

Brief report

Novelty seeking modulates medial prefrontal activity during the anticipation of emotional stimuli

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Abstract

In a functional magnetic resonance imaging experiment, expectancy cues signaling emotional stimuli were used to study the personality trait of novelty seeking. BOLD responses to emotional expectancy were positively correlated with novelty-seeking scores in the medial prefrontal cortex. This correlation was strongest for the sub-dimension of exploratory excitability.

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1. Introduction

The personality trait of novelty seeking is concerned with an individual's reaction to cues of emotionally salient stimulation (Cloninger et al., 1994). Individuals high in novelty seeking are characterized by frequent

exploratory activity, extravagance in approach to potential pleasures, and intense excitement during the anticipation of emotional stimulation. Given the anticipatory (i.e., "seeking") character of this personality trait, we expected that novelty seeking would be particularly relevant during the anticipation of emotionally salient stimuli.

Novelty seeking has been associated with the dopaminergic system. Support for this association comes from studies in substance abuse (Cloninger et al., 1988; Gerra et al., 2003), pathological gambling (Kim and Grant, 2001) and Parkinson's disease (Menza et al., 1993; Tsuchiya et al., 2000) as well as animal

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(Dulawa et al., 1999; Powell et al., 2003), receptor-binding PET (Suhara et al., 2001; Leyton et al., 2002), and genetic (Ebstein et al., 1996; but see Katsuragi et al., 2001) studies. The fact that dopamine is more important for appetitive (“wanting”) than for consummatory (“liking”) aspects of reward (Berridge and Robinson, 1998; Schultz, 2002; Burgdorf and Panksepp, 2006) points, again, to a role for the novelty-seeking trait in anticipatory processes.

Recent animal (Kabbaj and Akil, 2001), human lesion (Daffner et al., 2000), and resting state neuroimaging (Sugiura et al., 2000; Youn et al., 2002) studies have associated the personality trait of novelty seeking with a variety of dopamine-sensitive brain regions, including the ventral prefrontal cortex, anterior cingulate, insula, and caudate. However, the specific role for these regions in novelty seeking (and associated anticipatory processes) remains unclear.

The present study addressed the anticipatory character of novelty seeking. We hypothesized that novelty-seeking-dependent variation of activity in dopamine-sensitive brain regions would be directly related to differences in anticipatory processes prior to emotionally salient stimuli. To test this hypothesis, the present study relied on a functional magnetic resonance imaging (fMRI) activation paradigm employing the expectancy of emotional stimuli. While the group-average data of the study (17 healthy volunteers; 9 female) have been reported earlier (Berpohl et al., 2006a,b), the present report specifically relates the data to the personality trait of novelty seeking.

2. Methods

Details of the experimental design have been reported earlier (Berpohl et al., 2006a,b).

We used Cloninger’s *Temperament and Character Inventory* (Cloninger et al., 1994) to characterize the subjects’ personality trait of novelty seeking. The mean novelty-seeking score in our study sample was 20.3 (S.D.=6.4, range 6–34). During fMRI, upwards-pointing arrows were presented to subjects to induce the anticipation of emotional stimuli, followed by emotional photographs (Lang et al., 1999). Accounting for the uncertain (i.e., not always pleasant) outcome typically associated with novelty-seeking behavior, the paradigm incorporated both positive and negative emotional photographs. Horizontal arrows signaled neutral pictures. All photographs presented were novel for the subjects. Novelty-seeking scores were neither correlated with post hoc valence ratings for positive pictures (Pearson $r=-0.15$, $P=0.56$, n.s.) nor for negative pictures (Pearson $r=0.28$,

