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Original Article

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Neural basis of attentional deployment in affective forecasting of hypothetical medication outcome trade-offs

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Predicting the emotional impact of future events, known as affective forecasting, is central to decision-making. When outcomes are emotionally bivalent (i.e. contain mixed-valence elements), such as medical treatments involving both remission and adverse side effects, forecasts are often inaccurate. We used functional magnetic resonance imaging (fMRI) to investigate the neural basis of affective forecasting in medical treatment trade-offs and how it is shaped by attentional deployment, an emotion regulation strategy that directs attention toward or away from aspects of an outcome. Participants imagined undergoing a treatment providing pain relief but causing side effects, and forecasted their emotions while focusing on remission or side effects. Univariate analyses showed that attentional deployment modulated neural activity during forecasting: the side-effect-focus condition recruited the insula and frontal pole, whereas remission-focus trials recruited the superior frontal gyrus and frontal pole. Multivariate analyses revealed a broad and distributed network that differentially represented positive and negative forecasting. We conclude that attentional deployment modulates which brain regions are recruited for affective forecasting. We identify the frontal pole as a hub for sustaining emotion-regulation goals during prospective thought. Together, these findings advance models of affective forecasting and highlight potential mechanisms, such as attentional deployment, which may bias emotional predictions in medical trade-off scenarios.

Keywords **affective forecasting, attentional deployment, emotion regulation, fMRI, medical decision-making**

Introduction

Affective forecasting, the ability to predict our future emotional reactions to events, is central to planning and decision-making (Mellers and McGraw 2001; Baumgartner et al. 2008; Pezzulo and Rigoli 2011). Yet, research shows that humans are not always accurate forecasters, particularly when outcomes evoke bivalent or conflicting emotions (Gilbert and Wilson 2009). For example, a medical treatment might promise remission from illness while also carrying the risk of unpleasant side effects. Despite these inaccuracies, affective forecasting has both instrumental and experiential benefits. Some instrumental benefits of affective forecasting include helping guide decision-making by signaling the subjective value of an outcome (Sonnemans and Frijda 1995; Carlson et al. 2023) and providing motivation to achieve or avoid an outcome (Mellers and McGraw 2001; Morewedge and Buechel 2013; Carlson et al. 2023). Experiential benefits include, for example, later satisfaction with a choice made based on anticipated emotions (Carlson et al. 2023).

Neuroimaging studies have identified several brain regions that show increased activity for emotion anticipation, including the ventromedial prefrontal cortex (vmPFC) (Sharot et al. 2007; D'Argembeau et al. 2008; Bray et al. 2010), amygdala (Sharot et al. 2007), and insula (Knutson and Greer 2008; Greenberg et al. 2015). In studies using univalent positive stimuli, activity is also frequently observed in the ventral striatum (Knutson and Greer 2008; Greenberg et al. 2015) and the posterior cingulate cortex (PCC) (Sharot et al. 2007; D'Argembeau et al. 2008), regions previously associated with reward processing and

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self-referential thought, respectively. These studies, however, almost exclusively used univalent stimuli, which typically elicit only one emotional valence.

The present study aimed to advance previous work by examining affective forecasting for events that elicit mixed emotions, such as treatments that both alleviate symptoms and are associated with adverse side effects. We focused on attentional deployment, which refers to an emotion regulation strategy in which people direct their attention toward or away from particular aspects of a situation to influence their emotional response (Gross 1998; Mauss et al. 2007). For instance, a patient anticipating treatment might focus on the anticipated relief from their condition rather than on the anticipated distress of experiencing adverse treatment effects.

Inaccurate forecasts can have important consequences for decision-making, especially in medical contexts, where trade-offs are often unavoidable. Consistent with this, a meta-analysis of affective forecasting in medical decisions has shown that patients tend to overestimate quality of life when anticipating health improvements and underestimate it when anticipating health deterioration (Bosch et al. 2021). Such patterns suggest that patients may preferentially attend to anticipated feelings of benefit (e.g. relief from symptoms) or harm (e.g. side effects), depending on the expected health outcome. In medical decision-making, affect can function as a "spotlight," drawing attentional resources toward emotionally salient aspects of the available information while reducing attention to less affectively charged details. Such affect-driven selective attention can bias the perceived importance of decision attributes, e.g. by amplifying attention to potential benefits when in a positive affective state, or to potential risks when in a negative affective state (Peters et al. 2006). These modulations can influence how trade-offs are evaluated and ultimately shape choice preferences. While we do not investigate the effect of anticipatory emotions (i.e. emotions felt in the present in response to a future event as opposed to anticipated emotions which are predicted emotions) on attention in this study, such models highlight that the deliberate shifting of attention toward otherwise potentially neglected aspects of a decision could change one's emotional reactions and thus influence decisional processes.

To the best of our knowledge, there is only one prior study, which examined the neural basis of attentional deployment in affective forecasting with bivalent stimuli. Authors paired monetary gains (/losses) with aversive (/pleasant) sounds and instructed participants to focus on either the beneficial or adverse component (Kruschwitz et al. 2018). They found that focusing on the beneficial component triggered activations in the PCC, ventral striatum, and vmPFC, whereas focusing on the adverse one was linked to increased activity in the insula. These findings suggest that directing attention to different components of a mixed-valence outcome engages distinct neural systems.

