

Neural activity associated with repetitive simulation of episodic counterfactual thoughts

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ARTICLE INFO

Keywords:

Counterfactual thinking
Mental simulation
Autobiographical memory
Repetition

ABSTRACT

When people revisit past autobiographical events they often imagine alternative ways in which such events could have occurred. Often these episodic counterfactual thoughts (eCFT) are momentary and fleeting, but sometimes they are simulated frequently and repeatedly. However, little is known about the neural differences between frequently versus infrequently repeated eCFT. The current study explores this issue. In a three-session study, participants were asked to simulate alternative ways positive, negative, and neutral autobiographical memories could have occurred. Half of these eCFT were repeatedly re-simulated while the other half were not. Immediately after, participants were asked to simulate all these eCFT again while undergoing fMRI. A partial least squares analysis on the resultant fMRI data revealed that eCFT that were not frequently repeated preferentially engaged brain regions including middle (BA 21) and superior temporal gyri (BA 38/39), middle (BA 11) and superior frontal gyri (BA 9), and hippocampus. By contrast, frequently repeated eCFT preferentially engaged regions including medial frontal gyri (BA 10), anterior cingulate cortex, insula, and inferior parietal lobule (BA 40). Direct contrasts for each type of eCFT were also conducted. The results of these analyses suggest differential contributions of regions traditionally associated with eCFT, such as BA 10, anterior cingulate cortex, and hippocampus, as a function of kind of eCFT and frequency of repetition. Consequences for future research on eCFT and rumination are considered.

1. Introduction

When revisiting past autobiographical episodes, we often cannot help but imagine alternative ways in which such events could have occurred. These episodic counterfactual thoughts (eCFT; De Brigard and Giovanello, 2012)—which refer to imagined alternatives to past autobiographical episodes—tend to be distinguished from semantic counterfactual thoughts—imagined alternative ways in which non-personal facts could have been instead (e.g., “what if Iowa City was the capital of the US instead of Washington D.C.”, “what if kangaroos didn’t have tails”; see Roese and Epstude (2017), for a recent characterization). Recent research has shown that these pervasive and generally useful eCFT (Byrne, 2005, 2016; Epstude and Roese, 2008, Roese and Epstude, 2017) tend to engage core regions of the brain’s default network (DN; Buckner et al., 2008; Van Hoeck et al., 2013), a set of functionally connected brain regions including ventral medial prefrontal cortex (vMPFC), posterior cingulate cortex (PCC), inferior parietal lobule (IPL), lateral temporal cortex (LTC), dorsal medial prefrontal cortex (dMPFC), and the medial temporal lobes (MTL). Subsequent results

refined this initial observation by revealing that not all eCFT engaged DN regions to the same degree. For instance, De Brigard et al. (2013a) showed that eCFT that were judged by participants as being plausible engaged core regions of the DN associated with episodic autobiographical recollection, whereas eCFT participants judged as implausible recruited a significantly different brain pattern. Similarly, it has also been shown that DN is preferentially recruited in eCFT involving people rather than objects, and that this recruitment is modulated both by the familiarity and the similarity of the imagined character relative to the participant (De Brigard et al., 2015). More precisely, when we imagine eCFT featuring people we know and perceive as being similar to us, DN regions are recruited to a greater degree than when we imagine the same eCFT but featuring someone we are neither familiar with nor similar to. Finally, a recent study conducted by Parikh, Ruzic, Stewart, Spreng and De Brigard (in review) also revealed increased recruitment of DN regions for episodic relative to semantic counterfactuals, with perceived plausibility modulating the relative contribution of certain core regions of the DN, such as the hippocampus.

Normally, eCFT tend to be momentary and fleeting. However, in

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some instances, our eCFT are frequently and repeatedly simulated. Indeed, extant evidence suggests that some individuals cannot help but mentally simulate the same counterfactual thought over and over again (Roese et al., 2009). Moreover, for some of them, this repetitive counterfactual rumination—understood as the propensity to entertain repeated, frequent and uncontrollable eCFT—can become dysfunctional and debilitating (Brinker and Dozois, 2009; Tanner et al., 2013). Unfortunately, next to nothing is known about the neural correlates of eCFT that are frequently repeated relative to those that are simulated only infrequently. The current study employs a variation on a previously utilized paradigm (De Brigard et al., 2013b; Szpunar and Schacter, 2013; Szpunar et al., 2015) in an attempt to shed light on this issue. In this three-session study, participants came to the laboratory and provided specific negative, positive, and neutral autobiographical memories. A week later, they returned to generate eCFT based upon their reported episodic autobiographical memories. Specifically, participants were asked to generate upward (i.e., imagined better ways in which past negative events could have occurred), downward (i.e., imagined worse ways in which past positive events could have occurred), and neutral eCFT (i.e., alternative ways in which past neutral events could have occurred without changing the valence of the remembered experience). A day later participants came back for a final, two-part session. In the first part, participants were asked to repeatedly re-simulate half of the counterfactuals they generated. Immediately after, and while undergoing functional magnetic resonance imaging (fMRI), participants were presented with all the previously generated eCFT and were asked, for each of them, whether it had been previously re-simulated or not. As a result, this paradigm allows us to compare brain activity associated with eCFT that were recently repeated versus those that were only simulated once that day.

Two strategies for analyzing the resultant brain data were planned. First, a data-driven spatiotemporal analysis of event-related fMRI data using partial least squares (PLS; McIntosh et al., 2004) was employed to examine whether there were reliable differences in neural activity corresponding to frequently repeated versus non-repeated eCFT. Second, direct contrasts using non-rotated PLS analyses were also planned for each specific direction of eCFT—i.e., upward, downward and neutral—in order to explore differences in brain activity for each kind of eCFT as a function of frequent repetition. Given previous results on repetition-related neural activity in episodic future thinking—a related yet importantly different kind of episodic mental simulation (Schacter et al., 2015, 2017b)—we expected to find more engagement of core regions of the DN for eCFT simulated once relative to eCFT that were repeatedly simulated. This result would be consistent with a prior study, employing a repetition suppression paradigm (Grill-Spector et al., 2006), whereby core areas of DN exhibited neural adaptation as a function of repetition during episodic future thinking (Szpunar et al., 2014). Conversely, for the case of frequently repeated eCFT, we expected to find increased activation in precuneus, middle cingulate cortex, and pIPL, which are the brain areas composing the so-called “parietal memory network” (Gilmore et al., 2015): a functionally defined neural network that reliably shows increments in brain activity as a function of repetition and increased familiarity. Finally, the planned direct contrasts using non-rotated PLS analyses were more exploratory; while we expected to identify regions previously associated with each kind of eCFT (De Brigard et al., 2013a), there being no previous work exploring the effects of repetition on processing of counterfactual thinking, we had no prior hypothesis as to which regions would be more or less active as a function of repetition during downward, neutral or upward eCFT.

2. Materials and methods

2.1. Participants

Twenty-one healthy right-handed English-speaking adults with

normal or corrected-to-normal vision and no history of neurological or psychiatric conditions participated in the study. Since two participants failed to complete the second session, data from 19 participants ($M_{\text{age}} = 22.05$, $SD = 3.21$; 12 females) are included in the analyses. All participants provided written consent in accordance with the guidelines set by the Committee on the Use of Human Subjects in Research at Harvard University and received monetary compensation.

