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SHORT COMMUNICATION

Left medial orbitofrontal cortex volume correlates with skydive-elicited euphoric experience

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Abstract The medial orbitofrontal cortex has been linked to the experience of positive affect. Greater medial orbitofrontal cortex volume is associated with greater expression of positive affect and reduced medial orbital frontal cortex volume is associated with blunted positive affect. However, little is known about the experience of euphoria, or extreme joy, and how this state may relate to variability in medial orbitofrontal cortex structure. To test the hypothesis that variability in euphoric experience correlates with the volume of the medial orbitofrontal cortex, we measured individuals' ($N = 31$) level of self-reported euphoria in response to a highly anticipated first time skydive and measured orbitofrontal cortical volumes with structural magnetic resonance imaging. Skydiving elicited a large increase in self-reported euphoria. Participants' euphoric experience was predicted by the volume of their left medial orbitofrontal cortex such that, the greater the volume, the greater the euphoria. Further analyses indicated that the left medial orbitofrontal cortex and amygdalo-hippocampal complex independently explain variability in euphoric experience and that medial orbitofrontal cortex volume, in conjunction with other structures within the mOFC-centered corticolimbic circuit, can be used to predict individuals' euphoric experience.

Keywords Skydive · Euphoria · Medial prefrontal cortex · Reward · Hedonia

Introduction

A quintessential characteristic of being human is the subjective experience or 'feeling' that accompanies the emotional response to positive and negative life events. Although for many individuals positive affect is commonplace in daily life, there appears to be variability from individual-to-individual in their capacity to experience joy. At one end of the spectrum, anhedonia or diminished pleasure is a primary symptom of major depressive disorder (MDD) and a negative symptom of schizophrenia (Der-Avakian and Markou 2012; Millan et al. 2014; Kring and Barch 2014). Individuals with anhedonia find it difficult to take pleasure in enjoyable life experiences. However, even in individuals where positive affect is a common occurrence, the extreme state of euphoria is seldom experienced. Not surprisingly, very little is known about the neural mechanism(s) associated with variability in emotional experience at the upper end of hedonic capacity.

In the brain, the orbitofrontal cortex (OFC) is associated with reward processing across a number of dimensions including the subjective pleasantness experienced upon

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reward attainment (Kringelbach et al. 2003; Nitschke et al. 2003). Meta-analytical evidence suggests that the medial OFC (mOFC) in particular activates in response to a variety of pleasant or rewarding stimuli, whereas the lateral OFC is more responsive to negatively valenced stimuli (Kringelbach and Rolls 2004). Research has shown that greater expression of positive emotion is linked to larger medial, but not lateral, OFC volumes (Welborn et al. 2009). On the other hand, disorders associated with blunted affect have been linked to reduced mOFC volume. Evidence from postmortem studies (Rajkowska 2000), large scale volumetric studies (Grieve et al. 2013), literature reviews (Lorenzetti et al. 2009), and meta-analyses (Koolschijn et al. 2009; Kempton et al. 2011) suggest that at a group-level MDD is associated with decreased volume of the mOFC (among other areas). Similarly, at a group-level, patients with schizophrenia have reduced mOFC volumes (Liao et al. 2015; Baare et al. 1999; Gur et al. 2000) and severity of anhedonia is inversely correlated with mOFC activity in schizophrenia (Harvey et al. 2010). Furthermore, youth at risk for familial schizophrenia have reduced mOFC volumes and the extent of this volume reduction correlates with symptoms of anhedonia (Rosso et al. 2010). Collectively, these findings suggest that the mOFC is associated with neuro-typical reward processing and reduced mOFC volume is linked to disorders characterized by blunted positive affect. It is, therefore, possible that variability in mOFC volume might also be associated with differences in the ability to experience euphoria. However, this possibility remains untested.

