predict attention ability on a sustained attention task, with similar accuracy ($r=0.43$, $p=0.031$). Interestingly, though Rosenberg and colleagues did report a weak relationship between DMN-DMN connectivity and better performance, they did not find the DMN to be relatively informative, in contrast to motor and subcortical regions which contained the most information. This may be due to the different task, population, or rather more fine-grained and extensive brain parcellation used by Rosenberg and colleagues (Shen et al., 2013).

Other fcMRI studies implicate the DMN, with comparable effect sizes. Although not classification, Visintin et al. (2015) found posterior DMN (e.g. precuneus, ACC, right angular gyrus) connectivity to be associated with greater flanker interference effects. Kelly et al. (2008) confirmed that attention network-DMN communication increased with behavioral variability on incongruent ($r=0.67$, $p<0.001$) and congruent ($r=0.40$, $p<0.05$) trials, also on a flanker task. Finally, Sala-Llonch and colleagues (2012) extended the significance of DMN anti-correlations to working memory ability ($r=-0.65$, $p=0.012$), and interestingly DMN was the only significant network out of the eight considered. These studies offer additional evidence that the DMN connectivity is an important biomarker of attentional functioning.

A potentially fruitful future direction is to examine how other forms of distractor suppression and executive functions rely on similar and distinct components of intrinsic functional connectivity. For example, another commonly studied form of attentional capture by distraction is known as contingent capture (Folk et al., 1992; Serences et al., 2005), in which distractors share features with the targets, and thus distraction is modulated by top-down processing and task-set. While the distractors in our task are effective due to their low-level saliency (in this case, color), it could be that contingent capture relies on integrity of some partially distinct networks or regions. In particular, contingent capture has been related to working memory capacity (Mayer et al., 2012), and thus may be related to functional connectivity in other networks more often associated with working memory, rather than more strictly associated with attentional control. Also of interest is value-driven capture, when distractors hold previously rewarded visual information (Anderson et al., 2011). This type of capture is thought to rely on reward and learning mechanisms and thus it could be that the basal ganglia, frontal-striatal circuits, or medial prefrontal regions associated with reward and value learning would be more predictive of this type of distractibility. It would be useful for future work to determine the generalizability of the current findings with regard to these different types of distractor suppression effects and complement the findings presented here with task-based investigations of the roles of these networks. More broadly, distractor suppression ability is thought to be related to other aspects of attentional and executive functioning (Friedman and Miyake, 2004), and thus the current findings may generalize to other cognitive abilities, such as response inhibition.

One limitation of the current study is that our sample, comprised of returning Veterans with varying degrees of combat experience and PTSD, generally represent a different demographic than most studies of healthy cognition. Though few presented clinical levels of dysfunction, it may be that the results presented here are not entirely generalizable to those that have been observed in a more conventional sample. However, given the relatively intact performance and network integrity in these subjects and the expectation that we would be able to observe a greater dynamic range in their attentional performance, the sample is appropriate for the stated findings. It is also likely that our relatively modest sample size did not yield enough power to detect potential associations between capture performance and DAN-VAN connectivity or VAN-VAN/DAN-DAN connectivity. Finally, while the selection of the DAN, VAN, and DMN was based on clear hypotheses, other ways of defining networks and ROIs could possibly provide better predictive power and lead to converging or additional information regarding the role of intrinsic functional connectivity and attentional control.

5. Conclusions

Though the relationship between intrinsic brain activity and cognitive performance has been previously demonstrated, the current study is one of the first to use multivariate models of resting functional connectivity to predict individual variation in attentional ability. We demonstrate that the intrinsic functions of the DMN and its interactions with the attention networks can predict distractor suppression ability in a Veteran sample. It is our hope that this approach will encourage future characterization of intrinsic connectivity in a wide range of cognitive tasks and sample populations. These findings have particular implications for clinical populations with impaired attention, as the intrinsic integrity of these networks may be both diagnostic and serve as potential targets for rehabilitation (Fox and Greicius, 2010; Halko et al., 2014).