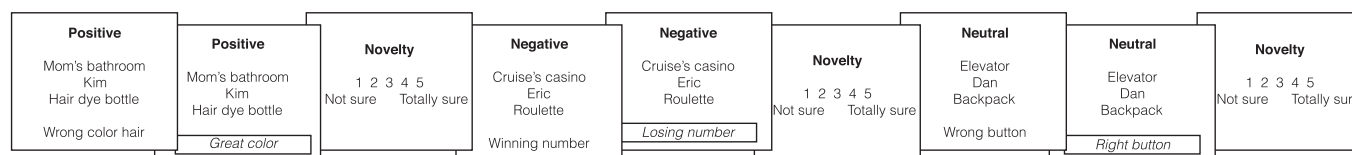
2.2. Pre-scan stimulus collection

In this session, participants were asked to provide 110 autobiographical memories of specific events from their personal past that occurred in the last 10 years. Participants were asked to recall discrete spatiotemporal events that involved either an action they performed or an event that occurred to them, where there was an immediate outcome. For each memory, participants were asked to provide a short description, a title, an approximate date and location, and one person and one object featured in the event. In addition, participants were asked to rate the emotion of each memory from (1) Negative to (5) Positive, with (3) being Neutral. Participants were asked to do their best to retrieve memories corresponding to all three emotions, and were encouraged to try to come up with as many negative, positive and neutral memories as possible. For retrieval support, participants were provided with a list of 100 common events and decisions culled from previous studies (De Brigard et al., 2013a, 2015). An experimenter would check on the participant every hour, verifying that they were providing memories for all emotions. When the participants reached 100 memories, the experimenter will tally the number of negative, neutral and positive memories to verify that there were around 30 memories of each emotion. If there were not enough memories corresponding to one of the emotions, participants would be asked to come up with memories specific to that emotion. The idea was to guarantee that, by the end of the first session, there would be at least 30 memories per emotion. To facilitate adherence to the instructions, participants were provided with examples of negative, positive and neutral specific autobiographical memories. This session took approximately 3 h.

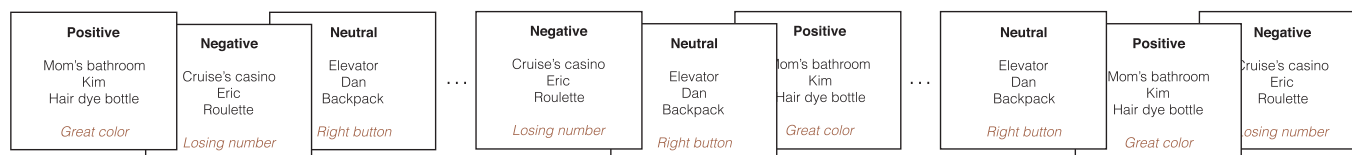
2.3. Counterfactual generation session

One week later, participants returned to the lab to generate eCFT based on the autobiographical memories collected the week before. Specifically, they were asked to generate 30 “upward” counterfactuals from negative memories (i.e., imagine *better* outcomes to events they previously rated as negatively valenced), 30 “downward” counterfactuals from positive memories (i.e., imagine *worse* outcomes to events they previously rated as positively valenced), and 30 neutral counterfactuals from neutral memories (i.e., imagine alternative outcomes that wouldn’t have modified the valence of the original memory). Trials were presented randomly on a computer screen, and in each, participants were shown a heading indicating whether the counterfactual they were asked to generate was upward (“positive”), downward (“negative”) or neutral (“neutral”). Below, four cues of the original memory were presented: the place, the person, the object and the short title they had provided for the original memory. Participants were required to remember this memory and to think of a relevant counterfactual. Once they had generated the counterfactual, they were asked to press a button that deleted the last cue on the screen (i.e., the title) revealing a text box for them to write a short title for the counterfactual just generated (Fig. 1). Participants were encouraged to do their best to imagine novel counterfactuals. At the end of each trial, participants were asked to rate how sure they were that it was the first time they generated such a counterfactual thought, with (1) being “Not sure” to (5) being “Completely sure.” Trials were presented using E-Prime 1.0 (Psychology Software Tools, Pittsburgh PA) on a Dell desktop computer, and participants used the keyboard to type their answers. This session took about 1 h.

Counterfactual generation session



Counterfactual re-simulation session



45 counterfactuals (15 positive, 15 negative, 15 neutral)

Same 45 counterfactuals, in new order, for the second time.

Same 45 counterfactuals, in new order, for a third time

Scanning session (sample run)

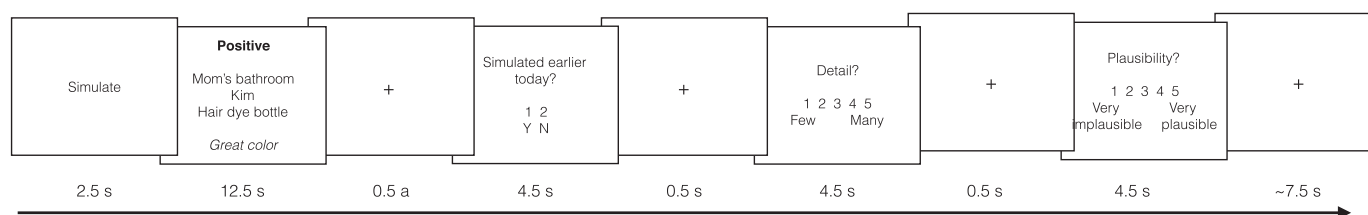


Fig. 1. Illustration of the experimental paradigm.

2.4. Counterfactual re-simulation session

A day later, participants returned for a final, two-part session. The first part occurred in a testing room right outside the MRI scanner. In this part, participants were asked to re-simulate half of the counterfactuals they generated the day before (i.e., 15 upward, 15 downward, and 15 neutral), three times each, in random order. Each trial was displayed with a similar structure as the day before, with a heading indicating the kind of counterfactual (“positive” for upward, “negative” for downward, and “neutral” for neutral), the place, person and object cues, and the new title they provided for each counterfactual during the initial counterfactual generation session. This new title was displayed in red font, for further emphasis and also to distinguish it from the title of the autobiographical memory the counterfactual simulation was derived from. Participants were given 12 s to re-simulate each counterfactual, and were told always to re-imagine the same alternative possibility, not a new one. This first part took approximately 30 min.