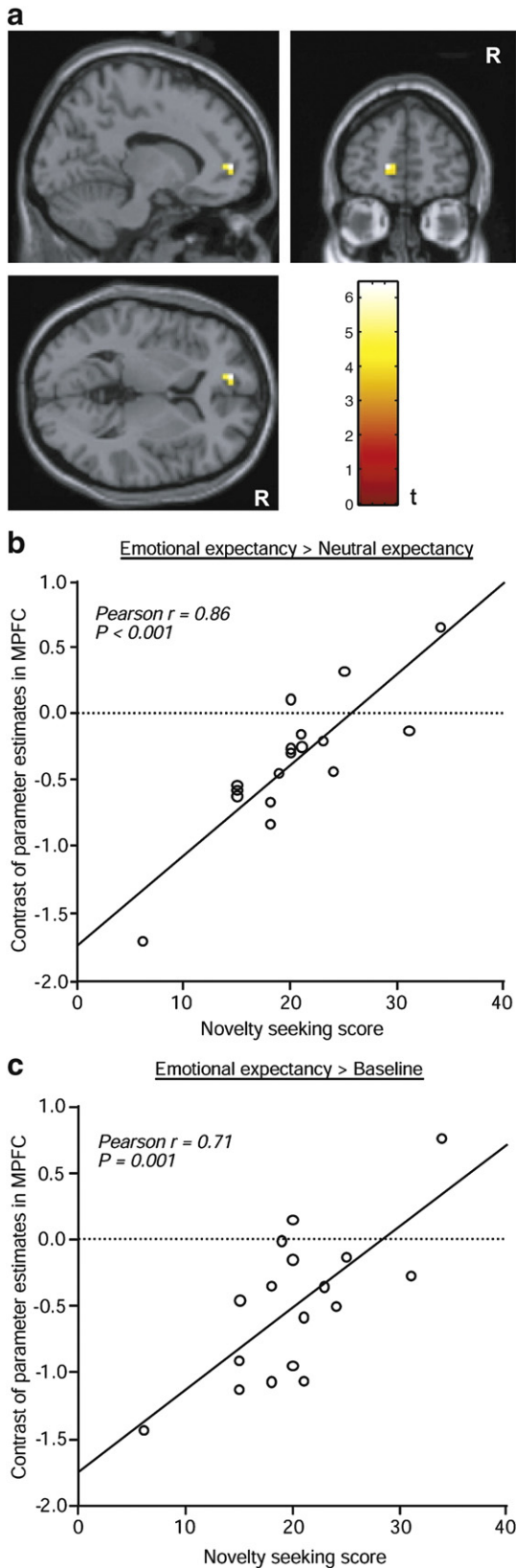
$P=0.28$, n.s.), suggesting that subjects high in novelty seeking did not show an affective processing preference (bias) during picture perception.

Statistical analysis was performed using SPM99 (Wellcome Department, London). Single-subject contrasts for the comparison “emotional versus neutral expectancy” were entered into a random-effects whole-brain linear regression analysis using the individual novelty-seeking scores as a covariate of interest ($n=17$). The height threshold was set to $P<0.001$ uncorrected and the extent threshold to $k=5$ voxels.

To further explore the correlation observed in the medial prefrontal cortex, contrasts of parameter estimates were extracted from the peak voxel ($x=-12$, $y=52$, $z=4$) for the comparison “emotional versus neutral expectancy” and correlated with the individual novelty seeking scores (two-tailed Pearson correlation, $n=17$). Analogous correlation analyses were carried out for three further contrasts. We were conservative in our post hoc correlation analyses and decided to use Bonferroni correction to account for the multiple testing. Including the separate analyses for the four novelty-seeking subscales, a total of eight tests were performed, resulting in a Bonferroni-corrected alpha level=0.00625.

3. Results

To study the association between novelty seeking and the anticipation of emotional stimuli, the individuals’ novelty-seeking scores were correlated with BOLD signals produced by the contrast “emotional > neutral expectancy”. This whole-brain analysis (Fig. 1a) revealed a positive correlation in the medial prefrontal cortex (MPFC; peak voxel $x=-12$, $y=52$, $z=4$, MNI space) at the border of the left medial frontal gyrus (BA 10) and the pregenual anterior cingulate gyrus (BA 32). Subjects with higher novelty-seeking scores showed larger BOLD signals in this region during emotional compared with neutral expectancy (Fig. 1b; Pearson $r=0.86$, $P<0.001$). Interestingly, this correlation did not hold during the actual perception of emotional versus neutral pictures (all emotional versus neutral pictures: Pearson $r=-0.21$, $P=0.42$, n.s.; positive emotional versus neutral pictures: Pearson $r=-0.03$, $P=0.90$, n.s.; negative emotional versus neutral pictures: Pearson $r=-0.18$, $P=0.48$, n.s.). Also the MPFC did not show a significant effect in the group-average contrast “emotional versus neutral expectancy”, i.e., independent of novelty seeking scores (SPM random-effects whole-brain analysis). Besides the MPFC, no brain region (dopamine-sensitive or -insensitive) was either positively or negatively correlated with novelty-seeking



scores in the whole-brain correlation analysis. Even when the height threshold was lowered on an exploratory basis to $P < 0.005$, no further dopamine-sensitive region was identified.

In agreement with these results, separate correlation analyses for each of the two expectancy conditions (emotional and neutral) relative to the fixation cross baseline revealed a significant positive correlation for the emotional expectancy (Fig. 1c; Pearson $r = 0.71$, $P = 0.001$), but not the neutral expectancy (Pearson $r = -0.15$, $P = 0.58$, n.s.) condition.

Analysis of the standard novelty-seeking sub-dimensions (Cloninger et al., 1994) (reported at the statistical maximum of the total score correlation finding) revealed that the correlation was strongest for *Exploratory Excitability* (Pearson $r = 0.74$, $P = 0.001$), followed by *Disorderliness* (Pearson $r = 0.69$, $P = 0.002$). Relatively weak effects were observed for *Impulsiveness* (Pearson $r = 0.60$, $P = 0.012$, n.s.) and *Extravagance* (Pearson $r = 0.46$, $P = 0.060$, n.s.).