Research into the neural correlates of euphoric experience has been limited by the fact that it is hard to produce true states of euphoria in laboratory settings. A small number of studies on drug induced euphoria (e.g., Drevets et al. 2001; Breiter et al. 1997) have linked this state to increased activity in the nucleus accumbens. Yet, very little is known about the neural correlates of endogenously produced states of euphoric experience and the potential relationship between brain structure and variability in euphoric experience. Anticipation of skydiving has previously been used as an effective probe of real-world stress reactivity (Chatterton et al. 1997; Dikecligil and Mujica-Parodi 2010; DeDora et al. 2011; Mujica-Parodi et al. 2014). Yet, experiencing a first-time skydive is an activity that most individuals—that freely volunteer to skydive—find extremely enjoyable. Indeed, prior research has shown that people are most anxious/stressed during the anticipatory period leading up to the jump and upon landing are extremely euphoric (Carlson et al. 2012). Thus, the period immediately following a skydive provides a unique opportunity to probe individuals' states of extreme euphoria.

In this study, to elicit a strong euphoric experience we went outside the laboratory to measure participants' reactions to a first-time skydive. In addition to measuring participants' feelings of euphoria in response to skydiving, we measured medial and lateral OFC volumes with structural magnetic resonance imaging. We hypothesized that individuals experiencing the greatest levels of euphoria while skydiving would be those with the largest mOFC volumes. In addition to the OFC, the nucleus accumbens (NAcc) is linked to a variety of reward-related processes from reward seeking and anticipation (Knutson et al. 2001a, b; O'Doherty et al. 2002; Greenberg et al. 2014) to reward valuation and attainment (Bartra et al. 2013). Thus, we conducted additional analyses to assess the relationship between euphoric experience and a broader mOFC-centered corticolimbic circuit including the nucleus accumbens, but also the amygdala and hippocampus, which have previously been shown to be part of the mOFC network associated with affective and reward processing (Berridge and Robinson 2003; Cha et al. 2014; Roy et al. 2012). We used path analysis to model the relationship between the volumes of the structures within the mOFC corticolimbic circuit that subserve euphoric experience, as well as, multivariate pattern recognition analysis to predict individuals' level of euphoric experience based on their "pattern" of brain volumes within the mOFC-centered corticolimbic circuit.

Method

Participants

We recruited individuals who independently contacted a local skydiving school (Skydive Long Island, Calverton, NY) to schedule their first tandem skydive. Thirty-one (13 female) healthy consenting adults ($M = 24.23$, SD $= 6.82$, 18–48) participated in the study. The Institutional Review Board of Stony Brook University approved all aspects of the study. The individuals and measures included in this study were part of a larger investigation of individual variability in physiological stress reactivity.

Procedure

Testing took place over two time-matched days: (1) skydive day and (2) control day. At the airfield, participants boarded the plane at 10:15 a.m., ascended for 15 min, and then jumped with a period of freefall lasting 1 min, which was followed by a 4-min descent under an open parachute. Landing occurred at 10:35 a.m. On both days participants were asked to rate their current state of euphoria (e.g., "I am euphoric" and "I feel blissful"; Carlson et al. 2012) and anxiety on a four-point scale (e.g., "I am worried" and "I am tense"; six-item short-form of the Spielberger state

anxiety scale; Marteau and Bekker 1992; Spielberger et al. 1970). Euphoria and anxiety levels were collected on the plane immediately prior to jumping and at the airfield immediately after landing. Baseline levels of euphoria and anxiety were collected on the control day at matched time-points. On the control day, Zuckerman Sensation Seeking values were also obtained (Zuckerman and Link 1968). One individual did not fill out this questionnaire. Sensation seeking scores for the remaining 30 participants ranged from 16 to 33 ($M = 24.77$, SD $= 4.09$) and were used as a control variable in subsequent analyses. Correlations between these self-report measures are shown in Supplementary Figure 1).