Building on this prior research, we investigated these processes using more ecologically valid medical decision-making scenarios. We used a cue-exposure paradigm in which participants imagined undergoing a hypothetical treatment while focusing either on the remission-related benefits (*remission-focus condition*) or adverse side-effect risks (*side-effect-focus condition*). We first conducted a behavioral validation of the cue-exposure paradigm to ensure participants could project themselves into these scenarios and effectively shift their focus before implementing the paradigm for functional magnetic resonance imaging (fMRI) scanning.

We predicted that affective forecasting for these medical trade-offs would involve regions relevant to affective future thinking, including vmPFC, (para) hippocampus, medial parietal regions, and lateral temporal cortex (D'Argembeau et al. 2008), as well as emotion-related regions, such as the amygdala (Holmes and Mathews 2010). Consistent with previous work on attentional deployment (Kruschwitz et al. 2018; Liu et al. 2020; Li et al. 2022), we expected side-effect-focus trials to show greater activity in the insula, and remission-focus trials to show greater activity in the ventral striatum and superior/medial frontal gyri.

In addition to neural measures, participants rated each stimulus for familiarity, anticipated distress, and vividness of emotion projection. We expected unfamiliar side effects to be associated with greater hippocampal engagement (Sasse et al. 2015). Although we did not have specific hypotheses for affect or vividness modulation, previous studies linked the ventral striatum to anticipated relief and insula activity to anticipated distress (Kruschwitz et al. 2018). Vividness is particularly relevant, as more vivid prospection is associated with greater affective arousal (Van Boven and Ashworth 2007), influences the effectiveness of behavioral intentions and episodic future thinking on intertemporal choice (Mazzocco et al. 2019; Rösch et al. 2022), and modulates neural activity triggered by mental projection (St-Laurent et al. 2015; Lee et al. 2021; Aupperle et al. 2024).

In summary, this study investigated how attentional deployment modulates the neural mechanisms of affective forecasting in realistic medical trade-off scenarios. Understanding these mechanisms may help inform strategies to improve decision support in complex medical contexts.

Materials and methods

Behavioral validation

Stimulus selection

First, we conducted an anonymous online survey ($n = 181$; duration ~5 min) in which participants rated the perceived severity of 30 potential side effects of common analgesics on a 5-point scale (1 = not at all severe, 5 = extremely severe). We selected the nine highest- and nine lowest-rated items (total = 18) for use in the experimental task.

Participants

A separate sample of 52 participants was recruited at the Belval campus of the University of Luxembourg (M age = 26.12, $SD = 4.86$, 35 Female, 16 Male, 1 undisclosed). Inclusion criteria were: age ≥18 yr, normal to corrected-to-normal vision, and no current physical or mental disorders. Inclusion criteria were included in recruitment materials and checked on the day of data collection through verbal and written confirmation. Data collection took place in the CLIPS laboratory at the University of Luxembourg. The study was approved by the institutional ethics board (ERP 23–090 AffMed).

Experimental task and procedure

Participants were instructed to imagine the following scenario: "Imagine that you have been suffering from chronic pain for the last two years. Every day, you feel pain throughout your body. This chronic pain has had a considerable impact on your life. At times, you are unable to work, eat properly, take part in physical activity, or enjoy life. Without treatment, your condition will never improve."

Participants were then asked to imagine as vividly as possible what their life would be like under these conditions. Following this, they were introduced to the cue-exposure paradigm.

They were informed that there was a medication that could cure their chronic pain, but also entailed a side effect. The cue-exposure

paradigm featured two conditions: (i) side-effect-focus, and (ii) remission-focus. In the side-effect condition, participants were instructed to project as vividly as possible their emotional state if experiencing the side effect. In the remission condition, they were asked to project as vividly as possible their emotional state if experiencing remission from chronic pain despite the side effect. Each condition consisted of three blocks with six trials each. The 18 side effects (dry mouth, flatulence, itching, chills, loss of appetite, fatigue, constipation, irritability, weakness, memory loss, hallucinations, depression, speech disorder, shortness of breath, anxiety, hair loss, blurry sight, insomnia) appeared in both conditions. Block order alternated between conditions, and the starting condition was counterbalanced across participants. At the start of each block, participants received a cue indicating which condition they were in (5 s). A trial occurred as follows: (i) 1–3 s intertrial interval (ITI), (ii) stimulus presentation during which they had to engage in emotional projection (10s), (iii) ratings on the vividness of their projection, the level of anticipated distress, and the level of anticipated relief on a 5-point Likert scale ranging from 1 (not at all vivid/distressed/relieved) to 5 (extremely vivid/distressed/relieved).