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References

Anderson, B.A., Laurent, P.A., Yantis, S., 2011. Value-driven attentional capture. Proc. Natl. Acad. Sci. 108, 10367–10371.
Andrews-Hanna, J.R., Snyder, A.Z., Vincent, J.L., Lustig, C., Head, D., Raichle, M.E., Buckner, R.L., 2007. Disruption of large-scale brain systems in advanced aging. Neuron 56, 924–935.
Anticevic, A., Cole, M.W., Murray, J.D., Corlett, P.R., Wang, X.-J., Krystal, J.H., 2012. The role of default network deactivation in cognition and disease. Trends Cognit. Sci. 16, 584–592.
Balthazar, M.L., Pereira, F.R., Lopes, T.M., da Silva, E.L., Coan, A.C., Campos, B.M., Duncan, N.W., Stella, F., Northoff, G., Damasceno, B.P., Cendes, F., 2014. Neuropsychiatric symptoms in Alzheimer's disease are related to functional connectivity alterations in the salience network. Hum. Brain Mapp. 35, 1237–1246.
Bishop, S.J., 2009. Trait anxiety and impoverished prefrontal control of attention. Nat. Neurosci. 12, 92–98.
Bonnelle, V., Ham, T.E., Leech, R., Kinnunen, K.M., Mehta, M.A., Greenwood, R.J., Sharp, D.J., 2012. Salience network integrity predicts default mode network function after traumatic brain injury. Proc. Natl. Acad. Sci. 109, 4690–4695.
Bourel-Ponchel, E., Querné, L., Le Moing, A.G., Delignières, A., de Broca, A., Berquin, P., 2011. Maturation of response time and attentional control in ADHD: evidence from an attentional capture paradigm. Eur. J. Paediatr. Neurol. 15, 123–130.
Buckner, R.L., Andrews-Hanna, J.R., Schacter, D.L., 2008. The brain's default network: anatomy, function, and relevance to disease. Ann. N Y Acad. Sci. 1124, 1–38.
Buschman, T.J., Miller, E.K., 2007. Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. Science 315, 1860–1862.
Castellanos, F.X., Margulies, D.S., Kelly, C., Uddin, L.Q., Ghaffari, M., Kirsch, A., Shaw, D., Shehzad, Z., Di Martino, A., Biswal, B., Sonuga-Barke, E.J., Rotrosen, J., Adler, L.A., Milham, M.P., 2008. Cingulate-precuneus interactions: a new locus of dysfunction in adult attention-deficit/hyperactivity disorder. Biol. Psychiatry 63, 332–337.
Christoff, K., Gordon, A.M., Smallwood, J., Smith, R., Schooler, J.W., 2009. Experience sampling during fMRI reveals default network and executive system contributions to mind wandering. Proc. Natl. Acad. Sci. U S A 106, 8719–8724.
Clapp, W.C., Gazzaley, A., 2012. Distinct mechanisms for the impact of distraction and interruption on working memory in aging. Neurobiol. Aging 33, 134–148.
Cole, M.W., Yarkoni, T., Repovs, G., Anticevic, A., Braver, T.S., 2012. Global connectivity of prefrontal cortex predicts cognitive control and intelligence. J. Neurosci. 32, 8988–8999.
Connor, C.E., Egeth, H.E., Yantis, S., 2004. Visual attention: bottom-up versus top-down. Curr. Biol. 14, R850–R852.
Corbetta, M., Patel, G., Shulman, G.L., 2008. The reorienting system of the human brain: from environment to theory of mind. Neuron 58, 306–324.
Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain. Nat. Rev. Neurosci. 3, 201–215.
Cox, R., 1996. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput. Biomed. Res. 29, 162–173.
De Havas, J.A., Parimal, S., Soon, C.S., Chee, M.W., 2012. Sleep deprivation reduces default mode network connectivity and anti-correlation during rest and task

performance. Neuroimage 59, 1745–1751.