Magnetic resonance image acquisition

Participants underwent T_1-weighted structural magnetic resonance imaging (sMRI) on the control day. Data were acquired from two 3-Tesla scanners. A Philips 3T Achieva whole body scanner with the following high-resolution MPRAGE sequence was used for the initial 11 scans: repetition time/echo time ion time (TR/TE) = 8.0/4.3 ms, flip angle (FA) = 18°, field of view (FOV) = 250 × 250 × 150 mm, 256 × 256 × 168 matrix, 1 mm isotropic voxels, sagittal partitions). The final 20 scans were collected on a 3T Siemens MAGNETOM Trio Tim MRI scanner with the following high-resolution MPRAGE sequence: TR/TE = 2500/1900 ms, FA = 9°, FOV = 250 mm × 250 mm × 250 mm, 1 mm isotropic voxels, sagittal partitions. It should be noted that Freesurfer morphometric procedures (described below) have been demonstrated to show good test–retest reliability across scanner manufacturers and across field strengths (Reuter et al. 2012; Han et al. 2006). In our sample, there were no significant volumetric differences between the two scanners for any of our OFC regions of interest (ROIs) or whole brain gray matter (all Ps $\geq$ 0.19).

Magnetic resonance image processing

We performed cortical reconstruction and volumetric segmentation with the Freesurfer image analysis suite (http://surfer.nmr.mgh.harvard.edu/). The technical details of these procedures have been described in detail in a number of earlier publications (Dale et al. 1999; Desikan et al. 2006; Fischl and Dale 2000; Fischl et al. 1999, 2002). Freesurfer image processing includes the following steps: motion correction, removal of non-brain tissue, automated normalization to Talairach space, segmentation into subcortical white matter and gray matter, normalization of overall image intensity, defining the gray and white matter boundary, topology correction, and surface deformation. This last step is accomplished by following intensity gradients to optimally place the gray/white and gray/cerebrospinal fluid borders at the location where the greatest shift in intensity defines the transition to the other tissue. Freesurfer then performs a number of additional procedures including surface inflation, registration to a spherical atlas based on individual cortical folding patterns, parcellation of the cerebral cortex into units based on gyral and sulcal structure, and the creation of surface based data including maps of curvature and sulcal depth.

Following these procedures, we derived mean gray matter volumes for three OFC ROIs in each hemisphere (Fig. 1) of each individual. Delineation of the OFC ROIs was defined using the Desikan–Killiany Atlas (Desikan et al. 2006) following the automated parcellation procedures described in Fischl et al. (2002). Three Desikan–Killiany masks were used to precisely characterize the topography of the OFC: (1) *medial OFC*: medial to olfactory sulcus, spanning the rectal gyrus ventrally and the medial orbital gyrus dorsally; (2) *lateral OFC*: between the olfactory sulcus and the lateral orbital sulcus, spanning the medial-to-lateral orbital gyrus; and (3) *pars orbitalis*: lateral to the lateral orbital sulcus, spanning the lateral orbital gyrus. All ROIs were visually inspected to ensure appropriate parcellation.

Analyses

We tested for a positive correlation between euphoric experience and OFC volume in each of the three OFC ROIs across both cerebral hemispheres (adjusted $\alpha = 0.0083$; i.e., $P = 0.05/6$ comparisons, 3 ROIs × 2 hemispheres). Using Pearson's partial correlations, we controlled for the effects of age, gender, handedness, scanner, state anxiety, sensation seeking, and intracranial volume (Ge et al. 2002; Tisserand et al. 2004; Welborn et al. 2009; Carlson et al. 2015).

Given that mOFC processing of threat versus safety cues (Greenberg et al. 2013a, b) has been linked to structural variability across a broader circuit (Cha et al. 2014), we performed a stepwise linear regression ($P < 0.05$ to enter and $P > 0.10$ for removal) analysis to test (1) the degree to which the correlation between the mOFC and euphoria holds when additional brain regions are considered and if so, (2) whether additional variance can be explained by adding other components of the circuit. For this regression model we included the following volumetric variables for each hemisphere: medial OFC, lateral OFC, pars orbitalis, nucleus accumbens, amygdala, hippocampus, and a total amygdalo-hippocampal complex, which is meant to represent the affective/limbic contribution to the mOFC-centered corticolimbic circuit (Pitkänen et al. 2006; Roy et al. 2012). In addition, we included the following control variables: age, gender, handedness, scanner, state anxiety,

