Functional connectivity predicts the dispositional use of expressive suppression but not cognitive reappraisal

Daisy A. Burr*, Tracy d'Arbeloff*, Maxwell L. Elliott, Annchen R. Knodt, Bartholomew D. Brigidi & Ahmad R. Hariri

Department of Psychology & Neuroscience, Duke University Box 104410, Durham, NC 27708, USA

Correspondence: daisy.burr@duke.edu

*These authors contributed equally to this work.

Abstract

Previous research has identified specific brain regions associated with regulating emotion using common strategies such as expressive suppression and cognitive reappraisal. However, most research focuses on a priori regions and directs participants how to regulate, which may not reflect how people naturally regulate outside the laboratory. Here, we used a data-driven approach to investigate how individual differences in distributed intrinsic functional brain connectivity predict emotion regulation tendency. Specifically, we used connectome-based predictive modeling to extract functional connections in the brain significantly related to the dispositional use of suppression and reappraisal. These edges were then used in a predictive model and cross-validated in novel participants to identify a neural signature that reflects individual differences in the tendency to suppress and reappraise emotion. We found a significant neural signature for the dispositional use of suppression, but not reappraisal. Within this whole-brain signature, the intrinsic connectivity of the default mode network was most informative of suppression tendency. In addition, the predictive performance of this model was significant in males, but not females. These findings help inform how whole-brain networks of functional connectivity characterize how people tend to regulate emotion outside the laboratory.

Keywords: emotion regulation, predictive modeling, functional connectivity, biomarker

Introduction

Individuals choose to regulate their emotions in response to stressors in a variety of ways. Two common emotion regulation strategies are cognitive reappraisal and expressive suppression (Gross, 2002). Expressive suppression is an avoidance-based regulation strategy characterized by masking your outward emotional responses (Gross, 2002; Gross & John, 1998). Conversely, cognitive reappraisal involves reframing the meaning of a stimulus to change the associated emotional response (Buhle et al., 2013; Gross & John, 1998).

A major goal of emotion regulation research has been to identify how individuals vary in their tendency to suppress and reappraise. For example, research has illustrated that increased use of suppression is associated with negative health outcomes, such as anxiety (Amstadter, 2008; Cisler & Olatunji, 2012; Gross, 2002; Gross & Levenson, 1997; Troy, Wilhelm, Shallcross, & Mauss, 2010), though increased use of reappraisal is associated with lower levels of anxiety (Denny, Inhoff, Zerubavel, Davachi, & Ochsner, 2015; Jamieson, Mendes, Blackstock, & Schmader, 2010). In addition, research has demonstrated sex differences in dispositional use of suppression and reappraisal. Women report using a wider range of regulation strategies than men (Aldao & Nolen-Hoeksema, 2013; Nolen-Hoeksema & Aldao, 2011) and men report using suppression more than reappraisal (Gross & John, 2003).

Emotion regulation research has aimed to characterize biomarkers associated with suppression and reappraisal (Cutuli, 2014; Dennis & Hajcak, 2009; Gross & John, 2003; Kalisch, Wiech, Herrmann, & Dolan, 2006; Kanske, Heissler, Schönfelder, & Wessa, 2012; Urry et al., 2006). For example, studies have linked reappraisal with increased activity in the dorsolateral and

ventromedial prefrontal cortices (Buhle et al., 2013; Goldin, McRae, Ramel, & Gross, 2008), and both reappraisal and suppression have been associated with decreased activity in the amygdala (Buhle et al., 2013; Chen, Chen, Yang, & Yuan, 2017). Similarly, research has identified how patterns of intrinsic functional connectivity differ between suppression and reappraisal. Decreased coupling between the amygdala and medial prefrontal cortex has been associated with reappraisal, whereas increased coupling between the amygdala and dorsal anterior cingulate cortex has been associated with suppression (Pan et al., 2018; Picó-Pérez et al., 2018; Uchida et al., 2015). Globally, intrinsic activity within the default mode network, which supports self-referential processes, has been associated with suppression (Pan et al., 2018) and reappraisal (Gao et al., 2018; Gao, Chen, Biswal, Lei, & Yuan, 2018; Martins & Mather, 2016; Sripada et al., 2013; Xie et al., 2016).

Although these findings have informed the brain basis of suppression and reappraisal, they have been limited in several key areas. First, most emotion regulation research often relies on instructing individuals to regulate in specific ways (Buhle et al., 2013; McRae et al., 2010; McRae, Misra, Prasad, Pereira, & Gross, 2012). However, this may not reflect how individuals tend to regulate outside the laboratory. Second, existing studies have largely focused on *a priori* regions of interest, though evidence has rapidly accrued that complex cognitive processes are more likely supported by distributed networks of brain regions (Chang, Gianaros, Manuck, Krishnan, & Wager, 2015; Pan et al., 2018). Third, existing research that explores whole-brain maps of cognitive processes are often subject to extreme issues of multiple comparisons and based on overfit models (Shen et al. 2017). Fourth, most existing studies have smaller sample sizes and amounts of data, which

limits reliability and the ability to map individual differences on to the dispositional use of suppression and reappraisal (Bennett and Miller, 2010; Elliott et al., 2019).

Here, we attempt to address these limitations by using a data-driven approach to identify patterns of distributed intrinsic functional connectivity predictive of dispositional use of suppression and reappraisal. In order to increase reliability and benefit from the most amount of data, we collapsed across task and resting-state scans into general functional connectivity (GFC; Elliott et al., 2019). We employed connectome-based predictive modeling (CPM; Shen et al., 2017) to select the most informative features (functional connections) from GFC matrices and predict individual differences in the dispositional use of suppression and reappraisal without overfitting the data. In light of the pronounced sex differences in the dispositional use of suppression and reappraisal (Aldao & Nolen-Hoeksema, 2013; Gross & John, 2003; Nolen-Hoeksema & Aldao, 2011), we examined how the predictive performance of this model varied based on sex.