DeGutis, J., Esterman, M., McCulloch, B., Rosenblatt, A., Milberg, W., McGlinchey, R., 2015. Posttraumatic psychological symptoms are associated with reduced inhibitory control, not general executive dysfunction. J. Int. Neuropsychol. Soc. 21, 342–352.
Eglin, M., Robertson, L.C., Knight, R.T., 1989. Visual search performance in the neglect syndrome. J. Cogn. Neurosci. 1, 372–385.
Esterman, M., DeGutis, J., Mercado, R., Rosenblatt, A., Vasterling, J.J., Milberg, W., McGlinchey, R., 2013a. Stress-related psychological symptoms are associated with increased attentional capture by visually salient distractors. J. Int. Neuropsychol. Soc. 19, 835–840.
Esterman, M., Liu, G., Okabe, H., Reagan, A., Thai, M., DeGutis, J., 2015. Frontal eye field involvement in sustaining visual attention: evidence from transcranial magnetic stimulation. Neuroimage 111, 542–548.
Esterman, M., Noonan, S.K., Rosenberg, M., Degutis, J., 2013b. In the zone or zoning out? Tracking behavioral and neural fluctuations during sustained attention. Cereb. Cortex 23, 2712–2723.
Esterman, M., Rosenberg, M.D., Noonan, S.K., 2014. Intrinsic fluctuations in sustained attention and distractor processing. J. Neurosci. 34, 1724–1730.
Esterman, M., Tamber-Rosenau, B.J., Chiu, Y.-C., Yantis, S., 2010. Avoiding non-independence in fMRI data analysis: leave one subject out. Neuroimage 50, 572–576.
Finn, E.S., Shen, X., Scheinost, D., Rosenberg, M.D., Huang, J., Chun, M.M., Papademetris, X., Constable, R.T., 2015. Functional connectome fingerprinting: identifying individuals using patterns of brain connectivity. Nat. Neurosci. 18, 1664–1671.
Fischl, B., Sereno, M.I., Dale, A.M., 1999a. Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system. Neuroimage 9, 195–207.
Fischl, B., Sereno, M.I., Tootell, R.B., Dale, A.M., 1999b. High-resolution intersubject averaging and a coordinate system for the cortical surface. Hum. Brain Mapp. 8, 272–284.
Folk, C.L., Remington, R.W., Johnston, J.C., 1992. Involuntary covert orienting is contingent on attentional control settings. J. Exp. Psychol. Hum. Percept. Perform. 18, 1030–1044.
Forbes, D., Creamer, M., Biddle, D., 2001. The validity of the PTSD checklist as a measure of symptomatic change in combat-related PTSD. Behav. Res. Ther. 39, 977–986.
Forstmann, B.U., van den Wildenberg, W.P., Ridderinkhof, K.R., 2008. Neural mechanisms, temporal dynamics, and individual differences in interference control. J. Cogn. Neurosci. 20, 1854–1865.
Fox, M.D., Greicius, M., 2010. Clinical applications of resting state functional connectivity. Front Syst. Neurosci. 4, 19.
Friedman, N.P., Miyake, A., 2004. The relations among inhibition and interference control functions: a latent-variable analysis. J. Exp. Psychol. Gen. 133, 101–135.
Halko, M.A., Farzan, F., Eldaief, M.C., Schmahmann, J.D., Pascual-Leone, A., 2014. Intermittent theta-burst stimulation of the lateral cerebellum increases functional connectivity of the default network. J. Neurosci. 34, 12049–12056.
Haufe, S., Meinecke, F., Görgen, K., Dähne, S., Haynes, J.D., Blankertz, B., Bießmann, F., 2014. On the interpretation of weight vectors of linear models in multivariate neuroimaging. Neuroimage 87, 96–110.
Hung, J., Driver, J., Walsh, V., 2011. Visual selection and the human frontal eye fields: effects of frontal transcranial magnetic stimulation on partial report analyzed by Bundesen's theory of visual attention. J. Neurosci. 31, 15904–15913.
Jenkinson, M., Beckmann, C.F., Behrens, T.E., Woolrich, M.W., Smith, S.M., 2012. Fsl. Neuroimage 62, 782–790.