After the task, participants answered four post-experimental questions: (i) "Did you find it difficult to project yourself into these scenarios?", (ii) "Were you able to switch focus between focusing on the negative (side effect condition) and the positive (remission condition)?", (iii) "Did you have enough time to visualize each event?", and (iv) "Across the 36 trials, did you project any other feelings/emotions other than distress or relief?"

Statistical analyses

We tested whether vividness, distress, and relief ratings differed significantly across conditions using linear mixed effects models (LMMs), computed in R Studio (R core team 2021) using the lme4 package (Bates et al. 2015). We examined any significant differences by testing a full model that included the condition against a null model that did not, using a likelihood ratio test. Random effects for the models included intercepts for participants and side effects.

fMRI experiment

Transparency and openness

The fMRI study, including method, hypotheses, and planned statistical analyses, was preregistered at https://osf.io/u9qpb. Raw data is available on the OpenNeuro platform (doi:10.18112/openneuro.ds006601.v1.0.0), and unthresholded statistical maps can be found on NeuroVault (https://identifiers.org/neurovault.collection:21775). Three participants did not consent to sharing their data.

Participants

Thirty-four participants (*Female* = 23, Age: $M = 21.56$ $SD = 5.26$) were recruited on the UCLouvain campus (Louvain-la-Neuve, Belgium). Sample size was based on Kruschwitz et al. (2018), who included between 16 and 28 participants for their experiments. Participants were healthy volunteers and met the following eligibility requirements: at least ≥18 yr, no electrical or mechanical implants, no current physical or mental disorders, including chronic conditions, and not pregnant. Interested participants were pre-screened for eligibility criteria using an MRI safety form (validated by the Ghent Institute for Functional and Metabolic Imaging, GIfMI). On the day of testing, participants completed the MRI safety form again to ensure their safety and compliance. The MRI safety form asked participants i) whether they ever had heart or head surgery, ii) if participants have electrical/mechanical implants or electrodes in their body, iii) if their eyes or skin has ever been damaged by metal fragments, iv) if they currently have a fever, and v) if there is a chance they are pregnant. The remaining eligibility criteria were detailed in the informed consent form, which participants were instructed to read and sign prior to participation. fMRI sessions took place in October/November 2024 at the GIfMI on the premises of the Gent University hospital (UZ Gent, Belgium). The study was approved by the ethics review boards of Gent University (ONZ-2023-0663) and the University of Luxembourg (ERP 24–030 MedCast).

Experimental task and MRI procedure

Figure 1 describes the cue-exposure task performed in the scanner. The task did not differ from the behavioral validation, except that participants did not provide ratings after each stimulus, and the intertrial interval was adjusted to 3 to 5 s for design efficiency. Additionally, due to feedback that some of the side effects were perceived as more severe than chronic pain, we updated the stimulus list to less severely rated side effects, resulting in the following 18 side effects: dry mouth, flatulence, itching, chills, loss of appetite, fatigue, constipation, irritability, headache, insomnia, confusion, vomiting, shortness of breath, anxiety, hair loss, blurry sight, chest pain, and fever.

Post-task questionnaires

After scanning, participants rated (1 to 5) each side effect for distress, familiarity, and average vividness in each condition. Finally, to ensure that participants did not vary considerably in their current health states, participants filled out the RAND-36 questionnaire (Hays et al. 1993), which assesses participants' global physical and mental health. Descriptive statistics of the rating scales are detailed in Tables S1 and S2 (see the Supplementary Materials).

Brain imaging data acquisition

The experimental task was implemented using Python and PsychoPy on an IBM-compatible computer. Imaging was conducted on a 3 T Siemens MAGNETOM Prisma scanner at the GIfMI center. 176 slice T1-weighted anatomical images were obtained using an MPRAGE sequence (TE = 4.18 ms, TR = 2250 ms, flip angle = 9°, 1-mm slice thickness). Fieldmaps were acquired using standard Siemens magnetic field maps using a multi-echo gradient echo acquisition (TR = 588 ms, TE 1 = 4.92 ms, TE 2 = 7.38 ms, flip angle = 60°). Finally, the fMRI scan used a z-shim gradient echo echo planar imaging (EPI) sequence (TE = 31 ms, TR = 1070 ms, flip angle = 52°, voxel size = $2.5 \times 2.5 \times 2.5$ mm^3).

Preprocessing of imaging data

Image preprocessing steps included: motion correction, distortion correction, co-registration, normalization, and spatial smoothing. All steps were implemented in the fMRI Expert Analysis Tool (version 6.0, part of the FSL package, FMRIB software library; Jenkinson et al. 2012). Motion correction was implemented using FSL's MCFLIRT algorithm. All participants demonstrated <1.0 mm of absolute or relative motion; thus, no participants were excluded. Data were temporally high-pass filtered. Geometric distortions caused by magnetic field inhomogeneities were corrected using the acquired field maps. The first magnitude image was brain extracted using FSL's bet2 algorithm, and the edges were then further eroded using the -ero function. We then used the fsl_prepare_fieldmaps function to transform the units of