4. Discussion

Our findings indicate that the personality trait of novelty seeking modulates brain activity in the MPFC during the expectancy of emotional stimuli. Extending previous lesion (Daffner et al., 2000) and resting state neuroimaging studies (Sugiura et al., 2000; Youn et al., 2002), our fMRI investigation offers a dynamic, function-oriented view on novelty seeking. Focusing on the *expectancy* of emotional stimuli, the paradigm accounts for the *anticipatory* character of novelty seeking. Our findings suggest that the MPFC is specifically linked to this “seeking” aspect of the personality trait. In the MPFC, BOLD signals correlate

Fig. 1. (a) Correlation map. Shown are regions of positive correlation between novelty-seeking scores and single-subject contrasts of parameter estimates (beta-values) for “emotional versus neutral expectancy” (random-effects whole-brain linear regression analysis). Peak voxel $x = -12$, $y = 52$, $z = 4$ (MNI space). $P < 0.001$ uncorrected, $k = 5$ voxels. R, right. (b), (c) Correlation diagrams. Displayed are individual novelty-seeking scores and contrasts of parameter estimates as well as the corresponding correlation curves. Two-tailed Pearson correlation analyses were carried out ($n = 17$). Contrasts of parameter estimates were extracted from the MPFC peak voxel identified in the correlation map for the comparisons “emotional versus neutral expectancy” and “emotional expectancy versus baseline”. From (b) and (c), it appears that two data points may be driving the effect. We therefore completed the respective correlation analyses without these two potential outliers. We found that the main correlation effect (reported in (b)) remained significant (Pearson $r = 0.62$, $P = 0.014$), while the secondary correlation analysis relying on the baseline contrast (reported in (c)) did not (Pearson $r = 0.38$, $P = 0.16$).

positively with novelty-seeking scores during the anticipation of emotional stimuli, but not during the anticipation of *neutral* stimuli or the *perception* of emotional stimuli. The correlation is strongest for the sub-dimension of *Exploratory Excitability*, where the “seeking” aspect can be expected to appear most pronounced.

Our finding is in accordance with functional neuroimaging studies implicating the MPFC in certain types of reward anticipation (Knutson et al., 2007) and appetitive states (Erk et al., 2002; Paulus and Frank, 2003; McClure et al., 2004). Although the MPFC is also involved in processing gain outcomes (Kuhnen and Knutson, 2005; Wrase et al., 2007), we did not find an association between novelty-seeking scores and BOLD signals obtained during the actual perception of emotional pictures, even if positive pictures were analyzed separately.

We do not find a significant average-group effect (i.e., independent of novelty-seeking scores) in the MPFC for the main contrast ‘emotional versus neutral expectancy’. Such a group contrast reveals signal increases in the supragenual anterior cingulate, as reported earlier (Birmpohl et al., 2006b). One might therefore suggest that emotional expectancy differentially involves the anterior cingulate, with general (i.e., novelty-seeking-independent) activation in the supragenual section and novelty-seeking-dependent signal changes in the pregenual section.

As the MPFC is a dopamine-sensitive region (Lewis et al., 1986), our findings add to previous studies associating novelty seeking with the dopaminergic system (Ebstein et al., 1996; Leyton et al., 2002; Powell et al., 2003). Our results are also in accordance with findings in animals associating the exploratory aspect of novelty seeking with the dopaminergic system (Dulawa et al., 1999; Powell et al., 2003). No dopamine-sensitive region (e.g., ventral striatum) besides the MPFC was identified in our study, even when the global height threshold was lowered on an exploratory basis to $P < 0.005$. This might be due to the paradigm employed. Focusing on the expectancy of emotional stimuli, the present paradigm accounted for the anticipatory (i.e., “seeking”) character of the novelty-seeking trait. Incorporating both positive and negative emotional stimuli, our paradigm accounted for the fact that the outcome of novelty-seeking behavior is often uncertain. It is acknowledged that different activation paradigms, focusing on other aspects of novelty seeking, may reveal a role for further components of the dopaminergic system. For instance, a paradigm that emphasized motor aspects of novelty-seeking behavior might have produced effects in the nigrostriatal system. The present findings suggest that the personality trait of

novelty seeking modulates medial prefrontal projections involved in anticipatory (appetitive) rather than consummatory aspects of positive and negative emotional stimulus processing (Burgdorf and Panksepp, 2006). These results in humans may have implications for patients with drug abuse, since alterations in this appetitive system, as suggested by increased novelty-seeking scores (Cloninger et al., 1988; Compton et al., 1996), may contribute to drug-seeking behavior (Bechara et al., 2002).

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