Kelly, A.M., Uddin, L.Q., Biswal, B.B., Castellanos, F.X., Milham, M.P., 2008. Competition between functional brain networks mediates behavioral variability. Neuroimage 39, 527–537.
Kucyi, A., Davis, K.D., 2014. Dynamic functional connectivity of the default mode network tracks daydreaming. Neuroimage 100, 471–480.
Laird, A.R., Fox, P.M., Eickhoff, S.B., Turner, J.A., Ray, K.L., McKay, D.R., Glahn, D.C., Beckmann, C.F., Smith, S.M., Fox, P.T., 2011. Behavioral interpretations of intrinsic connectivity networks. J. Cogn. Neurosci. 23, 4022–4037.
Leber, A.B., 2010. Neural predictors of within-subject fluctuations in attentional control. J. Neurosci. 30, 11458–11465.
Lindemer, E.R., Salat, D.H., Leritz, E.C., McGlinchey, R.E., Milberg, W.P., 2013. Reduced cortical thickness with increased lifetime burden of PTSD in OEF/OIF veterans and the impact of comorbid TBI. NeuroImage: Clin. 2, 601–611.
Lippa, S., Fonda, J., Fortier, C., Amick, M., Kenna, A., Milberg, W., McGlinchey, R., 2015. Deployment-related psychiatric and behavioral conditions and their association with functional disability in OEF/OIF/OND Veterans. J. Trauma. Stress 28, 25–33.
Mayer, J.S., Fukuda, K., Vogel, E.K., Park, S., 2012. Impaired contingent attentional capture predicts reduced working memory capacity in schizophrenia. PLoS. One 7, e48586.
Mennes, M., Kelly, C., Zuo, X.-N., Di Martino, A., Biswal, B.B., Castellanos, F.X., Milham, M.P., 2010. Inter-individual differences in resting-state functional connectivity predict task-induced BOLD activity. Neuroimage 50, 1690–1701.
Moser, J.S., Becker, M.W., Moran, T.P., 2012. Enhanced attentional capture in trait anxiety. Emotion 12, 213–216.
Mäki-Marttunen, V., Kuusinen, V., Brause, M., Peräkylä, J., Polvivaara, M., dos Santos Ribeiro, R., Öhman, J., Hartikainen, K.M., 2015. Enhanced attention capture by emotional stimuli in mild traumatic brain injury. J. Neurotrauma 32, 272–279.
Reineberg, A.E., Andrews-Hanna, J.R., Depue, B.E., Friedman, N.P., Banich, M.T., 2015. Resting-state networks predict individual differences in common and specific aspects of executive function. Neuroimage 104, 69–78.
Robinson, M.E., Lindemer, E.R., Fonda, J.R., Milberg, W.P., McGlinchey, R.E., Salat, D. H., 2015. Close-range blast exposure is associated with altered functional connectivity in Veterans independent of concussion symptoms at time of exposure. Hum. Brain Mapp. 36, 911–922.
Rosenberg, M.D., Finn, E.S., Constable, R.T., Chun, M.M., 2015. Predicting moment-to-moment attentional state. Neuroimage 114, 249–256.
Rosenberg, M.D., Finn, E.S., Scheinost, D., Papademetris, X., Shen, X., Constable, R.T., Chun, M.M., 2016. A neuromarker of sustained attention from whole-brain functional connectivity. Nat. Neurosci. 19, 165–171.
Sala-Llonch, R., Peña-Gómez, C., Arenaza-Urquijo, E.M., Vidal-Piñeiro, D., Bargalló, N., Junqué, C., Bartrés-Faz, D., 2012. Brain connectivity during resting state and subsequent working memory task predicts behavioural performance. Cortex 48, 1187–1196.
Schall, J.D., Hanes, D.P., 1993. Neural basis of saccade target selection in frontal eye field during visual search. Nature 366, 467–469.
Serences, J.T., Shomstein, S., Leber, A.B., Golay, X., Egeth, H.E., Yantis, S., 2005. Coordination of voluntary and stimulus-driven attentional control in human cortex. Psychol. Sci. 16, 114–122.