Methods

Participants

Data were available from 1,316 participants (age range = 18-22 years old; 43% men) who completed the Duke Neurogenetics Study between January 2010 and July 2014 (Table 1). This study was approved by the Duke University Medical Center Institutional Review Board. The authors assert that all procedures contributing to this work also complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

All participants provided informed consent before participation and were excluded in the present sample if they met any of the following criteria: (a) medical diagnoses of cancer, stroke, diabetes requiring insulin treatment, chronic kidney or liver disease, or lifetime history of psychotic symptoms (b) use of psychotropic, glucocorticoid, or hypolipidemic medication (c) conditions affecting cerebral blood flow and metabolism (e.g., hypertension) or (d) failed quality control criteria for functional magnetic resonance imaging (fMRI) data. Diagnosis of any past or current DSM-IV Axis I disorder or select Axis II disorders (antisocial personality disorder and borderline personality disorder) were assessed with structured clinical interviews (Sheehan et al., 1998). Such diagnoses were, however, not exclusion criteria, as the Duke Neurogenetics Study sought to establish broad variability in multiple behavioral phenotypes related to psychopathology. Of the 1,316 participants included in our analyses, 66 met criteria for major depressive disorder, 35 for bipolar disorder, 26 for panic disorder, 12 for social anxiety disorder, 24 for generalized anxiety disorder, 15 for obsessive compulsive disorder, 2 for post-traumatic stress disorder, 142 for alcohol abuse, 48 for substance abuse, 11 for eating disorder (bulimia or anorexia) and 3 experienced psychotic symptoms.

Self-report questionnaires

Individual differences in dispositional emotion regulation practices and negative affect were assessed with the following self-report questionnaires. The Emotion Regulation Questionnaire (ERQ), a 10-item self-report questionnaire, was used to measure individual differences in suppression and reappraisal (Gross & John, 2003). The ERQ has two subscales—ERQ-Suppression, including items such as “I control my emotions by not expressing them.” and ERQ-Reappraisal, including items such as “I control my emotions by changing the way I think about

the situation I'm in." All items are rated on a 7-point scale from 1 (strongly disagree) to 7 (strongly agree) and summed within each subscale to generate overall scores for suppression and reappraisal. The ERQ has been consistently shown to be a valid and reliable index of regulation tendency (Gross & John, 2003).

MRI data acquisition

Each participant was scanned using one of two identical research-dedicated GE MR750 3T scanners equipped with high-power high-duty-cycle 50-mT/m gradients at 200 T/m/s slew rate, and an eight-channel head coil for parallel imaging at high bandwidth up to 1MHz at the Duke-UNC Brain Imaging and Analysis Center. A semi-automated high-order shimming program was used to ensure global field homogeneity. A series of 34 interleaved axial functional slices aligned with the anterior commissure-posterior commissure plane were acquired for full-brain coverage using an inverse-spiral pulse sequence to reduce susceptibility artifacts (TR/TE/flip angle=2000 ms/30 ms/60; FOV=240mm; 3.75×3.75×4 mm voxels; interslice skip=0). Four initial radiofrequency excitations were performed (and discarded) to achieve steady-state equilibrium. For each participant, functional MRI was collected during various combinations of a single resting-state and four task scans. Due to the multi-phasic nature of the study, while all participants completed some fMRI scanning, not all participants had the same fMRI scans. See supplementary Figure 1 for a breakdown of the specific scans available for each participant.

MRI Preprocessing

Anatomical images for each participant were skull-stripped, intensity-normalized, and nonlinearly warped to a study-specific average template in the standard stereotactic space of the Montreal

Neurological Institute template using the ANTs SyN registration algorithm (Avants, Epstein, Grossman, & Gee, 2008; Klein et al., 2009). Time-series images for each participant were despiked, slice-time-corrected, realigned to the first volume in the time series to correct for head motion using AFNI tools (Cox, 1996), co-registered to the anatomical image using FSL's Boundary Based Registration (Cox, 1996; Greve & Fischl, 2009), spatially normalized into MNI space using the non-linear ANTs SyN warp from the anatomical image, resampled to 2mm isotropic voxels, and smoothed to minimize noise and residual difference in gyral anatomy with a Gaussian filter set at 6-mm full-width at half-maximum. All transformations were concatenated so that a single interpolation was performed.

Time-series images for each participant were further processed to limit the influence of motion and other artifacts. Voxel-wise signal intensities were scaled to yield a time series mean of 100 for each voxel. Motion regressors were created using each participant's 6 motion correction parameters (3 rotation and 3 translation) and their first derivatives (Jo et al., 2013; Satterthwaite et al., 2013) yielding 12 motion regressors. White matter and cerebrospinal fluid nuisance regressors were created using CompCorr (Behzadi, Restom, Liao, & Liu, 2007). Images were bandpass filtered to retain frequencies between .008 and .1 Hz, and volumes exceeding 0.25mm frame-wise displacement or 1.55 standardized DVARS (Nichols, 2017; Power et al., 2014) were censored. Nuisance regression, bandpass filtering and censoring for each time series was performed in a single processing step using AFNI's 3dTproject.

General Functional Connectivity

We combined all available BOLD data (task and resting-state) for each participant into a single time-series. Using our recently developed methods (Elliott et al., 2019), we extracted measures of GFC for each participant using a 264-region parcellation scheme derived in a large independent dataset (Power et al., 2011). BOLD time-series were averaged within 5 mm spheres surrounding each of the 264 coordinates in the parcellation and extracted time-series were concatenated. Importantly, we regressed out the task structure from each time-series to reduce the effect of task-related activation on estimates of functional connectivity (Elliott et al., 2019). Correlation matrices were derived from these time-series using Pearson correlation, resulting in 34,716 edges in the Power et al. parcellation. Sensitivity Analyses excluding participants with fewer than 400 TRs (Elliott et al., 2019) did not change our findings reported below.

Connectome-Based Predictive Modeling

Dispositional use of suppression and reappraisal were independently predicted from patterns of GFC using CPM, (Shen et al., 2017). This framework provides a general method to predict any measure from intrinsic connectivity matrices. Functional connections in the brain that had a $p < .01$ correlation with self-reported suppression and reappraise tendency were selected and used as features in a predictive model. Three linear regression predictive models are then built—one from the positive features (edges positively correlated with the measure of interest), one from the negative features (edges negatively correlated with the measure of interest) and one from the combination of positive and negative features (Shen et al., 2017). Here, we discuss the combined model that predicts dispositional regulation styles from positive and negative features in the brain (Shen et al., 2017).