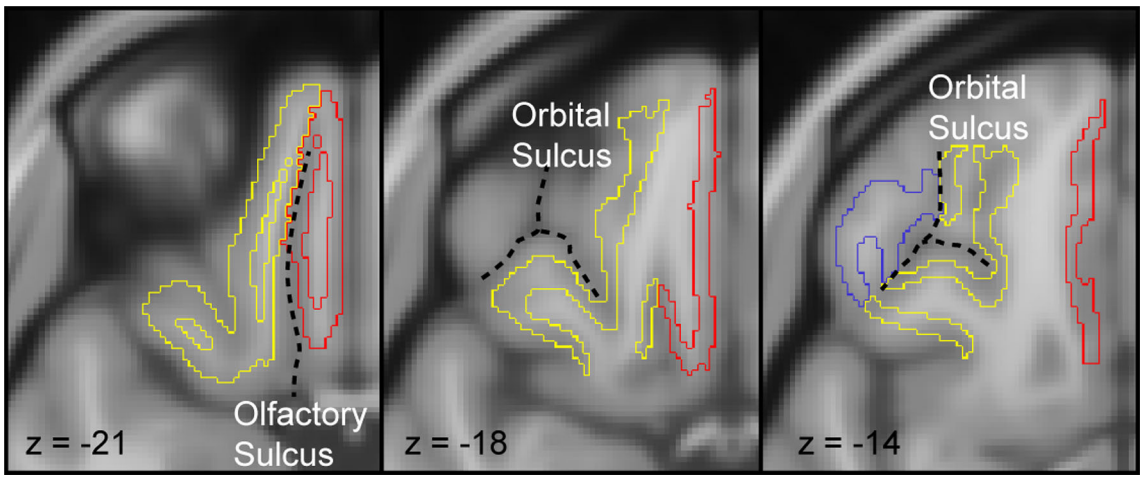

Fig. 1 Delineation of the orbitofrontal cortex (OFC) into three regions of interest (ROIs): (1) medial OFC (in *red*), medial to the olfactory sulcus, spanning the rectal gyrus and the medial orbital gyrus; (2) lateral OFC (in *yellow*), between the olfactory sulcus and the lateral orbital sulcus, spanning the medial-to-lateral orbital gyrus; and (3) pars orbitalis (in *blue*), lateral to the lateral orbital sulcus, spanning the lateral orbital gyrus. Three masks from the Desikan–Killiany Atlas (Desikan et al. 2006) were used to characterize the topographical architecture of the three OFC ROIs

sensation seeking, and intracranial volume. Correlations between these volume measures can be seen in Supplementary Figure 2).

Using linear stepwise regression to select our variables of interest, we then performed path analysis in AMOS 18 (SPSS, Inc.) to compare three models assessing the relationship between temporal lobe limbic structures (i.e., amygdala and hippocampus) and the mOFC on euphoric experience: (Model 1) limbic structures and the mOFC independently contribute to euphoric experience, (Model 2) limbic structures influence the mOFC, which in turn affects euphoric experience, and (Model 3) the mOFC influences limbic structures, which in turn affects euphoric experience. Given that our original set of control variables did not help explain variability in euphoric experience and their inclusion produced poor fit in preliminary path analyses, we restricted confounding variables during the model comparison phase to scanner and intracranial volume. For our model comparisons we considered goodness of fit measures, such as Akaike's Information Criterion (AIC), the root mean square error of approximation (RMSEA), and the comparative fit index (CFI). Cutoff criteria for RMSEA (<0.06) and CFI (0.95) were considered (Hu and Bentler 1999). Additionally, we employed a bootstrapping approach (Linhart and Zucchini 1986). Similar to previous work (Carlson et al. 2014), the bootstrapping approach used four steps: (1) Bootstrap samples were generated using the original data as the population. (2) Using the maximum likelihood function for each iteration (1000 bootstrap samples) the discrepancy between each sample and the population was calculated. (3) The average discrepancy across bootstrap samples for each model was calculated. (4) The models were compared based on the mean discrepancy.