2.5. fMRI scanning session

For this last part, which occurred ten minutes after the re-simulation part, participants were placed inside the MRI scanner. Participants were told that they will see all the counterfactuals they had created, one by one, and that their task was to ascertain whether or not each counterfactual was repeatedly re-simulated previously outside of the scanner (i.e., during the counterfactual re-simulation part) or not. In addition, they were asked to rate the amount of detail and perceived plausibility of the simulated counterfactual event. Each of the 90 counterfactuals was presented once, in random order, and in equal number across 5 runs, so each run had a total of 6 trials per condition (upward, downward, neutral). Half of these trials included counterfactuals that were re-simulated three times just before (i.e., repeatedly simulated) while the other half were not (non-repeatedly simulated). Each trial started with a “simulate” instruction, followed by a screen showing the

emotional direction of the counterfactual (i.e., “Positive” for upward, “Negative” for downward, and “Neutral” for neutral), the three components shown during the counterfactual generation session (i.e., place, person, object), and the new counterfactual title. Participants were asked to re-simulate, one last time, the relevant counterfactual for 12.5 s. Next, participants were asked to indicate whether each counterfactual was simulated earlier that day, by answering “yes” or “no” to the displayed question “Imagined earlier today?”, which was shown for 4.5 s. Next, participants were asked to give ratings of detail (1 = Few; 5 = Many) and plausibility (1 = Very implausible; 5 = Very plausible). The order of these phenomenological ratings was counterbalanced across trials, and each one was displayed for 4.5 s. Trials were interleaved with fixation crosses randomly lasting 12.5, 15 or 17.5 s, to introduce jitter (Fig. 1).

fMRI data were acquired on a 3 T Siemens Magnetom TimTrio Scanner, equipped with a 12-channel head coil. Participants’ heads were held in place with cushions. An initial localizer was followed by a high-resolution magnetization-prepared rapid gradient echo sequence (MPRAGE; 176 × 1 mm sagittal slices, TE=1.64 ms, TR = 2530 ms, flip angle = 7.0 deg., voxel size = 1 × 1 × 1 mm). Functional scans were collected during 5 runs using a whole brain, 2 T* gradient-echo, EPI sequence (TR = 2.5 s, TE = 30 ms, FOV = 216 mm, flip angle = 80°). Interleaved slices (39 × 3 mm slices; .5 mm skip) were acquired parallel to the AC/PC plane, as identified by the T1 structural scan. Stimuli were projected in black letters onto a screen at the head of the bore. Participants saw the screen on a mirror placed on the head coil. E-Prime Software (psychology Software Tools, Inc., Pittsburgh, PA) was used for stimuli presentation and to collect behavioral responses, for which participants used a five-button MR compatible response box with their right hand.

2.6. fMRI data pre-processing and analyses

Functional MRI data were preprocessed using SPM8 (Wellcome

Table 1

A) Ratings of novelty, detail and plausibility for all repeated and non-repeated upward, downward and neutral eCFT. B) Ratings of detail and plausibility for only novel upward, downward and neutral repeated and non-repeated eCFT.

A) All data			
	Upward	Downward	Neutral
Novelty			
Repeated	3.16 (.84)	3.54 (.84)	3.53 (.81)
Non-Repeated	3.16 (.85)	3.54 (.78)	3.46 (.93)
Detail			
Repeated	2.13 (.63)	2.29 (.53)	1.70 (.76)
Non-Repeated	2.49 (.57)	2.30 (.43)	2.17 (.61)
Plausibility			
Repeated	2.10 (.72)	2.07 (.61)	2.69 (.53)
Non-Repeated	1.98 (.70)	2.21 (.69)	2.61 (.49)
B) Phenomenological ratings for only novel counterfactuals			
	Upward	Downward	Neutral
Detail			
Repeated	2.84 (.70)	2.43 (.73)	2.48 (.60)
Non-Repeated	2.20 (.90)	2.26 (.73)	2.09 (.72)
Plausibility			
Repeated	1.73 (1.07)	2.51 (.77)	2.65 (.68)
Non-Repeated	1.90 (.76)	1.98 (.70)	2.81 (.60)

Department of Cognitive Neurology, London, UK) implemented in MATLAB (Mathworks, Natick, MA). Images were realigned, co-registered, segmented, normalized to MNI template, spatially smoothed using a 6 mm full-width at half maximum isotropic Gaussian kernel, and re-sliced ($2 \times 2 \times 2$ mm voxels). To explore the two main questions of the current study, data were analyzed using spatiotemporal PLS (Krishnan et al., 2011; McIntosh et al., 1996, 2004). Spatiotemporal PLS is a multivariate functional neuroimaging analysis tool designed to identify whole brain patterns of activity that are correlated with tasks. PLS assesses the covariance between brain voxels (BOLD signal) and the experimental design to identify a limited number of orthogonal components (Latent Variables, LVs) that optimally relate the two. This data-driven approach is similar to independent component analysis in that it determines orthogonal whole brain patterns of activity. Unlike independent component analysis, however, the number of latent structures is constrained by the experimental conditions. And unlike standard univariate analyses that examine the activity of any single voxel independently, PLS detects brain-wide systems that co-vary with the experimental design. Activity at each time point, relative to trial onset, for each voxel is averaged across trials of a given condition and normalized to activity in the first TR of the trial, and the data matrix is then expressed as voxel-by-voxel deviation from the grand mean across the entire experiment. This matrix is then analyzed with singular value decomposition to derive the optimal effects in the data.

In the current study, we employed PLS analyses to event-related fMRI data and the results provide a set of brain regions wherein activity is reliably related to the task conditions at 6 post-stimulus time points (i.e., 6 TRs = 15 s) for each LV. Each brain voxel is given a singular value weight, known as a salience (akin to a component loading in principal components analysis), which is proportional to the covariance of activity with the task contrast at each time point on each LV. Multiplying the salience by the BOLD signal value in that voxel and summing the product across all voxels gives a “brain score”

for each participant for each time point on a given LV (like a component score in principal components analysis). These brain scores can be used to examine differences in brain activity across conditions, as greater activity in brain areas with positive (or negative) weights on a latent variable will yield positive (or negative) mean scores for a given condition over each time point. The significance of each LV as a whole is determined by permutation testing, using 500 permutations. In a

second, independent step, the reliability of the saliences for the brain voxels across subjects, characterizing each pattern identified by a LV, is determined by bootstrap resampling, using 100 iterations, to estimate the standard errors for each voxel. Clusters larger than 10 mm^3 comprising voxels with a ratio of the salience to the bootstrap standard error values (i.e., the “bootstrap ratio”; BSR) greater than 3.2 ($p < .00024$) were reported. The local maximum for each cluster was defined as the voxel with a BSR higher than any other voxel in a 2-cm cube centered on that voxel. Because PLS identifies whole brain patterns of activity in a single analytic step no correction for multiple comparisons is required.

To explore differences in brain activation between repeated versus non-repeated eCFT, a data-driven mean-centered PLS analysis was conducted to examine maximal effects across conditions. Next, to explore specific differences in brain activity due to frequency of simulation for each kind of counterfactual, a non-rotated analysis was conducted. This analysis explores the strength of the cross-block correlation between the data matrix and a set of a priori contrasts. In the current case, the design matrix included three contrasts, with each condition weighed against the other while zeroing the weights of the remaining ones: 1) frequently repeated (i.e., repeatedly simulated) versus infrequently repeated (i.e., non-repeatedly simulated) upward eCFT, 2) frequently repeated versus infrequently repeated downward eCFT, and 3) frequently repeated versus infrequently repeated neutral eCFT. Statistical significance is tested the same way as in the mean-centered analysis.