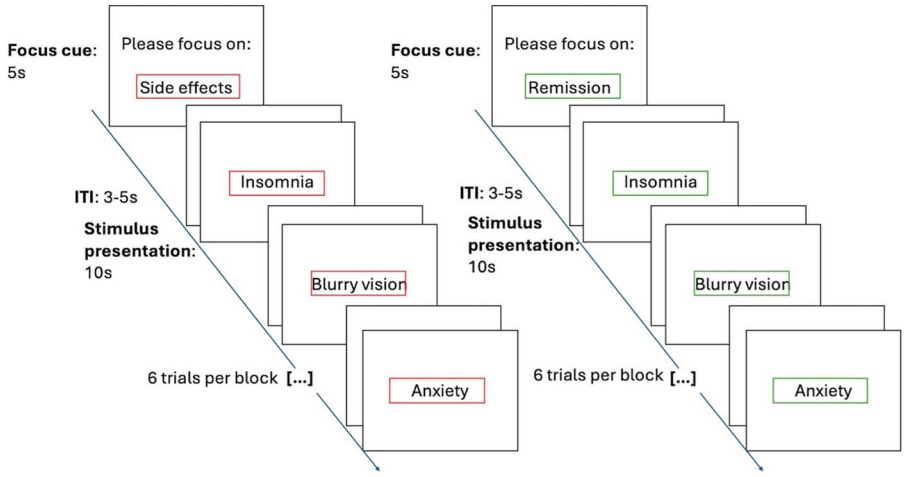

Figure 1 Depicted is the procedure for a block of the "side-effect-focus" condition and the "remission-focus" condition. To help participants remember the condition throughout the blocks, stimuli are framed in red for side effect and green for remission conditions.

the phase difference image into radians per second. FSL's BBR registration was used to co-register the anatomical and functional images using the information from the field maps to correct for geometric distortions. Normalization into MNI space was performed using FSL's FNIRT algorithm to perform a non-linear transformation. Finally, images were spatially smoothed using a 5-mm FWHM Gaussian kernel.

Statistical analyses

Whole-brain univariate analysis

To compare blood-oxygen-level-dependent (BOLD) activity during side-effect and remission conditions, we implemented a general linear model in FSL with the following explanatory variables (EVs): onsets for side-effect-focus trials (EV1), onsets for remission trials (EV2), parametric modulation (PM) assessing familiarity for side-effect-focus trials (EV3), PM assessing familiarity for remission-focus trials (EV4), PM assessing affective evaluation of side-effect-focus for side-effect trials (EV5), PM assessing affective evaluation of side-effect for remission-focus trials (EV6). We included six standard motion parameters as nuisance regressors. For group-level analyses, we performed a mixed-effects analysis using FLAME 1, with a height threshold of $z > 3.1$ and a cluster probability of $P < 0.05$ with family wise error (FWE) correction for multiple comparisons across the whole brain.

Multivariate analysis

We further conducted an exploratory multivariate intersubject pattern analysis using a whole-brain searchlight approach (Wang et al. 2020). Beta values for EV1 (side-effect-focus trials) and EV2 (remission-focus trials) were extracted from the univariate whole-brain GLM analysis. We then implemented a leave-one-subject-out cross-validation schema using Nilearn (Python v.3.9.20). Using a logistic regression as a classifying algorithm, all subjects but one were used as a training set, with the one left out participant serving as the test set. This was repeated until we had a single-fold accuracy map for every participant. To get a final accuracy map, we used $n = 1{,}000$ non-parametric permutations with correction for multiple comparisons at an FWE threshold of $P < 0.05$ in SnPM (v13.1.09).

Results

Behavioral validation

Vividness of projection

Average ratings of the vividness of projection were quite high for both side effect ($M = 4$ 0.13, $SD = 0.97$) and remission ($M = 4.09$, $SD = 0.95$) condition, and did not differ significantly, $\chi^2(1) = 0.8$, $P = 0.37$.

Emotion ratings

There was a significant effect of condition on both anticipated distress ($\chi^2(1) = 108.36$, $P < 0.001$) and anticipated relief ($\chi^2(1) = 198.3$, $P < 0.001$). Specifically, the estimated beta values indicate that distress ratings were higher in the side-effect-focus condition compared to the remission-focus condition, $\beta = 0.49$, $SE = 0.04$, and relief was lower in the side-effect-focus condition compared to the remission-focus condition, $\beta = -0.66$, $SE = 0.05$.

Post-experimental questions

Most participants indicated that they did not find it difficult to project their emotions (43/52), were able to switch focus between side effect and remission conditions (43/52), and had enough time to project their emotions (44/52). The most commonly mentioned emotions other than distress or relief were sadness ($n = 11$) and anger ($n = 8$), though relief and distress captured the primary emotional experience.

The behavioral validation confirmed that participants could vividly imagine the medical scenarios and shift attention between remission and side-effect components. This was evidenced by high vividness ratings and distinct distress/relief profiles across conditions.

fMRI experiment

Tables including all clusters and subclusters for each contrast can be found in the Supplementary Materials (Tables S3–S5).