For our final analysis, we used support vector regression (SVR), which unlike univariate analytical methods considers multivariate "patterns" of variables instead of each variable independently. Therefore, it may be more appropriate when a circuit-wide pattern is expected to be important. This approach allows for inferences at the level of the individual and thus allows us to predict an individual's euphoria level based on the pattern of brain volumes across the mOFC-centered corticolimbic circuit. Euphoria scores were fitted with a linear SVR machine with random feature elimination (RFE; Guyon et al. 2002) using the volumetric predictor variables included in the aforementioned regression model (i.e., bilateral medial OFC, lateral OFC, pars orbitalis, nucleus accumbens, amygdala, hippocampus, and a total amygdalo-hippocampal structure). To assess the predictive capacity of the variables, a two-tiered cross validation (CV) scheme was implemented. First, the data were split into leave-one-out (LOO) training and testing folds. For each training fold an additional LOO–CV was carried out to select model parameters—the soft margin of the SVM, and the number of features by applying RFE. Next, the SVR model was fitted to the entire training fold, and was used to predict the euphoria score of the test fold. This two-tiered LOO–CV resulted in a vector of predictions, which could be compared to the actual scores via the correlation coefficient. The significance of the resulting correlation was assessed through bootstrapping where we permuted the euphoria scores randomly 500 times, and then applied the same CV procedure to each of the resulting data sets to yield an empirical estimate of the

significance of the predication. SVR was performed using Neuroclass (Fekete et al. 2013) and the Library for SVM (LIB–SVM) toolbox (Chang and Lin 2011).

Results

Behavior

Relative to baseline levels, participants' self-report euphoria levels were greatly elevated (main effect, $F_{1,30} = 32.04$, $P = 0.000004$). An interaction between day (skydive vs. control) and time-point (pre-jump vs. post-jump) revealed that although euphoria was elevated immediately prior to jumping, it increased even further upon landing, $F_{1,30} = 12.35$, $P = 0.001$; see Fig. 2. Thus, as expected, skydiving was effective in eliciting a heightened level of euphoria.

Orbitofrontal cortex correlations with euphoric experience

As shown in Fig. 3, greater left mOFC volumes were predictive of greater levels of self-reported euphoria upon landing when euphoric experience was at its peak ($r_{partial} = 0.55$, $P = 0.003$). We found a similar association between the left mOFC and self-reported euphoria prior to jumping as well ($r_{partial} = 0.44$, $P = 0.019$); however, this effect did not reach significance when correcting for multiple comparisons. Such effects were not observed in other OFC regions (all Ps $\geq$ 0.19). In follow-up partial correlations controlling for age, handedness, scanner, gender, sensation seeking, and intracranial volume (Ge et al. 2002; Tisserand et al. 2004; Welborn et al. 2009) we show that no OFC regions correlated with state anxiety (all Ps $\geq$ 0.14). Therefore, individuals' experienced level of skydive-induced euphoria was uniquely linked to the volume of their left mOFC such that, greater mOFC volume was associated with greater euphoria.

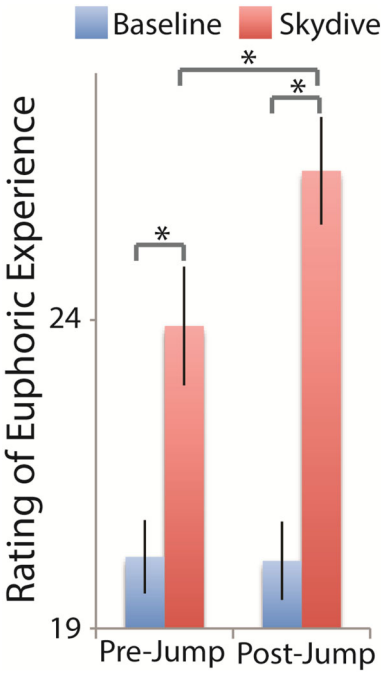

Fig. 2 A first-time tandem skydive was used to elicit a strong state of subjective euphoria. Self-report levels of subjective euphoria were elevated both pre-jump and post-jump relative to time-matched samples on a control day