Models were trained using a leave-one-out cross-validation scheme wherein data from all participants except one were used to predict the measure in the left-out participant. This was repeated until all participants had been left out. The Spearman correlation between predicted and true scores was adopted as an unbiased effect size measure of predictive utility. Model predictions of suppression and reappraisal tendency were assessed for significance using a parametric test for significance of correlations. All *p* values from correlations with suppression and reappraisal tendency were corrected for multiple comparisons using the false discovery rate (Benjamini & Hochberg, 1995). All confidence intervals for CPM prediction estimates were generated with bootstrap resampling, using AFNI's 1dCorrelate tool.

To first establish and then separate between- and within-network GFC, significant positive and negative edges for each of the 264 nodes were independently sorted into seven established neural networks (Yeo et al., 2011) based on pre-defined network assignments of each node. Any node that did not fall into one of these established networks was assigned to an “other” category. The number of edges within and between networks were then assessed for significance using random-sorted permutation testing to establish null distributions for comparison and determine how many connections would be expected by chance ($p < .001$; after correcting for multiple comparisons (.05/38 total within and between comparisons = .001)). In order to examine sex differences in the predictive performance of the models, we correlated the true and predicted dispositional regulation measures (i.e. the output of the CPM model) separately for males and females. Based on previous behavioral and neuroimaging literature noting that men use ES more than females (Aldao & Nolen-Hoeksema, 2013; Cai, Lou, Long, & Yuan, 2016; Gross & John, 2003; McRae, Ochsner, Mauss,

Gabireli, & Gross, 2008) Nolen-Hoeksema & Aldao, 2011), we predicted that this correlation would be stronger in males.

Results

Self-report measures

Means and standard deviations for the self-report questionnaires were as follows: ERQ-Suppression (3.79 ± 1.16 , range = 7) and ERQ-Reappraisal ($5.18 \pm .89$, range = 7). There were significant sex differences ($t(1223.7) = 6.05, p < 0.001$) in ERQ-Suppression subscores, with men (4.01 ± 1.13) scoring higher than women (3.63 ± 1.16). There were significant sex differences ($t(1159.2) = -3.78, p < 0.001$) in ERQ-Reappraisal subscale scores as well, with women (5.26 ± 0.86) scoring higher than men (5.07 ± 0.92). ERQ-Reappraisal and ERQ-Suppression subscales were not significantly correlated ($r = -.04, p = .97$).

Connectome-based predictive modeling

We investigated if there was a whole-brain signature for the dispositional use of suppression and reappraisal using a predictive and cross-validated model. There was no pattern of distributed functional connectivity in the brain that predicted individual differences in the dispositional use of reappraisal ($r = .02, p = .37$). We compared the correlations between actual and predicted ERQ-Reappraisal scores (i.e., the output and predictive utility of the CPM models) in men and women and found no sex difference ($r_{\text{male}} = -.009, p = .8; r_{\text{female}} = .039, p = .36$; Figure 2).

In contrast, there was a whole-brain signature for the dispositional use of suppression ($r = .135, p < .001$). 176 functional connections were positively correlated and 123 functional connections were

negatively correlated with ERQ-Suppression (Table 2). Within-network analyses revealed that the visual network had the most (41) positive predictive edges (Figure 1A) and the somatomotor network had the most (25) negative predictive edges (Figure 1B). The most (35) between-network positive connections were across frontoparietal and default mode networks and the most (32) between-network negative connections were across somatomotor and default mode networks (Figure 1A and B). Random sampling permutation tests of within-network patterns confirmed significant positive associations for visual, default mode, and frontoparietal networks, and significant negative associations for the somatomotor network. The only between-network connections expected above chance were across default mode and frontoparietal networks (positive) and default mode and somatomotor networks (negative).

When examining sex differences in the neural signature of dispositional suppression, we found that the predictive performance of the model (the correlation between actual and predicted ERQ-Suppression scores) was only significant in men ($r_{\text{male}} = .17, p < .001$; $r_{\text{female}} = .05, p = .09$; Figure 3). Moreover, the correlation coefficients between men and women were significantly different ($z = 1.96, p = .049$). In addition, we re-ran our CPM model with past or present psychiatric diagnosis as a covariate, which confirmed the neural signature associated with suppression was not driven by diagnosis ($r = .13, p < .001$). Because not all data were collected on the same scanner (Table 1), we conducted a final sensitivity analysis using scanner as a covariate, which confirmed the significant whole-brain signature of the dispositional suppression ($r = .11, p < .001$).

Discussion

In a large sample of 1,316 participants, we used a data-driven and theory-free approach to examine if there is a neural signature for how people tend to regulate their emotions. Instead of limiting patterns of functional connectivity to the typical 5 to 10 minutes of resting-state scans (Elliott et al., 2019), we used GFC to leverage shared features of task and resting-state fMRI and generate more reliable estimates of intrinsic functional connectivity. Most available research investigating individual differences in intrinsic connectivity is based on resting-state scans. However, most resting-state scans are typically not sufficiently long enough to generate reliable estimates of intrinsic functional connectivity. GFC has been shown to be a reliable measure of stable, trait-like individual differences in behavior, such as dispositional regulation tendency (Elliott et al., 2019). By adopting GFC, we increased our ability to investigate neural signatures of individual differences in emotion regulation strategies.

In addition to benefiting from using all available functional data, our findings begin to address other limitations often present in emotion regulation research. For example, existing research often finds overlapping patterns of neural activity for suppression and reappraisal, confounding the ability to distinguish between them. As our approach is wholly data-driven, we are able to analyze distributed patterns for each strategy separately. In addition, existing neuroimaging research that explores brain-behavior relationships is often biased toward specific regions of interest or explores whole-brain maps that may be overfit and vulnerable to false positives (Shen et al. 2017). Using CPM, we circumvent these limitations and generate a predictive model that is cross-validated in novel samples.

As with prior research on whole-brain networks associated with suppression, our results indicate that functional connectivity between the frontoparietal and default mode networks is positively correlated with the tendency to suppress negative emotion (Pan et al., 2018). The default mode network, initially named so because it is active in the absence of an explicit goal or task, is commonly implicated in self-reflection, mind wandering, and self-generated thought (Andrews-Hanna, 2012; Andrews-Hanna, Smallwood, & Spreng, 2014). The default mode network has been implicated in suppression in prior studies employing a univariate analysis approach as well (Goldin, McRae, Ramel, & Gross, 2008). This dual recruitment of default mode and frontoparietal networks is consistent with prior research indicating that the default mode network may support emotional processing and reflection, and the frontoparietal network may support emotional control—abilities that align to primary descriptions of suppression as the conscious inhibition of emotional expression (Gross & Levenson, 1993).