Univariate analyses

Figure 2 shows the activation for the "side-effect minus remission" and "remission minus side-effects" contrasts. For the "side-effect-focus minus remission-focus" contrast, there were three clusters of activations (see Fig. 2a). The first (cluster size = 209) has its peak of activation in the left frontal pole (−36, 62, −6; $z_{max} = 4.32$). The second cluster of

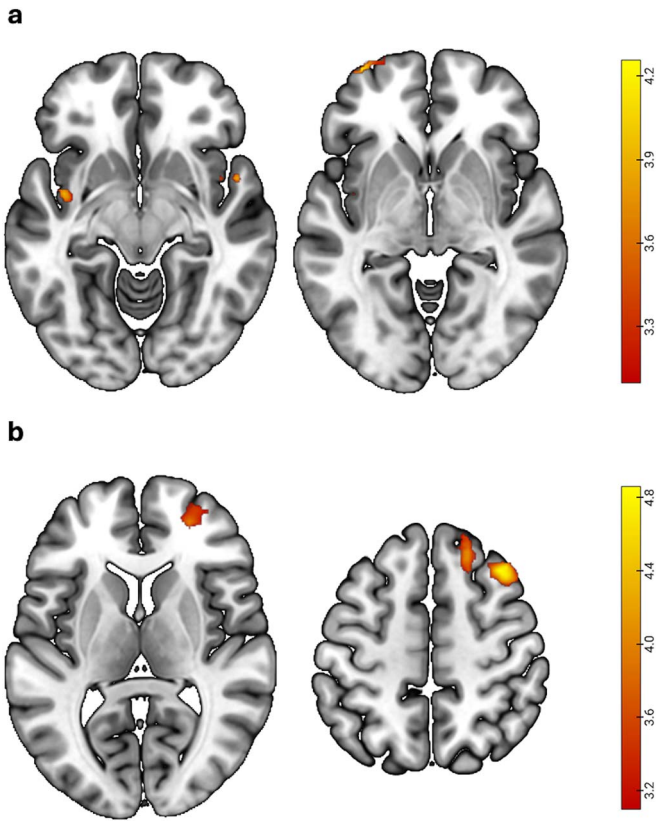

Figure 2 Depicted are the univariate whole-brain activation for side effect and remission conditions. Panels A and B show activations for "side effect minus remission" and "remission minus side effect", respectively. These images were thresholded using FSL FLAME 1, with a height threshold of $z > 3.1$ and a cluster probability of $P < 0.05$, FWE corrected for multiple comparisons across the whole brain.

activation (cluster size = 169) peaks in the right planum polare (50, 6, −8; $z_{max} = 4.09$) and extends into the temporal pole. The third cluster (cluster size = 119) peaks in the left insular cortex (−40, −2, −10; $z_{max} = 4$) and extends into the central opercular cortex and planum polare.

The "remission-focus minus side-effect-focus" contrast resulted in two clusters of activation (see Fig. 2b), the first of which (cluster size = 492) peaks in the right middle frontal gyrus (36, 25, 52; $z_{max} = 4.91$) extending into the superior frontal gyrus. The second cluster (cluster size = 283) peaks in the right frontal pole (26, 50, 8; $z_{max} = 3.98$).

Figure 3 shows the activations for "side-effect minus baseline" and "remission minus baseline" contrasts. We found six clusters for the "side-effect minus baseline" contrast (see Fig. 3a). The first cluster (cluster size = 2,068) peaks in the insular cortex (−40, 8, −2, $z_{max} = 5.26$) and extends into opercular cortices, inferior frontal gyrus, and temporal pole. The second cluster (cluster size = 1742) peaks in the left occipital pole (−24, −98, −8, $z_{max} = 6.28$) and extends into the inferior lateral occipital cortex. The third cluster (cluster size = 1,307) peaks in the left juxtapositional lobule cortex (−4, 6, 58, $z_{max} = 5.37$) and extends into the superior frontal gyrus. The fourth cluster (cluster size = 1,263) is centered on the right occipital pole (32, −96, − 4, $z_{max} = 6.19$) and extends into the inferior lateral occipital cortex. Cluster five (cluster size = 399) is in the right cerebellum crus I and II (38, −80, −36, $z_{max} = 4.74$). Finally, the sixth cluster (cluster size = 252) peaks in the

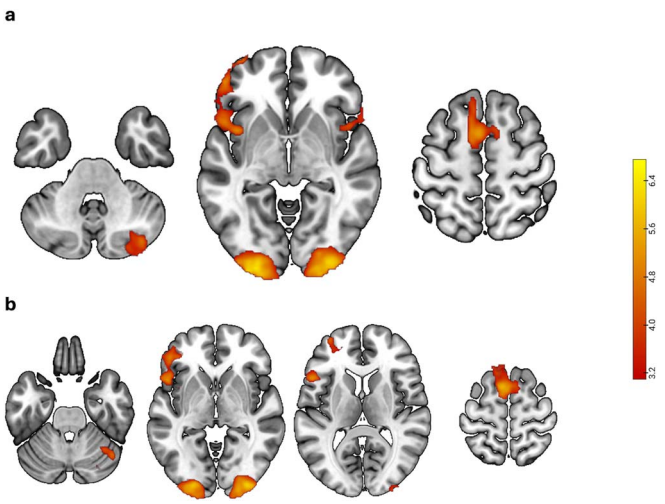

Figure 3 Depicted are univariate whole-brain activations for affective forecasting compared to baseline. Panel A shows the contrast for "side effect minus baseline" and Panel B shows "remission minus Baseline". These images were thresholded using FSL FLAME 1, with a height threshold of $z > 3.1$ and a cluster probability of $P < 0.05$, FWE corrected for multiple comparisons across the whole brain.

central opercular cortex and extends into the insular cortex, inferior frontal gyrus, and frontal and temporal pole (46, 10, 0, $z_{max} = 4.92$).