Orbitofrontal circuit-level predictors of euphoric experience

Stepwise linear regression indicated that prejump levels of euphoric experience were predicted by the left mOFC ($\beta = 0.40$, $P = 0.002$), left amygdalo-hippocampal complex ($\beta = -0.50$, $P = 0.001$), and prejump state anxiety[1] ($\beta = -0.35$, $P = 0.01$), $F_{3,29} = 13.41$, $P = 0.00002$, $R^2 = 0.61$. Post-jump euphoria was predicted by the left mOFC ($\beta = 0.45$, $P = 0.005$) and left amygdalo-hippocampal complex ($\beta = -0.60$, $P = 0.0004$), $F_{3,29} = 10.43$, $P = 0.0004$, $R^2 = 0.44$. Thus, in addition to the relationship between euphoric experience and the left mOFC, the left amygdalo-hippocampal complex also appears to be associated with euphoric experience; however, the nature of this relationship suggests that smaller amygdalo-hippocampal volumes are associated with greater reported euphoria.

Given that linear regression identified the left mOFC and amygdalo-hippocampal complex as significantly explaining variability in euphoric experience, we performed a path analysis on these structures to model the relationship between the structures in this circuit and euphoric experience. As displayed in Table 1, the results suggest that the parallel model in which the left mOFC and amygdalo-hippocampal complex directly influence euphoric experience independently outperforms the serial models as indicated by the best goodness of fit: lowest Akaike's Information Criterion (pre-jump: 48.10, post-jump: 47.95) and bootstrap discrepancy (pre-jump: 48.65, post-jump: 47.45) as well as the best comparative fit index (pre-jump: 1.00, post-jump: 1.00) and root mean square error of approximation (pre-jump: <0.00, post-jump: <0.00). In the pre-jump parallel model the effect of the mOFC on

[1] Note that the volume of the amygdalo-hippocampal complex was positively correlated with prejump (*left* $r = 0.39$, $P = 0.03$, *right* $r = 0.34$, $P = 0.05$) and postjump (*left* $r = 0.47$, $P = 0.01$, *right* $r = 0.39$, $P = 0.03$) state anxiety in partial correlations controlling for age, gender, handedness, sensation seeking, scanner, and intracranial volume.