3. Results

3.1. Behavioral results

Participants' memory performance (Hit rate = .97) clearly indicated that they were able to follow instructions, and discriminate between frequently repeated and non-repeated counterfactual simulations. Behavioral results are displayed in Table 1. To explore differences in ratings of novelty as a function of simulation, a 2 (Repetition: repeated, non-repeated) $\times$ 3 (Direction: upward, downward, neutral) repeated measures ANOVA was conducted. This analysis revealed a main effect of Direction, $F(2, 14) = 10.933$, $p = .001$, partial $\eta^2 = .610$, with no interaction. Direct contrasts revealed that upward counterfactuals were less novel than both downward and neutral counterfactuals (smallest $p = .001$). Next, to explore differences in ratings of detail, a 2 (Repetition) $\times$ 3 (Direction) repeated measures ANOVA was conducted. This analysis revealed main effects of Repetition, $F(1, 18) = 9.694$, $p = .006$, partial $\eta^2 = .350$, and Direction, $F(2, 17) = 5.636$, $p = .007$, partial $\eta^2 = .238$, with a Repetition-by-Direction interaction, $F(2, 17) = 7.188$, $p = .002$, partial $\eta^2 = .285$. To clarify this interaction, Bonferroni-corrected direct contrasts for each Direction were conducted. This analysis revealed higher ratings of detail for non-repeated upward, $t(18) = 2.67$, $p = .016$, Cohen's $d = .59$, and neutral counterfactuals, $t(18) = 4.30$, $p < .001$, Cohen's $d = .68$, relative to repeated ones. However, there was no difference for downward counterfactuals, $t(18) = .09$, $p = .92$. Finally, to explore differences in ratings of plausibility, a 2 (Repetition) $\times$ 3 (Direction) repeated measures ANOVA was conducted. This analysis revealed a main effect of Direction, $F(1, 18) = 18.231$, $p < .001$, partial $\eta^2 = .682$, with no interaction. Direct contrasts revealed that neutral counterfactuals were considered more plausible than both upward and downward counterfactuals ($p < .001$).

Since the ratings of novelty indicated that not all the counterfactuals generated by the participants were novel, and given that some of the effects previously reported in the literature pertained only to novel counterfactuals (e.g., De Brigard et al., 2013b), we analyzed differences in detail and plausibility for only those counterfactuals that participants judged as being novel (i.e., novelty ratings of 4 and 5). To investigate differences in ratings of detail for novel counterfactuals, a 2

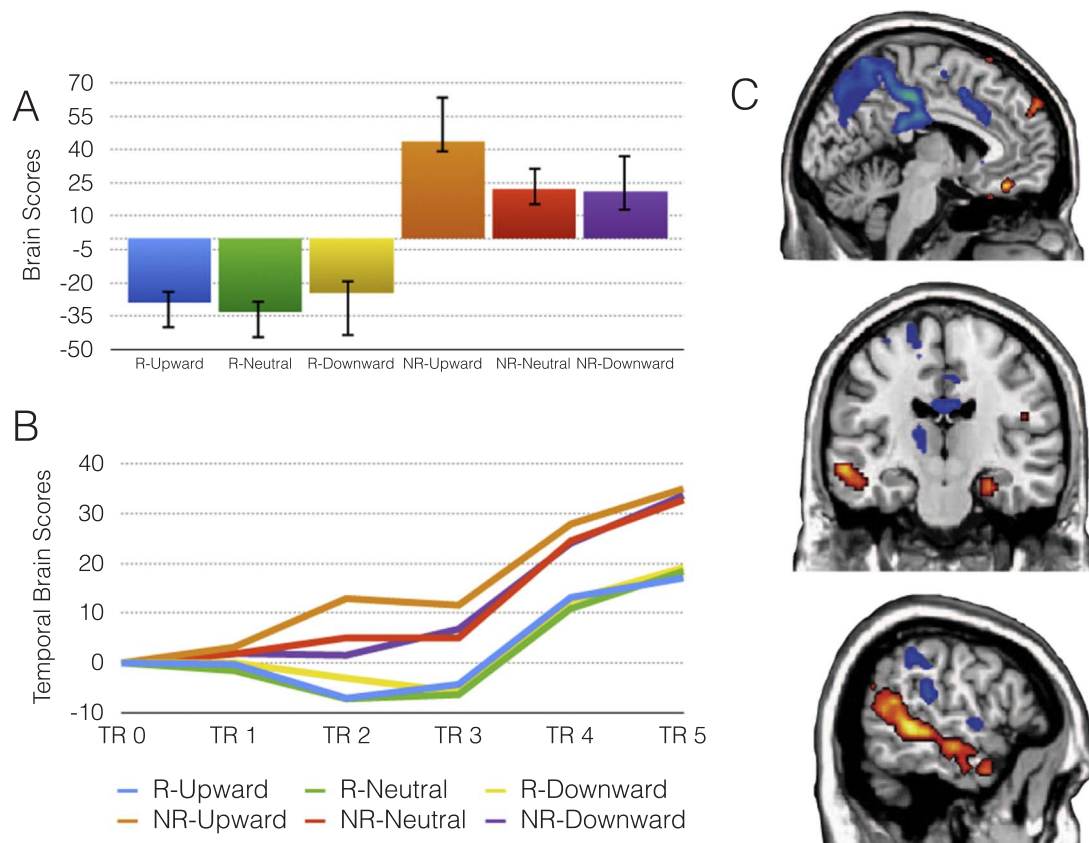


Fig. 2. Results from the mean-centered PLS analysis: LV 1. (A) Plot of brain scores with confidence intervals. (B) Plot of temporal brain scores indicating weighed average of activation across all voxels in all participants during the length of the counterfactual simulation. (C) Regions with negative saliences (cold colors) were engaged by frequently repeated eCFT while regions with positive saliences (hot colors) were engaged by non-repeated eCFT. All regions are shown at a threshold of $p < .001$.

(Repetition) $\times$ 3 (Direction) repeated-measures ANOVA was conducted. This analysis revealed an effect of Repetition, $F(1, 9) = 6.331$, $p = .033$, $\eta^2 = .413$, with no interaction, indicating that novel counterfactuals that were repeated received higher ratings of detail than those that were simulated only once. Finally, to investigate differences in ratings of plausibility for novel counterfactuals, a 2 (Repetition) $\times$ 3 (Direction) repeated-measures ANOVA was conducted. No effects were revealed.

3.2. Mean-centered PLS analysis

This analysis revealed one significant latent variable (LV1; $p < .001$) accounting for 42% of the crossblock co-variance. LV1 clearly differentiated neural patterns of brain activation for repeated versus non-repeated counterfactuals (Fig. 2A). During the window of maximal differentiation, TRs 3–4 (Fig. 2B), regions associated with non-repeated counterfactuals included bilateral middle temporal gyrus (BA 21), bilateral superior temporal gyrus (BA 38/39), left parahippocampal gyrus (BA 35), right hippocampus, right inferior occipital gyrus (BA 18), left fusiform gyrus (BA 37), and middle (BA 11) and superior frontal gyrus (BA 9). By contrast, regions associated with repeated counterfactuals included bilateral medial frontal gyrus (BA 6), bilateral cingulate gyrus (BA 31/32), bilateral middle frontal gyrus (BA 10), bilateral superior temporal gyrus (BA 22), bilateral insula (BA 13), right putamen, left thalamus, left inferior parietal lobule (BA 40), right cuneus (BA 18), and left globus pallidus (Fig. 2C; Table 2).