Consistent with demonstrated sex differences in emotion regulation, the neural signature of dispositional use of suppression identified in our current study was specific to men who tend to habitually use and are more successful at implementing suppression (Cai et al., 2016; Gross & John, 2003). Similarly, electromyography findings have shown that men show reduced emotional expressions when viewing negative emotional stimuli (Grossman & Wood, 1993). Prior research has shown that men are socialized to refrain from expressing emotion and therefore have more developmental experience with suppressing negative emotion (Brody & Hall, 2010; Katkin & Hoffman, 1976; Williams & Best, 1990). Such differences may contribute to our sex-specific effects. Future work is necessary to replicate this sex difference.

Importantly, the neural signature of dispositional suppression remained significant after excluding participants with psychiatric diagnoses, suggesting that clinical manifestations associated with suppressing emotion are not driving the predictive relationship between patterns of functional connectivity and suppression tendency. Although the tendency to suppress negative emotion is one characteristic of depression and anxiety (Amstadter, 2008; Cisler & Olatunji, 2012; Gross, 2002; Gross & Levenson, 1997; Troy, Wilhelm, Shallcross, & Mauss, 2010), healthy adults may also use suppression in certain situations (Doré, Silvers, & Ochsner, 2016; Suri, Sheppes, Young, Abraham, McRae, & Gross, 2018). Thus, the use of suppression is likely not categorically maladaptive and, indeed, may be adaptive in particularly stressful situations (Doré, Silvers, & Ochsner, 2016).

We found a pronounced whole-brain signature of the tendency to suppress negative emotion, but found no comparable signature for reappraisal. Specifically, despite prior research implicating the default mode network in the reappraisal of negative emotion, we found no such signature. However, these findings typically come from studies with small sample sizes, which increase the likelihood of false positives (Chen, Biswal, Lei, & Yuan, 2018; Gao et al., 2018). Moreover, emotion regulation research typically involves instructing participants to employ an explicit strategy (Cutuli, 2014; Dennis & Hajcak, 2009; Gross & John, 2003; Kalisch, Wiech, Herrmann, & Dolan, 2006; Kanske, Heissler, Schönfelder, & Wessa, 2012; Urry et al., 2006). But, emotion regulation during laboratory protocol may not accurately reflect how people tend to choose to regulate their emotions in the real world (Aldao, Nolen-Hoeksema, & Schweizer, 2010; Gross & John, 2003; Moore, Zoellner, & Mollenholt, 2008). Thus, the differences between our current

null findings and the positive findings of prior studies may reflect our focus on typical, daily strategies for regulation versus directed use of an experimental strategy for regulation.

One possibility for not identifying a neural signature for reappraisal specifically could be that reappraisal is a more heterogeneous construct with numerous subtypes than suppression (Doré, Silvers, & Ochsner, 2016). For example, although reappraisal is predominantly thought to be implemented in the service of reframing a stimulus to be less negative, individuals may use reappraisal to reframe a stimulus to be more positive (Doré, Silvers, & Ochsner, 2016). In addition, people can reappraise stimuli to feel less personal and more detached (Ossenfort, Harris, Platzeck, & Isaacowitz, 2018). In contrast, suppression is a more homogenous strategy with less variability in its implementation. As opposed to having numerous possible goals and subtypes, expressive suppression is a less complicated technique that invariably involves trying to mask your feelings from the outside world (Gross, 2002; Gross & John, 1998). Therefore, it may be more difficult to capture a stable neural signature of something as variable and multifaceted as reappraisal in comparison with suppression. The behavioral phenotypes predicted by our models are based on the ERQ-Suppression and Reappraisal subscales. The heterogeneity of reappraisal may be adding too much noise for the scale to be significantly predicted from patterns of functional connectivity. Relatedly, it may be difficult to self-report on a cognitively demanding and multifaceted technique such as reappraisal, making it difficult for a brain-behavior relationship to be identified.

Our study is not without limitations. Although GFC explicitly removes task-related activation from estimates of functional connectivity, such connectivity may nevertheless be affected by the inherent task performed during data acquisition (Elliott et al., 2019). Future research could

investigate how functional connectivity estimated only from resting-state data maps onto the dispositional use of reappraisal and suppression. Future studies may also aim to include a more diverse sample, as our sample was comprised of relatively high-functioning university students. Similarly, our data was cross-sectional, which limits our ability to determine if GFC patterns drive the use of suppression or if the use of suppression drives changes in GFC. In addition, our measure of regulation tendency was based on self-report. Thus, examining the neural signature of suppression we have identified during experimentally-controlled emotion regulation will be important. Lastly, the ERQ measures the tendency to use either suppression or reappraisal, but does not capture alternative strategies that people may adopt.

Acknowledgements

This work was supported by Duke University and National Institutes of Health (NIH) Grants R01DA033369 and R01DA031579 to the Duke Neurogenetics Study; NIH Grant R01AG049789 to A.R.H.; and the National Science Foundation Graduate Research Fellowship, Grant NSF DGE-1644868 to M.L.E. We thank the Duke Neurogenetics Study participants and the staff of the Laboratory of NeuroGenetics. In addition, the Brain Imaging and Analysis Center received support from the Office of the Director, National Institutes of Health under Award Number S10OD021480. The authors declare no competing financial interests.

Figure 1. A. The number of predictive positive edges within each network (i) and the number of predictive positive edges between each network that predict typical use of expressive suppression (ii). B. The number of predictive negative edges within each network (iii) and the number of predictive negative edges between each network that predict typical use of expressive suppression (iv). * denotes networks that are significantly ($p < 0.001$; based on a multiple corrections comparison) above the null distribution. Glass Brain Figures created by <http://bisweb.yale.edu/connviewer/> (Shen et al. 2017).

Figure 2. Correlation between actual and predicted Emotion Regulation Questionnaire-Reappraisal subscale scores from the connectome-based predictive model ($r_{\text{male}} = .039$, $p = .36$; $r_{\text{female}} = -.009$, $p = .8$).