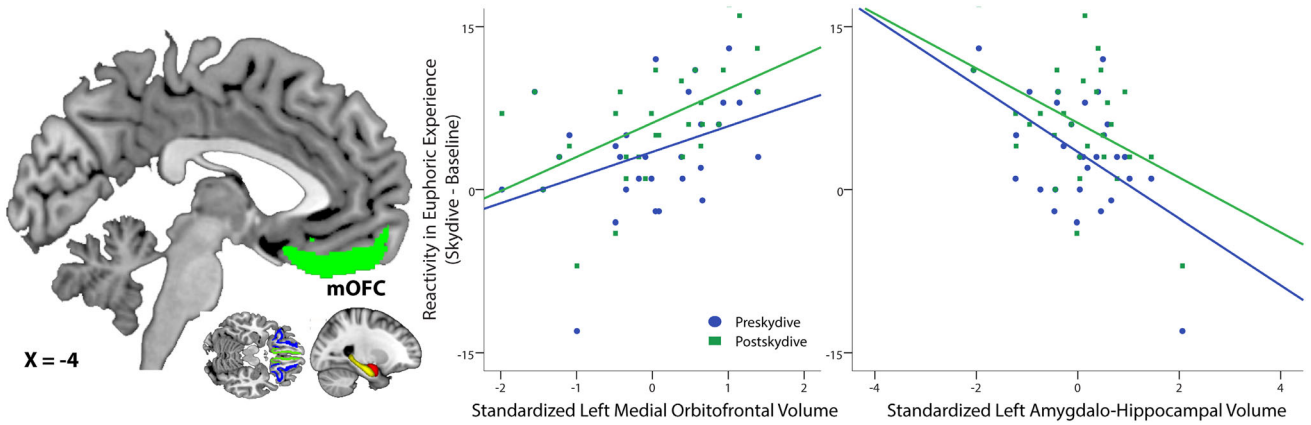

Fig. 3 The medial orbitofrontal cortex (OFC) region of interest (Freesurfer Atlas averaged across all participants; Desikan et al. 2006) is shown in *green* (*Left*). Scatter plot of individuals' level of experienced euphoric reactivity both pre-skydive and post-skydive (relative to baseline levels collected on separate day) were positively correlated with medial OFC volume (*Right*). The results show that greater OFC volume was associated with greater euphoric experience

Table 1 Model comparisons for euphoric experience

	χ^2, *df*	Bootstrapping[1]	AIC	CFI	RMSEA
Prejump euphoria					
Parallel model	4.10, 5	48.65	48.10	1.00	<0.00
Serial model 1	19.96, 5	68.46	63.96	0.64	0.32
Serial model 2	18.94, 5	67.46	62.94	0.66	0.31
Independent model	56.00	–	80.00	–	0.30
Postjump euphoria					
Parallel model	3.95, 5	47.45	47.95	1.00	<0.00
Serial model 1	18.24, 5	66.03	62.24	0.64	0.30
Serial model 2	13.90, 5	62.55	57.90	0.76	0.24
Independent model	51.74, 15	–	75.74	–	0.29

Model contains the combined volume of the amygdala/hippocampus (limbic) and medial orbitofrontal cortex (mOFC) in the left hemisphere as predictors and scanner, intracranial volume, and age as control variables

[1] Discrepancy between samples and population in bootstrapping. *Note* Serial model 1 = limbic to mOFC, Serial model 2 = mOFC to limbic, Parallel model = separate limbic and mOFC paths

euphoria was 0.57, $P < 0.001$ and the effect of the left amygdalo-hippocampal complex was −0.59, $P < 0.001$. Similarly, in the post-jump parallel model the effect of the mOFC on euphoria was 0.47, $P < 0.001$ and the effect of the left amygdalo-hippocampal complex was −0.59, $P < 0.001$.

The results of our path analysis suggest that the volumes of the left mOFC and amygdalo-hippocampal complex independently explain variability in euphoric experience. Given that left mOFC volume was positively associated with euphoric experience while left amygdalo-hippocampal volume was negatively correlated with euphoric experience, it seems that euphoric experience would be greatest when mOFC volumes are larger and amygdalo-hippocampal volumes are smaller. To further test this possibility, we calculated the ratio of left mOFC/amygdalo-hippocampal volume and tested for a positive relationship with euphoric experience pre- and post-skydive. As expected, the results of this analysis suggest that a larger mOFC/amygdalo-hippocampal volume ratio is highly correlated with increased euphoric experience (pre-jump $R = 0.64$, $P < 0.001$; post-jump: $R = 0.75$, $P < 0.001$; these partial correlations controlled for age, handedness, scanner, gender, state anxiety, sensation seeking, and intracranial volume).

Multivariate predictive analysis

We used support vector regression to predict individuals' level of euphoric experience based on brain volumes across the following regions: medial OFC, lateral OFC, pars orbitalis, nucleus accumbens, amygdala, hippocampus, and the total amygdalo-hippocampal complex. The volumes of the left mOFC, left hippocampus, and right accumbens

were found to be the best classifiers for pre-jump euphoric experience, $R = 0.38$, $P < 0.05$ (bootstrapping corrected). On the other hand, the volumes of the left mOFC and left amygdalo-hippocampal complex were the best classifiers for post-jump euphoric experience, $R = 0.56$, $P < 0.005$ (bootstrapping corrected).