3.3. Non-rotated PLS analysis

This analysis revealed three significant latent variables, one for each contrast entered in the model. The first significant latent variable (LV 2;

$p < .008$), accounting for 40.56% of the cross-block covariance, clearly differentiated neural patterns of activation for Repeated versus Non-repeated upward counterfactuals (Fig. 3A). For Non-repeated > Repeated upward counterfactuals only one region was identified: right middle frontal gyrus (BA 11). By contrast, Repeated > Non-repeated upward counterfactuals identified a number of regions, including left cingulate gyrus (BA 31), bilateral middle frontal gyrus (BA 10), bilateral superior frontal gyrus (BA 10, BA 6), bilateral inferior parietal lobule (BA 40), left inferior occipital gyrus (BA 18), left globus pallidus, right putamen, precuneus (BA 7) and caudate (Fig. 3B; Table 3).

The second significant latent variable (LV 3; $p < .054$), accounting for 30.05% of the cross-block covariance, differentiated neural patterns of activation for Repeated versus Non-repeated neutral counterfactuals (Fig. 4A). For Non-repeated > Repeated neutral counterfactuals this analysis identified a number of regions, including bilateral middle temporal gyrus (BA 21), right precentral gyrus (BA 6), left inferior frontal gyrus (BA 47), right posterior cingulate gyrus (BA 23), right superior temporal gyrus (BA 38/39), and bilateral superior frontal gyrus (BA 9/8). By contrast, for Repeated > Non-repeated the identified regions included right precuneus (BA 7), left middle frontal gyrus (BA 6), left cingulate gyrus (BA 23), left middle frontal gyrus (BA 10), left anterior cingulate (BA 24), right precuneus (BA 7), left claustrum, and right cuneus (BA 19; Fig. 4B; Table 4).

Finally, the third significant latent variable (LV 4, $p < .046$), accounting for 29.39% of the cross-block covariance, differentiated neural patterns of activation for Repeated versus Non-repeated downward counterfactuals (Fig. 5A). For the Non-repeated > Repeated contrast, this analysis identified regions including left inferior frontal gyrus (BA 45), bilateral superior temporal gyrus (BA 38, BA 22), bilateral middle temporal gyrus (BA 21), left uncus (BA 28), and right middle frontal gyrus (BA 11). By contrast, Repeated > Non-repeated included left

Table 2

Regions associated with repeated and non-repeated eCFT (LV 1). All activations reported survived a threshold of $p < .00024$ (BSR = 3.2), with a cluster size $k = 10$. BA = approximate Brodmann area. L = Left; R = Right. *The bootstrap ratio (BSR) is the parameter estimate for that voxel over its standard error. It is proportional to a z score.

Region of activation	Hemisphere	BA	Voxels	MNI coordinates			BSR*
				x	y	z	
Non-repeated > Repeated							
Middle temporal gyrus	R - L	21	679	−60	−39	0	6.883
Superior temporal gyrus	R - L	38/39	22	45	15	−36	6.339
Parahippocampal gyrus	L	35	15	−21	−9	−27	4.864
Hippocampus	R		12	27	−21	−21	4.424
Inferior occipital gyrus	R	18	12	33	−81	−9	5.121
Fusiform gyrus	R	37	11	42	−57	−15	4.365
Middle Frontal gyrus	R - L	11	15	42	39	−21	4.168
Superior frontal gyrus	L	9	31	−12	57	42	3.877
Repeated > Non-repeated							
Medial Frontal Gyrus	L - R	6	96	−15	6	60	−8.859
Cingulate gyrus	L - R	31/32	1699	−9	−30	42	−8.013
Middle frontal gyrus	R - L	10	246	33	39	27	−6.165
Superior temporal gyrus	R - L	22	232	63	−39	21	−6.139
Insula	R - L	13	55	39	12	12	−5.428
Putamen	R		15	21	0	9	−5.268
Thalamus	L		51	−21	−27	9	−4.928
Inferior parietal lobule	L	40	58	−51	−36	36	−4.249
Cuneus	R	18	23	15	−90	21	−4.328
Globus pallidus	L		13	−15	−3	−6	−4.195

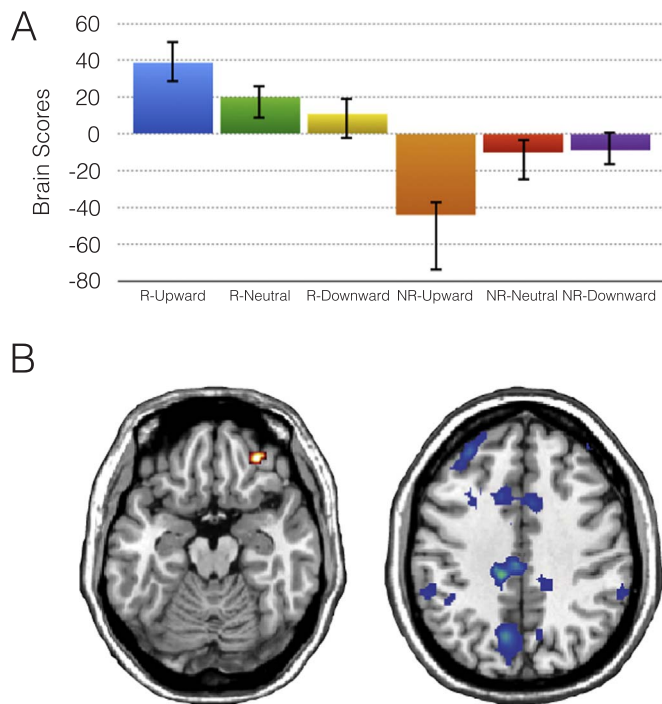


Fig. 3. Results for LV 2 for the contrast Repeated versus Non-Repeated upward eCFT. (A) Plot of brain scores from the non-rotated analysis with confidence intervals (B) Regions in hot colors (positive saliences) were preferentially associated with Non-Repeated upward eCFT, whereas regions in cold colors (negative saliences) were preferentially associated with Repeated upward eCFT. All regions are shown at a threshold of $p < .001$.

middle frontal gyrus (BA 10), left hippocampus (BA 10), right medial frontal gyrus (BA 9), right insula (BA 13), right inferior frontal gyrus (BA 45), right cingulate gyrus (BA 31), and right supramarginal/inferior parietal lobule (BA 40; Fig. 5B, Table 5).

4. Discussion

The current study sought to investigate differences in brain activity associated with frequently repeated versus non-repeated eCFT. A data driven approach was employed to identify patterns of brain activation

Table 3

Regions associated with repeated versus non-repeated upward eCFT (LV 2). All activations reported survived a threshold of $p < .00024$ (BSR = 3.2), with a cluster size $k = 10$. BA = approximate Brodmann area. L = Left; R = Right. *The bootstrap ratio (BSR) is the parameter estimate for that voxel over its standard error. It is proportional to a z score.