Figure 3. Correlation between actual and predicted Emotion Regulation Questionnaire-Suppression subscale scores from the connectome-based predictive model ($r_{\text{male}} = .17$, $p < .001$; $r_{\text{female}} = .062$, $p = .09$).

Table 1

Demographics

	Total (N = 1316)	Women (n = 755)	Men (n = 561)
Age (years)	19.70 ± 1.25	19.66 ± 1.23	19.75 ± 1.27
ERQ Reappraisal (1-7)	5.18 ± 0.89	5.26 ± 0.85	5.07 ± 0.92
ERQ Suppression (1-7)	3.79 ± 1.16	3.63 ± 1.16	4.01 ± 1.13
Any Diagnoses (n)	268	134	134
<i>MDD (n)</i>	66	44	22
<i>Bipolar (n)</i>	35	19	16
<i>Panic Disorder (n)</i>	26	20	6
<i>Social Anxiety (n)</i>	12	5	7
<i>GAD (n)</i>	24	15	9
<i>OCD (n)</i>	15	7	8
<i>PTSD (n)</i>	2	1	1
<i>Alcohol Abuse (n)</i>	142	61	81
<i>Substance Abuse (n)</i>	48	21	27
<i>Eating Disorder (n)</i>	11	8	3
Scanner			
<i>Scanner 1 (n)</i>	1089	625	464
<i>Scanner 2 (n)</i>	227	130	97

Table 2

Number of predictive positive and negative connections within and between networks

<u>Network</u>	<u>Direction</u>	
	<i><u>Positive</u></i>	<i><u>Negative</u></i>
<i>Within</i>		
Visual (VisN)	41 *	0
Default Mode (DMN)	27 *	1
Frontoparietal (FPN)	7 *	0
Dorsal Attention (DAN)	2	0
Somatomotor (SMN)	0	25 *
Ventral Attention (VAN)	0	1
Limbic (LimN)	0	0
Other (Othr)	0	0
<i>Between</i>		
FPN - DMN	35 *	2
VisN - DAN	12	0
VAN - DMN	9	10
Othr - SMN	8	4
LimN - FPN	5	1
VAN - FPN	5	0
VisN - DMN	3	12
VisN - LimN	3	4
SMN - FPN	3	3
DAN - FPN	3	0
Othr - VAN	3	0
VisN - FPN	3	0
Othr - DMN	2	2
Othr - VisN	1	3
SMN - VAN	1	3
VisN - SMN	1	3
LimN - DMN	1	0
Othr - LimN	1	0
SMN - DMN	0	32 *
VisN - VAN	0	8
SMN - DAN	0	5
SMN - LimN	0	2
DAN - DMN	0	1
VAN - LimN	0	1
DAN - LimN	0	0
DAN - VAN	0	0
Othr - DAN	0	0
Othr - FPN	0	0
<i>Total</i>	176	123

References

- Aldao, A., & Nolen-Hoeksema, S. (2013). One versus many: capturing the use of multiple emotion regulation strategies in response to an emotion-eliciting stimulus. *Cognition & Emotion*, 27(4), 753–760.
- Aldao, A., Nolen-Hoeksema, S., & Schweizer, S. (2010). Emotion-Regulation Strategies across Psychopathology: A Meta-Analytic Review. *Clinical Psychology Review*, 30, 217-237.
- Andrews-Hanna, J. R., Smallwood, J., & Spreng, R. N. (2014). The default network and self-generated thought: component processes, dynamic control, and clinical relevance. *Annals of the New York Academy of Sciences*, 1316(1), 29–52.
doi:10.1111/nyas.12360
- Amstadter, A. (2008). Emotion regulation and anxiety disorders. *Journal of Anxiety Disorders*, 22(2), 211–221.
- Andrews-Hanna, J. R. (2012). The brain's default network and its adaptive role in internal mentation. *The Neuroscientist: A Review Journal Bringing Neurobiology, Neurology and Psychiatry*, 18(3), 251–270.
- Andrews-Hanna, J. R., Smallwood, J., & Spreng, R. N. (2014). The default network and self-generated thought: component processes, dynamic control, and clinical relevance. *Annals of the New York Academy of Sciences*, 1316, 29–52.
- Avants, B. B., Epstein, C. L., Grossman, M., & Gee, J. C. (2008). Symmetric diffeomorphic image registration with cross-correlation: evaluating automated labeling of elderly and neurodegenerative brain. *Medical Image Analysis*, 12(1), 26–41.
- Behzadi, Y., Restom, K., Liau, J., & Liu, T. T. (2007). A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *NeuroImage*, 37(1), 90–101.

- Benjamini, Y., & Hochberg, Y. (1995). Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society: Series B (Methodological)*, Vol. 57, pp. 289–300. <https://doi.org/10.1111/j.2517-6161.1995.tb02031.x>
- Bennett, C.M. & Miller M.B. (2010). How reliable are the results from functional magnetic resonance imaging? *Ann. N. Y. Acad. Sci.* 1191, 133–155. doi: 10.1111/j.1749-6632.2010.05446.x.
- Brody, L. R., & Hall, J. A. (2010). Gender, Emotion, and Socialization. *Handbook of Gender Research in Psychology*, pp. 429–454. https://doi.org/10.1007/978-1-4419-1465-1_21
- Buhle, J. T., Kober, H., Ochsner, K. N., Mende-Siedlecki, P., Weber, J., Hughes, B. L., ... Wager, T. D. (2013). Common representation of pain and negative emotion in the midbrain periaqueductal gray. *Social Cognitive and Affective Neuroscience*, 8(6), 609–616.
- Cai, A., Lou, Y., Long, Q., & Yuan, J. (2016). The Sex Differences in Regulating Unpleasant Emotion by Expressive Suppression: Extraversion Matters. *Frontiers in Psychology*, Vol. 7. <https://doi.org/10.3389/fpsyg.2016.01011>.
- Chang, L. J., Gianaros, P. J., Manuck, S. B., Krishnan, A., & Wager, T. D. (2015). A Sensitive and Specific Neural Signature for Picture-Induced Negative Affect. *PLOS Biology*, Vol. 13, p. e1002180. <https://doi.org/10.1371/journal.pbio.1002180>.
- Chen, S., Chen, C., Yang, J., & Yuan, J. (2017). Trait self-consciousness predicts amygdala activation and its functional brain connectivity during emotional suppression: an fMRI analysis. *Scientific Reports*, Vol. 7. <https://doi.org/10.1038/s41598-017-00073-3>.
- Cisler, J. M., & Olatunji, B. O. (2012). Emotion regulation and anxiety disorders. *Current Psychiatry Reports*, 14(3), 182–187.