We found seven clusters for the "remission minus baseline" contrast (see Fig. 3b). The first (cluster size = 1,642) peaks in the left juxtapositional lobule (−6, 8, 64, $z_{max} = 5.68$) and extends into the superior frontal gyrus, paracingulate gyrus, and frontal pole. The second cluster (cluster size = 1,544) is centered on the left occipital pole (−24, −96, −6, $z_{max} = 6.75$) and extends into the inferior lateral occipital cortex. The third cluster (cluster size = 1,478) peaks in the inferior frontal gyrus (−50, 16, 0, $z_{max} = 5.35$) and extends into the frontal opercular cortex and frontal pole. The fourth cluster (cluster size = 1,184) spans the same regions as the second cluster but in the right hemisphere and also peaks in the occipital pole (32, −94, −2, $z_{max} = 6.17$). Cluster five (cluster size = 583) spans the left frontal pole (−34, 58, 10, $z_{max} = 4.55$). The last two clusters are in the right cerebellum, one spanning Crus I (cluster size = 178, 44, −62, −28, $z_{max} = 4.61$), the other Crus I and II (cluster size = 150, 28, −80, −40, $z_{max} = 4.56$). See Table S4 (Supplementary Materials) for a complete list of activations.

Parametric modulation of familiarity, emotion, and vividness

No significant activation was observed when comparing the parametric modulation (PM) of familiarity between the side-effect-focus and remission-focus conditions. Furthermore, we did not find PMs of emotion at a height threshold of $z > 3.1$. At a more lenient threshold of $z > 2.3$, we identified six clusters in the "side-effect-focus minus remission-focus" contrast (see Fig. 4a). The first cluster (cluster size = 1,608) peaks in the right cerebellum in region VI and extends into right VII and Crus I (30, −60, −26, $z_{max} = 3.92$). The second cluster (cluster size = 1,570) peaks in the left superior lateral occipital cortex and extends into the precuneus, cuneal cortex, and occipital pole (−16, −74, 58, $z_{max} = 3.39$). The third cluster (cluster size = 602) peaks in the left cerebellum in region Crus I and extends to left VI (−42, −58, −28, $z_{max} = 3.5$). Cluster four (cluster size = 552) peaks in the left middle frontal gyrus and extends into the inferior frontal gyrus,

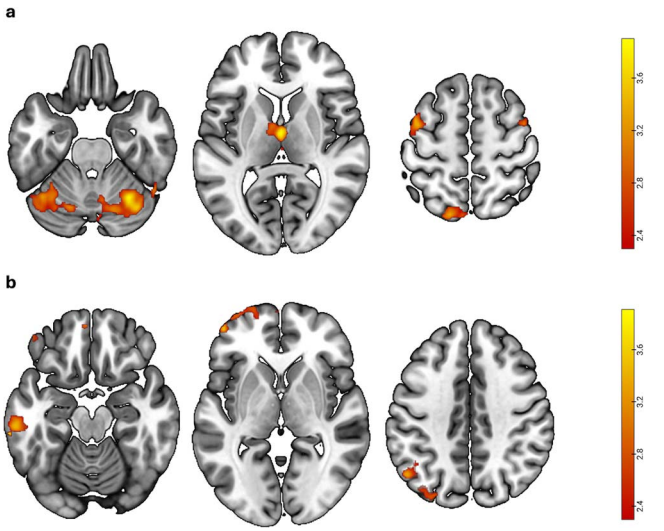

Figure 4 Depicted are the results of the parametric modulation of anticipated distress. Panel A shows PM for "side effect minus baseline" contrast, and Panel B shows PM for "remission minus baseline" contrast. Results were computed using FSL FLAME 1 with a height threshold of $z > 2.3$ and a cluster probability of $P < 0.05$, FWE corrected for multiple comparisons across the whole brain.

precentral gyrus, and postcentral gyrus (−40, −2, 62, $z_{max} = 3.49$). Cluster five (cluster size = 513) spans the left and right thalamus (0, −8, 8, $z_{max} = 3.95$) and extends into the caudate. Finally, cluster six (cluster size = 443) peaks in the right precentral gyrus and extends into the middle frontal gyrus, superior frontal gyrus, and precentral gyrus (50, 4, 50, $z_{max} = 3.53$).