Region of activation	Hemisphere	BA	Voxels	MNI coordinates			BSR*
				x	y	z	
Non-repeated > Repeated							
Middle frontal gyrus	R	11	10	24	30	−18	−3.855
Repeated > Non-repeated							
Cingulate gyrus	L	31	1332	−12	−30	39	9.129
Middle frontal gyrus	L - R	8	303	−36	36	42	7.788
Superior frontal gyrus	R	10	196	30	57	27	6.971
Superior frontal gyrus	L	6	400	−18	6	60	5.748
Inferior parietal lobule	R - L	40	123	60	−39	33	5.281
Inferior occipital gyrus	L	18	14	−36	−90	−18	5.236
Lateral globus pallidus	L		184	−18	−3	−6	5.210
Cerebellum	R		17	48	−54	−39	4.761
Middle frontal gyrus	L	11	84	−33	45	−12	4.649
Putamen	R		11	18	0	9	4.434
Precuneus	R	7	20	12	−63	36	4.400
Caudate	R		13	12	9	9	3.818

associated with eCFT that were simulated repeatedly immediately prior to undergoing fMRI versus eCFT that were only simulated once in the scanner. As expected, and consistent with previous neuroimaging studies on eCFT (e.g., van Hoeck et al., 2013; De Brigard et al., 2013b, 2015), a significant latent variable (LV1) revealed by the mean-centered PLS analysis identified a number of DN regions associated with non-repeated relative to repeated eCFT. Specifically, large clusters in the middle and superior temporal cortex, as well as the parahippocampal and hippocampal regions, were preferentially associated with non-repeated relative to repeated eCFT. We interpret these results in the context of a recent influential proposal put forth by Andrews-Hanna et al. (2014). According to this proposal, the DN is composed of

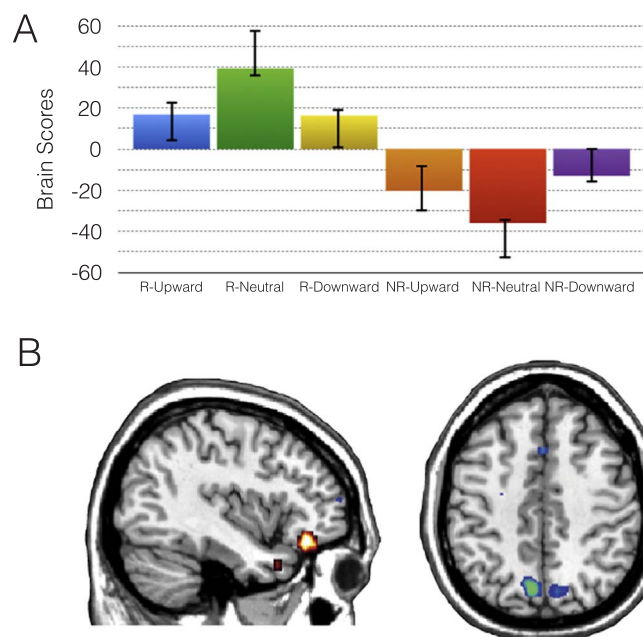


Fig. 4. Results for LV 3 for the contrast Repeated versus Non-Repeated neutral eCFT. (A) Plot of brain scores from the non-rotated analysis with confidence intervals (B) Regions in hot colors (positive saliences) were preferentially associated with Non-Repeated neutral eCFT, whereas regions in cold colors (negative saliences) were preferentially associated with Repeated neutral eCFT. All regions are shown at a threshold of $p < .001$.

three interacting sub-systems: a *dorsal-medial* sub-system, comprising dMPFC, TPJ, LTC and temporal pole, a *core* sub-system, comprising pCC and aMPFC, and a *medial-temporal* sub-system, comprising the hippocampus and parahippocampal formation, retrosplenial cortex, pIPL, and vMPFC. Consistent with previous studies using repetition suppression during episodic simulation (Szpunar et al., 2014), we take the results revealed by the Non-repeated > Repeated contrast in LV1 as identifying regions that show more neural adaptation as a result of repetition (Grill-Spector et al., 2006). Accordingly, the current data would suggest that repeated simulation of eCFT reduces the engagement of the core-sub-system of the DN relative to the medial-temporal and the dorsal-medial subsystem, which are likely to be required for the generation and maintenance of both the social and contextual components of a mental simulation online.

The pattern of brain activity revealed by LV1 as associated with the

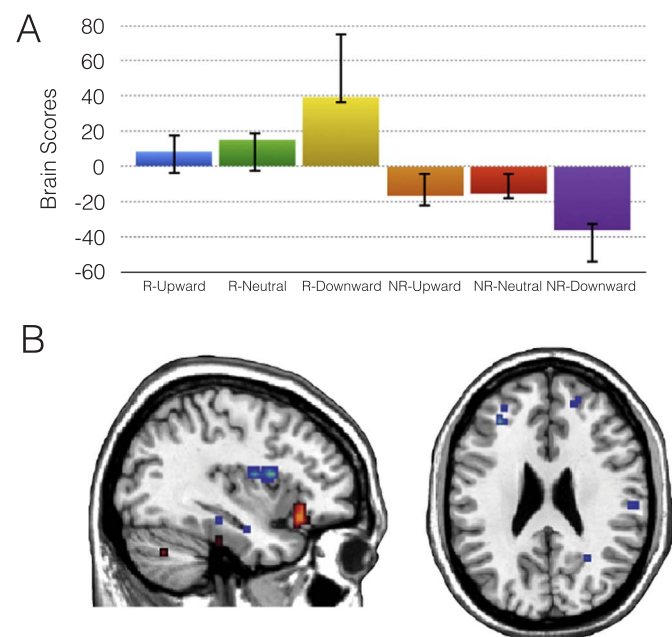


Fig. 5. Results for LV 4 for the contrast Repeated versus Non-Repeated downward eCFT. (A) Plot of brain scores from the non-rotated analysis with confidence intervals (B) Regions in hot colors (positive saliences) were preferentially associated with Non-Repeated downward eCFT, whereas regions in cold colors (negative saliences) were preferentially associated with Repeated downward eCFT. All regions are shown at a threshold of $p < .001$.

Repeated > Non-repeated contrast supports this interpretation, as large clusters in the pCC and the aMPFC were identified. These two regions constitute the core sub-system of the DN (Andrews-Hanna et al., 2014). However, this contrast also revealed a pattern of activation consistent with the so-called *parietal memory network* (PMN): a functionally coherent set of brain regions, different from the DN, that appears to be preferentially associated with increased repetition and familiarity (Gilmore et al., 2015). A large cluster centered around what Gilmore and collaborators identify as the middle cingulate cortex was preferentially associated with repeated eCFT, as well as a cluster of activation toward posterior IPL. Both of these regions belong to the PMN. The one difference is perhaps the fact that the occipital activation identified in our findings is more posterior than the one associated with the PMN, as the peak of the occipital cluster revealed by LV1 fell in the

Table 4

Regions associated with repeated versus non-repeated neutral eCFT (LV 3). All activations reported survived a threshold of $p < .00024$ (BSR = 3.2), with a cluster size $k = 10$. BA = approximate Brodmann area. L = Left; R = Right. *The bootstrap ratio (BSR) is the parameter estimate for that voxel over its standard error. It is proportional to a z score.