- Clarke, M. J., Marks, A. D. G., & Lykins, A. D. (2015). Effect of normative masculinity on males' dysfunctional sexual beliefs, sexual attitudes, and perceptions of sexual functioning. *Journal of Sex Research*, 52(3), 327–337.
- Cox, R. W. (1996). AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research, an International Journal*, 29(3), 162–173.
- Cutuli, D. (2014). Cognitive reappraisal and expressive suppression strategies role in the emotion regulation: an overview on their modulatory effects and neural correlates. *Frontiers in Systems Neuroscience*, 8, 175.
- Dennis, T. A., & Hajcak, G. (2009). The late positive potential: a neurophysiological marker for emotion regulation in children. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, 50(11), 1373–1383.
- Denny, B. T., Inhoff, M. C., Zerubavel, N., Davachi, L., & Ochsner, K. N. (2015). Getting Over It: Long-Lasting Effects of Emotion Regulation on Amygdala Response. *Psychological Science*, 26(9), 1377–1388.
- Doré, B. P., Silvers, J. A., & Ochsner, K. N. (2016). Toward a Personalized Science of Emotion Regulation. *Social and Personality Psychology Compass*, 10(4), 171–187.
- Elliott, M. L., Knodt, A. R., Cooke, M., Kim, M. J., Melzer, T. R., Keenan, R., ... Hariri, A. R. (2019). General functional connectivity: Shared features of resting-state and task fMRI drive reliable and heritable individual differences in functional brain networks. *NeuroImage*, 189, 516–532.
- Gao, W., Chen, S., Biswal, B., Lei, X., & Yuan, J. (2018). Temporal dynamics of spontaneous default-mode network activity mediate the association between reappraisal and depression.

Social Cognitive and Affective Neuroscience. <https://doi.org/10.1093/scan/nsy092>.

- Goldin, P. R., McRae, K., Ramel, W., & Gross, J. J. (2008). The neural bases of emotion regulation: reappraisal and suppression of negative emotion. *Biological Psychiatry*, 63(6), 577–586.
- Greve, D. N., & Fischl, B. (2009). Accurate and robust brain image alignment using boundary-based registration. *NeuroImage*, 48(1), 63–72.
- Gross, J. J. (2002). Emotion regulation: affective, cognitive, and social consequences. *Psychophysiology*, 39(3), 281–291.
- Gross, J. J., & John, O. P. (1998). Mapping the domain of expressivity: multimethod evidence for a hierarchical model. *Journal of Personality and Social Psychology*, 74(1), 170–191.
- Gross, J. J., & John, O. P. (2003). Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *Journal of Personality and Social Psychology*, Vol. 85, pp. 348–362. <https://doi.org/10.1037/0022-3514.85.2.348>
- Gross, J. J., & Levenson, R. W. (1997). Hiding feelings: the acute effects of inhibiting negative and positive emotion. *Journal of Abnormal Psychology*, 106(1), 95–103.
- Grossman, M., & Wood, W. (1993). Sex differences in intensity of emotional experience: a social role interpretation. *Journal of Personality and Social Psychology*, 65(5), 1010–1022.
- Jamieson, J. P., Mendes, W. B., Blackstock, E., & Schmader, T. (2010). Turning the knots in your stomach into bows: Reappraising arousal improves performance on the GRE. *Journal of Experimental Social Psychology*, 46(1), 208–212.
- Jo, H. J., Gotts, S. J., Reynolds, R. C., Bandettini, P. A., Martin, A., Cox, R. W., & Saad, Z. S. (2013). Effective Preprocessing Procedures Virtually Eliminate Distance-Dependent Motion Artifacts in Resting State FMRI. *Journal of Applied Mathematics*, 2013.

<https://doi.org/10.1155/2013/935154>.

- Kalisch, R., Wiech, K., Herrmann, K., & Dolan, R. J. (2006). Neural correlates of self-distraction from anxiety and a process model of cognitive emotion regulation. *Journal of Cognitive Neuroscience*, 18(8), 1266–1276.
- Kanske, P., Heissler, J., Schönfelder, S., & Wessa, M. (2012). Neural correlates of emotion regulation deficits in remitted depression: the influence of regulation strategy, habitual regulation use, and emotional valence. *NeuroImage*, 61(3), 686–693.
- Katkin, E. S., & Hoffman, L. S. (1976). Sex differences and self-report of fear: a psychophysiological assessment. *Journal of Abnormal Psychology*, 85(6), 607–610.
- Klein, A., Andersson, J., Ardekani, B. A., Ashburner, J., Avants, B., Chiang, M.-C., ... Parsey, R. V. (2009). Evaluation of 14 nonlinear deformation algorithms applied to human brain MRI registration. *NeuroImage*, 46(3), 786–802.
- Martins, B., & Mather, M. (2016). Default mode network and later-life emotion regulation: Linking functional connectivity patterns and emotional outcomes. *Emotion, Aging, and Health*, pp. 9–29. <https://doi.org/10.1037/14857-002>.
- McLean, C. P., & Anderson, E. R. (2009). Brave men and timid women? A review of the gender differences in fear and anxiety. *Clinical Psychology Review*, 29(6), 496–505.
- McRae, K., Hughes, B., Chopra, S., Gabrieli, J. D. E., Gross, J. J., & Ochsner, K. N. (2010). The neural bases of distraction and reappraisal. *Journal of Cognitive Neuroscience*, 22(2), 248–262.
- McRae, K., Misra, S., Prasad, A. K., Pereira, S. C., & Gross, J. J. (2012). Bottom-up and top-down emotion generation: implications for emotion regulation. *Social Cognitive and Affective Neuroscience*, Vol. 7, pp. 253–262. <https://doi.org/10.1093/scan/nsq103>.

McRae, K., Ochsner, K. N., Mauss, I. B., Gabrieli, J., & Gross, J. J. (2008). Gender Differences

in Emotion Regulation: An fMRI Study of Cognitive Reappraisal. *Group processes & intergroup relations : GPIR*, 11(2), 143–162. doi:10.1177/1368430207088035

Moore, S. A., Zoellner, L. A., & Mollenholt, N. (2008). Are expressive suppression and

cognitive reappraisal associated with stress-related symptoms?. *Behaviour research and therapy*, 46(9), 993–1000. doi:10.1016/j.brat.2008.05.001

Nichols TE (2017). Notes on Creating a Standardized Version of DVARS.