We also found three significant clusters of activation in the PM for emotion in the "remission-focus minus baseline" contrast (see Fig. 4b). The first (cluster size = 654) peaks in the left lateral occipital cortex and extends into the angular gyrus (−50, −66, 40, $z_{max} = 3.39$). Cluster two (cluster size = 606) peaks in the left frontal pole and extends into the medial frontal cortex (−46, 52, 0, $z_{max} = 3.61$). Cluster three (cluster size = 509) peaks in the left middle temporal gyrus and extends into the inferior and superior temporal gyrus (−66, −32, −18, $z_{max} = 4.1$).

With regards to PM of the vividness of projection we found one cluster for the parametric weights of the vividness for side effects (cluster size = 121, −56, −26, 24, $z_{max} = 4.18$) in the "side-effect-focus minus baseline" contrast, which peaks in the supramarginal gyrus, and extends into the postcentral gyrus and the central/parietal operculum cortex.

Multivariate analysis

The intersubject pattern analysis uncovered a wide network of regions that discriminate between side-effect-focus and remission-focus conditions (see Fig. 5). Cluster 1 (cluster size = 1,867) peaks in the right thalamus (22,–32,–4) and extends into the right hippocampus, parahippocampal gyrus, and PCC. The second cluster (cluster size = 3,343) peaks (2, −68, 60) in the precuneus cortex and extends into the cuneal cortex, lateral occipital cortex, and postcentral gyrus. Cluster 3 (cluster size = 1,279; 3, −20, 18) spans the left putamen and caudate, as well as extending into the left accumbens and amygdala. Cluster 4 (cluster size = 3,947; −40, −44, −16) peaks in the left temporal fusiform cortex, temporal occipital fusiform cortex, inferior temporal gyrus, middle temporal gyrus, and extends into the cerebellum. Cluster 5 (cluster size = 755; 26, −66, 6) peaks in the right intracalcarine cortex and extends into the occipital pole and the lingual gyrus. Finally, cluster 6 (cluster size = 1,334; 12, 14, −4) peaks in the right caudate, extending into the right putamen and insular cortex as well as frontal orbital cortex.

Discussion

The present study sought to identify the neural correlates underlying affective forecasting in bivalent medical decision contexts and to investigate how attentional deployment influences this process. We extend prior work on affective forecasting by shifting focus from univalent or abstract stimuli typically used in prior research (e.g. monetary gains/losses) to more ecologically valid and emotionally complex scenarios: imagining remission from chronic pain in the presence of potential treatment side effects.

The contrasts between the *side-effect-focus* and *remission-focus* conditions partially supported our hypotheses. Focusing on remission was associated with increased activity in the superior frontal gyrus and frontal pole. These regions are implicated in both cognitive control and emotion regulation. Notably, the frontal pole has been linked to maintaining and manipulating representations in working memory (Kroger and Kim 2022), managing competing goals (Mansouri et al. 2017), self-referential processing (Burgess et al. 2007), and prospective thought (Okuda et al. 2003). In our paradigm, its activity likely reflects the deliberate maintenance of the attentional goal. Similarly, the superior frontal gyrus recruitment aligns with findings showing increased activation when participants focused on collected gains in risky choices (Liu et al. 2020; Li et al. 2022). Such recruitment likely reflects the effortful shift required to override the attentional capture of negative information (Kahneman and Tversky 1979; Vuilleumier and Schwartz 2001; Tom et al. 2007). Consequently, the prefrontal activations in our study appear to reflect the strategic deployment of attention during the simulation of desirable outcomes, rather than generic emotion processing.

Consistent with our hypotheses and prior work (Kruschwitz et al. 2018), focusing on side effects engaged the bilateral insula. The insular cortex has been broadly linked to interoception (Critchley et al. 2004; Zaki et al. 2012; Hassanpour et al. 2018; Fermin et al. 2022), emotion processing (Craig 2009; Zaki et al. 2012; Duerden et al. 2013), and aversive prediction (Wicker et al. 2003; Wright et al. 2004; Sarinopoulos et al. 2006; Liljeholm et al. 2014). Its recruitment in our study supports the interpretation that envisioning one's own response to side effects engages embodied simulations of aversive states. This may be especially true when anticipating one's affective state in response to a side effect, as such anticipation may involve recalling or constructing the physical sensations associated with these outcomes.

The fact that the frontal pole was active across both focus conditions suggests that this region may serve as a valence-independent hub integrating emotional and goal-related information, rather than exclusively supporting positive or negative simulation. This view aligns with recent models that place the frontal pole at the center of emotional set-shifting and high-order emotion regulation (Roelofs et al. 2023).

The intersubject pattern analysis revealed a broad, distributed network distinguishing remission-focus from side-effect-focus trials. Consistent with previous work on prospective thinking of emotional events, this included the PCC, hippocampus, parahippocampal cortex, and lateral temporal cortices (Sharot et al. 2007; D'Argembeau et al.