Region of activation	Hemisphere	BA	Voxels	MNI coordinates			BSR*
				x	y	z	
Non-repeated > Repeated							
Middle temporal gyrus	L - R	21	251	− 57	− 30	− 3	− 7.354
Precentral gyrus	R	6	30	51	− 9	60	− 7.237
Inferior frontal gyrus	L	47	101	− 45	33	− 15	− 5.758
Posterior cingulate	R	23	22	3	− 57	21	− 5.060
Superior temporal gyrus	R	39/38	51	51	− 57	27	− 4.720
Superior frontal gyrus	L - R	9/8	36	− 9	54	42	− 4.215
Repeated > Non-repeated							
Precuneus	R	7	292	6	− 78	45	6.445
Middle frontal gyrus	L	6	15	− 27	− 12	42	5.684
Cingulate gyrus	L	23	45	− 6	− 27	24	5.667
Middle frontal gyrus	L	10	58	− 39	57	15	5.426
Anterior cingulate	L	24	19	0	27	21	4.715
Cerebellum	L		19	− 36	− 48	− 45	4.712
Precuneus	R	7	49	3	− 60	66	4.465
Clastrum	L		12	− 27	− 3	18	4.456
Cuneus	R	19	17	15	− 90	24	4.041

Table 5

Regions associated with repeated versus non-repeated downward eCFT (LV 4). All activations reported survived a threshold of $p < .00024$ (BSR = 3.2), with a cluster size $k = 10$. BA = approximate Brodmann area. L = Left; R = Right. *The bootstrap ratio (BSR) is the parameter estimate for that voxel over its standard error. It is proportional to a z score.

Region of activation	Hemisphere	BA	Voxels	MNI coordinates			BSR*
				x	y	z	
Non-repeated > Repeated							
Inferior frontal gyrus	L	45	304	−51	21	6	−6.753
Superior temporal gyrus	R	38	77	48	12	−27	−5.884
Middle temporal gyrus	L - R	21	58	−60	−18	−12	−4.910
Superior temporal gyrus	L	22	112	−60	−51	15	−4.445
Uncus	L	28	14	−30	3	−27	−4.015
Middle frontal gyrus	R	11	17	36	39	−21	−3.979
Repeated > Non-repeated							
Middle frontal gyrus	L	10	110	−36	39	24	7.486
Hippocampus	L		10	−36	−27	−15	5.502
Medial frontal gyrus	R	9	11	18	24	36	5.497
Insula	R	13	33	36	15	9	5.230
Inferior frontal gyrus	R	45	19	30	30	12	5.096
Cingulate gyrus	R	31	18	6	−30	42	4.093
Supramarginal/ IPL	R	40	13	54	−48	36	3.952

cuneus rather than the precuneus. Nevertheless, we believe that these findings highlight the need of further research to understand the interaction between DN and PMN during repeated mental simulations, as both networks seem to be engaged during these kinds of cognitive processes.

The findings of the mean-centered analysis should also be discussed in the context of similar findings in the field of episodic future thinking. For instance, in a recent study, *van Mulukom et al. (2013)* explored neural differences as a function of repetition in episodic future thinking (i.e., one, two, or three simulations of a future event), and identified a linear increase in neural activity in right dMPFC, IPL and cingulate cortex. More recently, *Szpunar et al. (2015)* also examined brain activity associated with repetition of emotional episodic future thoughts, and identified a set of regions closely resembling those revealed by our study, including IPL, right MFG, aCC and insula. Finally, using a different paradigm that also explored brain activity as a function of repeated simulation, *Szpunar, St Jacques and colleagues (2014)* identified a cluster in the right cuneus/precuneus region closely resembling that identified by the current analysis. These commonalities suggest that there may be shared mechanisms involved in frequently repeated episodic simulations, regardless of whether they are oriented toward a possible future, as in episodic future thinking, or toward a possible past, as in eCFT (*De Brigard and Gessell, 2016; Schacter et al., 2015*).

To a certain extent, the commonalities between future and past thinking also extend to regions associated with non-repeated relative to repeated simulations. In the aforementioned study by *van Mulukom et al. (2013)*, it was reported that both the hippocampus and surrounding parahippocampal gyrus showed increased activity for non-repeated relative to repeated episodic future thoughts. *Szpunar et al. (2014)* also reported similar findings for the hippocampus, as it was preferentially associated with novel rather than previously simulated episodic future thoughts. In the current study, we see a similar pattern of increased activation for the MTL, particularly left parahippocampal

gyrus and right hippocampus. Consistent with prior reports on episodic future thinking, we interpret these findings as highlighting the role of the hippocampus and the hippocampal formation in the construction of the mental simulation (for a recent review, see *Schacter et al., 2017a*). This interpretation is also consistent with the role of the medial-temporal sub-system of the DN mentioned above (*Andrews-Hanna et al., 2014*).

Previous studies on repeated eCFT have shown that while ratings of detail increase as a function of repetition, perceived plausibility of the counterfactual event decreases (*De Brigard et al., 2013b; Stanley et al., 2017*). These effects, however, have only been reported for novel eCFT—that is, eCFT that participants are certain of not having imagined before. In the current study, we included ratings of detail and plausibility in the hopes of exploring the role these factors may play in the underlying differences in brain activity as a function of frequent repetition. Unfortunately, although we encouraged participants to generate only novel eCFT, the ratings collected during the second session indicated that only a small proportion of those eCFT were surely novel. When we compared repeated versus non-repeated novel eCFT, repetition did show an increase in detail, as previously reported (e.g., *De Brigard et al., 2013b; Stanley et al., 2017*), but the difference in plausibility failed to reach significance. Surprisingly, however, when all eCFT (i.e., both novel and non-novel) were included in the model, ratings of detail decreased, rather than increased, as a function of repetition for upward and neutral counterfactuals. What can explain these seemingly inconsistent results? One possibility is that regret-producing upward eCFT that have been rehearsed in the past—i.e., non-novel eCFT—simply succumb to a fading affect bias: the tendency for negative experiences to be forgotten more quickly than positive ones (*Walker et al., 2003; Walker and Skowronski, 2009*). As such, when compared with novel eCFT freshly created in the lab, they are comparatively less detailed. This further suggests that changes in perceived detail for eCFT may follow an inverse U-shape, so that they tend to increase with frequent repetition shortly after being generated—just as it occurs with other kinds of imaginations (*Koehler, 1991*)—but then their perceived details start to fade over time. It is unclear, however, if this explanation also applies to neutral eCFT, as it remains to be determined whether the fading affect bias affects only negative valenced memories, or whether it may also affect neutral memories that have been mentally modified. Given scant data on repeated simulations of eCFT, which so far has only employed novel ones, this conjecture is merely speculative, and further research is needed to clarify the role of repetition and temporal retention in eCFT. Moreover, given previously reported differences in hippocampal activity due to detail and perceived plausibility in both episodic future (*Addis and Schacter, 2008; Weiler et al., 2010*) and counterfactual thinking (*De Brigard et al., 2013b; Parikh et al., in progress*), further studies should be conducted to clarify the role of these factors in frequently repeated eCFT.