<http://arxiv.org/abs/1704.01469>.

Nolen-Hoeksema, S., & Aldao, A. (2011). Gender and age differences in emotion regulation

strategies and their relationship to depressive symptoms. *Personality and Individual Differences*, Vol. 51, pp. 704–708. <https://doi.org/10.1016/j.paid.2011.06.012>

Ossenfort, K.L., Harris, J.A., Platzek, C., & Isaacowitz, D.M. (2018). Positive and detached

reappraisal in older adulthood: A temporal examination of gaze patterns. *Aging & Mental Health*.

Pan, J., Zhan, L., Hu, C., Yang, J., Wang, C., Gu, L., ... Wu, X. (2018). Emotion Regulation and

Complex Brain Networks: Association Between Expressive Suppression and Efficiency in the Fronto-Parietal Network and Default-Mode Network. *Frontiers in Human Neuroscience*, 12, 70.

Picó-Pérez, M., Alonso, P., Contreras-Rodríguez, O., Martínez-Zalacaín, I., López-Solà, C.,

Jiménez-Murcia, S., ... Soriano-Mas, C. (2018). Dispositional use of emotion regulation strategies and resting-state cortico-limbic functional connectivity. *Brain Imaging and Behavior*, 12(4), 1022–1031.

Power, J. D., Cohen, A. L., Nelson, S. M., Wig, G. S., Barnes, K. A., Church, J. A., ... Petersen,

- S. E. (2011). Functional Network Organization of the Human Brain. *Neuron*, Vol. 72, pp. 665–678. <https://doi.org/10.1016/j.neuron.2011.09.006>
- Power, J. D., Mitra, A., Laumann, T. O., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2014). Methods to detect, characterize, and remove motion artifact in resting state fMRI. *NeuroImage*, 84, 320–341.
- Satterthwaite, T. D., Elliott, M. A., Gerraty, R. T., Ruparel, K., Loughead, J., Calkins, M. E., ... Wolf, D. H. (2013). An improved framework for confound regression and filtering for control of motion artifact in the preprocessing of resting-state functional connectivity data. *NeuroImage*, 64, 240–256.
- Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., ... Dunbar, G. C. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *The Journal of Clinical Psychiatry*, 59 Suppl 20, 22–33;quiz 34–57.
- Shen, X., Finn, E. S., Scheinost, D., Rosenberg, M. D., Chun, M. M., Papademetris, X., & Constable, R. T. (2017). Using connectome-based predictive modeling to predict individual behavior from brain connectivity. *Nature Protocols*, 12(3), 506–518.
- Sripada, R. K., Marx, C. E., King, A. P., Rajaram, N., Garfinkel, S. N., Abelson, J. L., & Liberzon, I. (2013). DHEA enhances emotion regulation neurocircuits and modulates memory for emotional stimuli. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology*, 38(9), 1798–1807.
- Suri, G., Sheppes, G., Young, G., Abraham, D., McRae, K. & Gross, J. (2018) Emotion regulation choice: the role of environmental affordances, *Cognition and Emotion*, 32(5), 963-97.

- Troy, A. S., Wilhelm, F. H., Shallcross, A. J., & Mauss, I. B. (2010). Seeing the silver lining: cognitive reappraisal ability moderates the relationship between stress and depressive symptoms. *Emotion*, 10(6), 783–795.
- Uchida, M., Biederman, J., Gabrieli, J. D. E., Micco, J., de Los Angeles, C., Brown, A., ... Whitfield-Gabrieli, S. (2015). Emotion regulation ability varies in relation to intrinsic functional brain architecture. *Social Cognitive and Affective Neuroscience*, 10(12), 1738–1748.
- Urry, H. L., van Reekum, C. M., Johnstone, T., Kalin, N. H., Thurow, M. E., Schaefer, H. S., ... Davidson, R. J. (2006). Amygdala and ventromedial prefrontal cortex are inversely coupled during regulation of negative affect and predict the diurnal pattern of cortisol secretion among older adults. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 26(16), 4415–4425.
- Williams, J. E., & Best, D. L. (1990). *Measuring sex stereotypes: a multination study*. Sage Publications, Inc.
- Xie, X., Mulej Bratec, S., Schmid, G., Meng, C., Doll, A., Wohlschläger, A., ... Sorg, C. (2016). How do you make me feel better? Social cognitive emotion regulation and the default mode network. *NeuroImage*, 134, 270–280.
- Yeo, B. T. T., Thomas Yeo, B. T., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., ... Buckner, R. L. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, Vol. 106, pp. 1125–1165. <https://doi.org/10.1152/jn.00338.2011>.

Supplementary Figures

Amygdala Reactivity Task	Ventral Striatum Task	Hippocampal Task	Working Memory Task	Resting State Scan	# Subjects
					960
					306
					29
					8
					3
					3
					2
					2
					1
					1

					1
				Total	1316

Figure 1. Breakdown by task of available Magnetic Resonance Imaging data for participants (N = 1,316). Mean available Repetition Time (TRs) across all participants was 620.2 (1st Quartile = 494, 3rd Quartile = 622). Colored squares signify data availability. See Supplementary Material for detailed descriptions of each task.

Supplementary Material*Amygdala Task*

The experimental fMRI paradigm consists of four blocks of a perceptual face-matching task interleaved with five blocks of a sensorimotor control task. The Duke Neurogenetics Study version of this paradigm consists of one block each of fearful, angry, surprised, and neutral facial expressions presented in a pseudorandom order across participants. During face-matching blocks, participants view a trio of faces and select one of two faces identical to a target face. Each face processing block consists of six images, balanced for gender, all of which were derived from a standard set of pictures of facial affect (Ekman & Friesen, 1976). During the sensorimotor control blocks, participants view a trio of simple geometric shapes (circles and vertical and horizontal ellipses) and select one of two shapes that are identical to a target shape. Each sensorimotor control block consists of six different shape trios. All blocks are preceded by a brief instruction ("Match Faces" or "Match Shapes") that lasts 2 s. In the task blocks, each of the six face trios is presented for 4 s with a variable interstimulus interval (ISI) of 2-6 s (mean = 4 s) for a total block length of 48 s. A variable ISI is used to minimize expectancy effects and resulting habituation, and maximize amygdala reactivity throughout the paradigm. In the control blocks, each of the six shape trios is presented for 4 s with a fixed ISI of 2 s for a total block length of 36 s. Total task time is 390 s.