Sheline, Y.I., Raichle, M.E., Snyder, A.Z., Morris, J.C., Head, D., Wang, S., Mintun, M.A., 2010. Amyloid plaques disrupt resting state default mode network connectivity in cognitively normal elderly. Biol. Psychiatry 67, 584–587.
Shen, X., Tokoglu, F., Papademetris, X., Constable, R.T., 2013. Groupwise whole-brain parcellation from resting-state fMRI data for network node identification. Neuroimage 82, 403–415.
Spreng, R.N., Grady, C.L., 2010. Patterns of brain activity supporting autobiographical memory, prospection, and theory of mind, and their relationship to the default mode network. J. Cogn. Neurosci. 22, 1112–1123.
Sridharan, D., Levitin, D.J., Menon, V., 2008. A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. Proc. Natl. Acad. Sci. 105, 12569–12574.
Sripada, R.K., King, A.P., Welsh, R.C., Garfinkel, S.N., Wang, X., Sripada, C.S., Liberzon, I., 2012. Neural dysregulation in posttraumatic stress disorder: evidence for disrupted equilibrium between salience and default mode brain networks. Psychosom. Med. 74, 904–911.
Theeuwes, J., 1992. Perceptual selectivity for color and form. Percept. Psychophys. 51, 599–606.
Theeuwes, J., 2004. Top-down search strategies cannot override attentional capture. Psychon. Bull. Rev. 11, 65–70.
Theeuwes, J., 2010. Top-down and bottom-up control of visual selection. Acta Psychol. (Amst.) 135, 77–99.
Theeuwes, J., 2013. Feature-based attention: it is all bottom-up priming. Philos. Trans. R. Soc. Lond. B Biol. Sci. 368, 20130055.
Theeuwes, J., Burger, R., 1998. Attentional control during visual search: the effect of irrelevant singletons. J. Exp. Psychol. Hum. Percept. Perform. 24, 1342–1353.
Uddin, L.Q., Kelly, A.M., Biswal, B.B., Margulies, D.S., Shehzad, Z., Shaw, D., Ghaffari, M., Rotrosen, J., Adler, L.A., Castellanos, F.X., Milham, M.P., 2008. Network homogeneity reveals decreased integrity of default-mode network in ADHD. J. Neurosci. Methods 169, 249–254.
Vincent, J.L., Kahn, I., Snyder, A.Z., Raichle, M.E., Buckner, R.L., 2008. Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. J. Neurophysiol. 100, 3328–3342.
Visintin, E., De Panfilis, C., Antonucci, C., Capecci, C., Marchesi, C., Sambataro, F., 2015. Parsing the intrinsic networks underlying attention: a resting state study. Behav. Brain Res. 278, 315–322.
Vossel, S., Geng, J.J., Fink, G.R., 2014. Dorsal and ventral attention systems distinct neural circuits but collaborative roles. Neuroscientist 20, 150–159.
Weathers, F.W., Litz, B., Huska, J., Keane, T., 1994. PCL-C for DSM-IV. National Center For PTSD-Behavioral Sciences Division,, Boston.
Weissman, D.H., Roberts, K.C., Visscher, K.M., Woldorff, M.G., 2006. The neural bases of momentary lapses in attention. Nat. Neurosci. 9, 971–978.
Wotruba, D., Michels, L., Buechler, R., Metzler, S., Theodoridou, A., Gerstenberg, M., Walitza, S., Kollias, S., Rössler, W., Heekeren, K., 2014. Aberrant coupling within and across the default mode, task-positive, and salience network in subjects at risk for psychosis. Schizophr. Bull. 40, 1095–1104.
Yeo, B.T., Krienen, F.M., Sepulcre, J., Sabuncu, M.R., Lashkari, D., Hollinshead, M., Roffman, J.L., Smoller, J.W., Zöllei, L., Polimeni, J.R., Fischl, B., Liu, H., Buckner, R. L., 2011. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J. Neurophysiol. 106, 1125–1165.