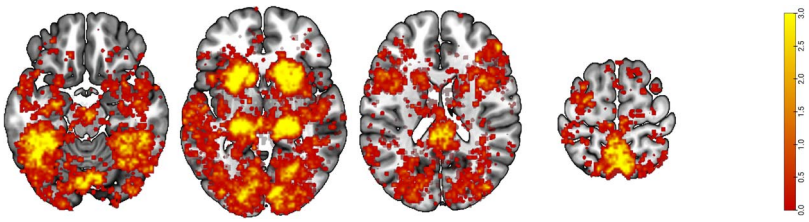

Figure 5 Depicted are the clusters of voxels that significantly decoded side effect and remission conditions across participants. They were computed using $n = 1000$ non-parametric permutations with correction for multiple comparisons using an FWE threshold of $P < 0.05$.

2008). These areas are thought to support the construction and contextualization of emotional simulations by drawing on autobiographical memory and spatial processing.

The network also encompassed reward-related regions (ventral striatum, orbitofrontal cortex) and emotion-processing regions (amygdala and insula), indicating that core circuits for valuation and emotion are differentially engaged depending on the attentional goal (i.e. side-effect or remission focus). This finding supports the notion that affective forecasting engages distinct neural representations depending on whether attention is directed toward potential gains or losses.

In addition, contributions from sensorimotor and cerebellar regions point toward the role of embodied simulation in forecasting. Recent literature has increasingly implicated the cerebellum in emotional and cognitive processing (Van Overwalle 2024; Baumann and Mattingley 2022; Ciapponi et al. 2023), suggesting that these activations may reflect the integration of sensory, motor, and emotional information during simulation.

Compared to previous research on affective forecasting using univalent gain-loss paradigms, our task elicited more anterior frontal activations, including robust engagement of the frontopolar cortex across conditions. This likely reflects the cognitive and emotional complexity inherent to the task. Forecasting, in the context of medical trade-offs, requires the participants to handle emotionally conflicting information, sustain task-relevant attentional goals, and simulate their future affective state. Collectively, these elements appear to have placed substantial demands on higher-order cognitive systems.

Although parametric modulation effects should be interpreted cautiously, given our modest sample size and exploratory threshold, we found that higher anticipated distress in the remission-focus condition was associated with stronger frontopolar activation. This suggests that maintaining focus on positive aspects becomes more effortful as anticipated distress increases. This is in line with the negativity bias by which negative affect tends to attract attention through its motivational salience in signaling threat (Kahneman and Tversky 1979; Vuilleumier and Schwartz 2001; Tom et al. 2007).

Our findings should be considered in light of several limitations. First, the moderate sample size may have reduced power to detect subtler modulations of neural activity, such as parametric effects of familiarity. Second, the use of hypothetical scenarios, where participants do not experience the actual outcomes, limits the generalizability of the results to real-world medical decision-making. It would be essential for future work to investigate these processes in (patient) populations who have to deliberate on treatment options. Third, our healthy young-adult sample may not reflect the experiences of (older) adults or individuals with chronic health conditions. Finally, we cannot exclude the possibility that participants also experienced anticipatory emotions while engaging in affective forecasting. Future research could measure participants' anticipatory affect concurrently to disentangle their respective contributions more systematically (e.g. Clayton McClure et al. 2024).

Additionally, we did not preregister specific hypotheses for the parametric modulation of distress and vividness. As such, these exploratory findings should be validated in larger samples and replicated with stimulus sets that systematically vary distress, vividness, and familiarity. Such an approach would enable fine-grained and informed investigation of these modulations.

This study demonstrates that attentional deployment shapes the neural mechanisms of affective forecasting in response to emotionally bivalent and medically relevant contexts. Side-effect-focus selectively recruited the insula, while remission-focus engaged the superior frontal gyrus. Across both conditions, the frontal pole emerged as a central hub for sustaining attentional goals in the face of emotionally conflicting prospection. Multivariate analyses further revealed a large-scale network, including valuation, emotion, memory, and sensory integration systems, that represents remission- and side-effect-focused forecasting differently. Together, these findings underscore the neural complexity underlying our ability to anticipate future feelings when facing consequential emotional trade-offs.

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Author contributions

Roxane Philips (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing—original draft, Writing—review & editing), Claus Vögele (Funding acquisition, Project administration, Supervision, Writing—review & editing), Chris Baeken (Project administration, Resources, Writing—review & editing), İrem Tuğçe Öz (Investigation, Writing—review & editing), James M. Harris (Investigation, Writing—review & editing), Mathieu Petieau (Software), and Damien Brevers (Conceptualization, Investigation, Methodology, Project administration, Resources, Supervision, Writing—review & editing).

Supplementary material

Supplementary material is available at *Cerebral Cortex* online.

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Conflicts of interest

The authors have no relevant financial or non-financial interests to disclose. We have no known conflicts of interest to disclose.

Data availability

This study, including method, hypotheses, and planned statistical analyses, was preregistered at https://osf.io/u9qpb. Raw data is available on the OpenNeuro platform (doi:10.18112/openneuro.ds006601.v1.0.0), and unthresholded statistical maps can be found on NeuroVault (https://identifiers.org/neurovault.collection:21775). Three participants did not consent to sharing their data.

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