Ventral Striatum Task

As described previously (Forbes et al. 2009), our blocked-design number-guessing paradigm consists of a pseudorandom presentation of three blocks of predominantly positive feedback (80% correct guess), three blocks of predominantly negative feedback (20% correct guess) and three

control blocks. There are five trials in 3 seconds to guess, via button press, whether the value of a visually presented card is lower or higher than 5 (index and middle finger, respectively). The numerical value of the card is then presented for 500 milliseconds and followed by appropriate feedback (green upward-facing arrow for positive feedback; red downward-facing arrow for negative feedback) for an additional 500 milliseconds. A crosshair is then presented for 3 seconds, for a total trial length of 7 seconds. Each block comprises five trials, with three blocks each of predominantly positive feedback (80% correct) and three of predominantly negative feedback (20% correct) interleaved with three control blocks. During control blocks, participants are instructed to simply make button presses during the presentation of an "x" (3 seconds), which is followed by an asterisk (500 milliseconds) and a yellow circle (500 milliseconds). Each block is preceded by an instruction of "Guess Number" (positive or negative feedback blocks) or "Press Button" (control blocks) for 2 seconds resulting in a total block length of 38 seconds and a total task length of 342 seconds. Participants were unaware of the fixed outcome probabilities associated with each block and were led to believe that their performance would determine a net monetary gain at the end of the scanning session. Instead, all participants received \$10. We included one incongruent trial within each task block (eg, one of five trials during positive feedback blocks was incorrect resulting in negative feedback) to prevent participants from anticipating the feedback for each trial and to maintain participants' engagement and motivation to perform well.

Hippocampus Task

Our fMRI paradigm consists of the encoding and subsequent recall of novel face-name pairs (Zeineh et al., 2003). A distractor task (odd/even number identification) is interleaved between encoding and recall blocks to prevent maintenance of information in working memory. During each of four encoding blocks, participants view six novel face-name pairs for 3.5 seconds each. During each of four recall blocks, participants view six faces each presented for 2 seconds and immediately followed by an incomplete name fragment for 1 second during which they are required by forced-choice to determine if the fragment is correct or incorrect. A 1 second inter-trial interval is used during recall blocks. During each of four distractor blocks, participants view six different numbers for 3.5 seconds each and are required to determine if the numbers are odd or even (see [diagram](#)). Total task length is 324 seconds.

Prefrontal Task

Activity of the dlPFC was measured during BOLD fMRI using an event-related working memory paradigm adapted from Tan et al. (Tan et al., 2007, Scult et al. 2016). The paradigm included 10 trials for each of 6 different conditions, including 3 control conditions, consisting only of a 3s response phase, and 3 working memory conditions, consisting of a 0.5s encoding phase followed by a 4s maintenance interval and a 3s response phase. Control and working memory conditions were interleaved with jittered rest intervals lasting 4s to 8.5s for a total scan length of 11m 48s. Responses were recorded via an MR-compatible button box using the index (left button) and middle (right button) fingers of the dominant hand.

During the control conditions, participants performed 1) a simple motor task in which they pressed either the left or the right button according to a prompt, 2) a numerical size judgment task in which they chose the number on the left or right based on an instruction to choose either the larger or the smaller number, and 3) a numerical computation and size judgment task in which they performed a numerical subtraction of 2 or 3 from either the left or right number, and made a numerical size judgment as instructed.

In the first working memory condition, participants viewed 2 numbers during the brief encoding phase, then recalled the numbers and performed a numerical size judgment as instructed. In the second working memory condition, the participants additionally performed subtraction of 2 or 3 from one of the remembered numbers as indicated before making the numerical size judgment during recall. In the final working memory condition, participants performed subtraction of 2 or 3 from one of the 2 numbers during the brief encoding phase, then recalled the resulting two numbers and performed a numerical size judgment as instructed during the response phase after the maintenance interval. In each working memory condition trial, all the numbers were single digits from 0 to 9; the two numbers on which the numerical size judgment was ultimately performed (after numerical computation if applicable) were equally balanced across 0 to 9, and equally likely to differ by either 1 or 3 units. Numerical computation was equally likely on the left or right number, with correct responses equally balanced on the left or right, and equally likely to be the larger or smaller number for each working memory trial type. The trials were performed in an order that was optimized using a sequencing program (Wager & Nichols, 2003).

Supplementary References

Ekman P, Friesen W. Pictures of Facial Affect. Palo Alto, CA: Consulting Psychologists Press;

1976.

Forbes, EE, Brown, SM, Kimak, M, Ferrell, RE, Manuck, SB, Hariri, AR (2009). Genetic variation in components of dopamine neurotransmission impacts ventral striatal reactivity associated with impulsivity. *Molecular Psychiatry* 14, 60-70. Scult, M. A., Knodt, A. R.,

Swartz, J. R., Brigidi, B. D., & Hariri, A. R. (2016). Thinking and Feeling: Individual Differences in Habitual Emotion Regulation and Stress-Related Mood Are Associated With Prefrontal Executive Control. *Clinical Psychological Science*, 2167702616654688.

Tan, H.-Y., Chen, Q., Goldberg, T. E., Mattay, V. S., Meyer-Lindenberg, A., Weinberger, D. R., & Callicott, J. H. (2007). Catechol-O-methyltransferase Val158Met modulation of prefrontal-parietal-striatal brain systems during arithmetic and temporal transformations in working memory. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 27(49), 13393-401. doi:10.1523/JNEUROSCI.4041-07.2007

Wager, T. D., & Nichols, T. E. (2003). Optimization of experimental design in fMRI: A general framework using a genetic algorithm. *NeuroImage*, 18(2), 293-309. doi:10.1016/S1053-8119(02)00046-0

Zeineh MM, Engel SA, Thompson PM, Bookheimer SY. Dynamics of the hippocampus during encoding and retrieval of face-name pairs. *Science*. 2003;299:577–580.