With regard to the specific contrasts, the non-rotated analyses identified three significant latent variables corresponding to each independent contrast in the model. For upward eCFT, LV2 identified only a small cluster in vMPFC associated with increased activity for non-repeated relative to repeated eCFT. This cluster of activation is consistent with the vMPFC node of the medial-temporal subsystem of the DN (*Andrews-Hanna et al., 2014*), and thus suggestive of the engagement of such a sub-system in the generation and online maintenance of upward eCFT. By contrast, LV2 identified large clusters of activation preferentially associated with repeated relative to non-repeated upward eCFT. As with the results from LV1, we see recruitment of the PMN for repeated relative to non-repeated upward eCFT, with large clusters in mid-cingulate cortex, pIPL and precuneus. This finding again reinforces the suggestion that PMN, which is sensitive to increases in repetition and familiarity, is recruited by repeated simulation of upward eCFT. The commonalities between the areas revealed for repeated eCFT in general and upward eCFT in particular extend beyond the engagement of the PMN. For instance, in both cases we identified increased

activation of dMPFC and SFG, toward the rostral-polar cortex (BA 10). These regions are consistently reported in the counterfactual literature and appear to be associated with regret producing counterfactual tasks. Whether the engagement of these frontal regions during eCFT correspond to the positive imagined alternative or the negative regretful feeling associated with its not having occurred is hard to tell from the present data. Further studies isolating these two factors should be able to clarify this issue. Finally, it is worth noting an interesting difference between the findings from LV1 and LV2: the size of the cluster of activation in the globus pallidus associated with repeated upward eCFT in particular, relative to repeated eCFT in general, was significantly larger. Medial to the putamen, and an integral part of the basal ganglia, the globus pallidus has been associated with fictive learning, a counterfactual generating task where a reward signal is propagated, not as a result of what the individual received, but rather as a response for what she could have gotten (Kishida et al., 2016). It is possible that this increased activity in the globus pallidus as a result of repeatedly simulating unattained better outcomes to past events reflects an increase in the reward signal that supports fictive learning.

The second latent variable of the non-rotated analysis, LV3, corresponded to the contrast between repeated and non-repeated *neutral* eCFT. Here, the pattern of activity associated with non-repeated *neutral* eCFT closely paralleled that identified by LV1 as common for all non-repeated eCFT. First, the contrast neutral Non-repeated > Repeated identified a large bilateral cluster in MTL and IFG, which we interpret as reflecting the involvement of the medial-temporal subsystem of the DN in the construction and maintenance of mental simulations (Andrews-Hanna et al., 2014). Likewise, as with the case of LV1, non-repeated neutral eCFT preferentially recruited LTC and the temporal pole, further suggesting the engagement of the dorsal-medial subsystem of the DN. Interestingly, however, a large cluster of inferior frontal activation, too lateral to be considered part of either the DN or the PMN, was associated with non-repeated relative to repeated neutral eCFT. It is possible that this cluster reflects some attentional or control process specific to this task. It is also worth noting, once again, that the pattern of activity revealed by this contrast is remarkably consistent with those reported by Szpunar et al. (2014), who also identified dlPFC, SFG, pCC and STG during novel relative to repeated episodic future thoughts. As suggested before, these commonalities suggest shared mechanisms in episodic hypothetical simulation (De Brigard, 2014) which may be indifferent to whether the mental simulation refers to a possible future or a possible counterfactual event (De Brigard and Gessell, 2016).

The third and final significant latent variable identified by the non-rotated analysis, LV4, corresponded to the contrast between repeated and non-repeated downward counterfactuals. We see again a similar pattern of activation for downward non-repeated eCFT, whereby regions of the medial-temporal and the dorsal-medial sub-systems of the DN are preferentially recruited, whereas regions of the core sub-system of the DN are associated with repeated rather than non-repeated downward eCFT. Paralleling the results of LV1, repeated downward eCFT also seem to recruit the PMN (Gilmore et al., 2015), as activity in the dIPL and middle cingulate cortex was identified for the Repeated > Non-Repeated contrast. Insula activation was also evident for repeated downward eCFT, although lateralized to the right hemisphere, in contrast to the bilateral activation of insula identified for repeated eCFT, regardless of specific direction. Given the multi-functionality of insula activation (e.g., Menon and Uddin, 2010), it is difficult to tell, from our current data alone, what role it may have during repeated eCFT. Further studies would be needed to settle this issue. Finally, it is worth noting the engagement of left hippocampus during repeated downward eCFT. Contrary to van Mulukom et al. (2013), who found reductions in hippocampal activity as a function of repetition during episodic future thinking, LV 4 showed the opposite pattern for repeated downward eCFT. The hippocampal region identified by LV4, however, is more dorsal than that reported by van Mulukom and colleagues.

Clarifying the role of the hippocampus during repeated simulation of episodic counterfactual and future thinking is a fruitful avenue for future research.

The current study explored neural differences between frequently repeated and non-repeated eCFT, regardless of the direction of the counterfactual modification, as well as differences specific to upward, downward and neutral eCFT as a function of repetition. Our results consistently identified regions of the medial-temporal and dorsal-lateral subsystems of the DN as being preferentially recruited for non-repeated relative to repeated eCFT, whereas regions of the core-subsystem of the DN were preferentially associated for repeated relative to non-repeated eCFT. In addition, the PMN, which is sensitive to increases in familiarity and repetition of stimuli, was also associated with repeated relative to non-repeated eCFT. The current study mirrored a paradigm previously employed with episodic future thinking (Szpunar et al., 2015), a closely related variant of episodic simulation (Schacter et al., 2015). This paradigm, in turn, was built upon similar experimental designs, aimed at exploring brain activity preferentially associated with frequently repeated information during mental simulation (e.g., Szpunar et al., 2014; see also, Baron et al., 2016; Schacter et al., 2007). Following this line of research, we have interpreted our results as suggesting that the repetition suppression pattern (i.e., non-repeated > repeated) is reflected in regions that serve to represent key content associated with counterfactual simulations and that increasingly less engagement is required within these regions in order to re-activate that content across repeated simulations, whereas the enhanced pattern (i.e., repeated > non-repeated) reflects either a familiarity or recognition memory signal. Given the similarities between the results of the current studies, and those employing episodic future simulations, we suspect this interpretation is on the right track. Nevertheless, it is critical to acknowledge that the current experimental design does not allow to rule out some alternative interpretations, such as the possibility that the neural dissimilarities are largely due to differences in the strength of the recognition signal, which may be greater for repeated relative to non-repeated trials. Further studies would be needed to fully understand the differences between content and process related activity in eCFT as a function of repetition.

To the best of our knowledge, the current study constitutes the first exploration of the neural underpinnings involved in processing repetitive episodic counterfactual simulation (for related findings, see St Jacques et al., 2017) and, as such, we hope it can contribute to the nascent research in the phenomenon of repetitive counterfactual rumination, one of the four main sub-classes of pathological ruminative thinking—the other three being problem-focused, repetitive, and anticipatory thoughts (Brinker and Dozois, 2009; Tanner et al., 2013). Many studies have shown that excessive eCFT—and usually, but not exclusively, upward counterfactuals (Roese and Olson, 1995; Markman et al., 1995)—are strongly associated with a number of psychological disorders, including anxiety, depression (Roese et al., 2009), and post-traumatic stress disorder (for a review, see Watkins, 2008). An important caveat of the current study is that it explores laboratory-induced repetition, which may or may not differ in important respects from the naturally occurring frequent repetition of eCFT associated with regret and rumination (Summerville and Roese, 2008). Our hope, however, is that our results can provide a first step toward fully understanding the neural underpinnings of repetitive counterfactual thinking. Unveiling the neural and cognitive mechanisms underlying this cognitive process may constitute a critical step toward developing strategies for potential clinical and therapeutic interventions (De Brigard and Hanna, 2015).

Acknowledgments

This work was supported by grant NIMH MH060941 for DLS.

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