Discussion

We found that first time skydiving increased levels of self-reported euphoric experience both prior to jumping and immediately upon landing (Fig. 2). Greater left mOFC volume was found to correlate with greater euphoric experience. Regression analyses indicated that in addition to the left mOFC, the volume of the left amygdalo-hippocampal complex also explained variability in euphoric experience. These two volumetric variables were the primary predictors of euphoric experience, while sensation seeking[2] and other participant variables such as age and gender did not predict euphoria. However, whereas left mOFC volume, was positively correlated with euphoric experience, left amygdalo-hippocampal complex volume was negatively correlated with euphoric experience. Together these two volumetric variables explained approximately 40 % of the variance in euphoric experience. Path analysis suggested that mOFC and amygdalo-hippocampal complex volumes did not interact directly, but rather correlate with euphoria in a parallel manner—providing evidence for multiple distinct pathways to euphoric states. Additionally, multivariate predictive analysis showed that left mOFC volume in conjunction with the volume of other structures including the amygdalo-hippocampal complex and nucleus accumbens can be used to predict euphoria on an individual-by-individual basis.

A large number of neuroimaging studies suggest that the OFC responds to a variety of reward-related stimuli including pleasant tastes (Kringelbach et al. 2003; O'Doherty et al. 2002), pleasant sounds (Royet et al. 2000), pleasant visual images and attractive faces (O'Doherty et al. 2003; Ishai 2007; Royet et al. 2000; Nitschke et al. 2003), monetary rewards (Carlson et al. 2011; O'Doherty et al. 2001), social cooperation (Rilling et al. 2002), erotic images (Walter et al. 2008), and sexual chemosensory signals (Zhou and Chen 2008). Activity in the OFC has also been linked to the subjective feeling of pleasantness (Kringelbach et al. 2003; Nitschke et al. 2003). Meta-analytic data suggest that it is the mOFC in particular that is responsive to pleasant or rewarding stimuli, whereas the lateral OFC is more responsive to negatively valenced stimuli (Kringelbach and Rolls 2004). However, most of these reward stimuli either directly (e.g., food and sex) or indirectly (e.g., money) aid an organism's survival. On the other hand, skydive-induced euphoria is not driven by survival, but rather is done for pure entertainment or play. Although play is an important aspect of development in many species (Fagen 1974), the extreme-level of play represented by skydiving seems to be specific to humans and the pleasantness of this experience is person-specific (Carlson et al. 2012). Another non-need-based experience that humans find uniquely pleasant is music, which can elicit great pleasure in the form of musical chills. Similar to skydiving, the type of music that elicits such chills is person-specific and is linked to the mOFC as well as additional emotion and reward-related brain regions (Blood and Zatorre 2001).

Much empirical and theoretical work has linked the nucleus accumbens to reward anticipation or wanting and the prefrontal cortex/OFC with reward attainment (O'Doherty et al. 2002; Knutson et al. 2001b; Berridge and Robinson 2003). However, a recent meta-analysis of the functional neuroimaging data suggests that both structures are active prior to and after reward attainment (Bartra et al. 2013). The differential involvement of brain regions pre versus post reward is particularly relevant for motivational and learning-related reward processes, respectively. However, reward processing is not limited to motivation and cognitive learning processes, but also contains a subjective affective component. The mOFC is thought to serve as a hub of multimodal integration across sensory and cognitive systems (Cha et al. 2014; Kringelbach 2005; Roy et al. 2012), which supports a unified state of subjective awareness—including hedonic experience (Kringelbach 2005). Our results suggest that the left mOFC is associated with the subjective experience of euphoria, whether this affective experience precedes or follows the actual reward. On the other hand, our multivariate predictive analysis identified the nucleus accumbens as a predictor of euphoric experience pre-jump/reward, but not post, which provides partial support for the idea that the nucleus accumbens is associated with the wanting or anticipation phase of reward processing (O'Doherty et al. 2002; Knutson et al. 2001b; Berridge and Robinson 2003) and in particular during anticipatory euphoric experience.

Beyond the left mOFC and reward circuit structures we found an inverse association between euphoric experience and the volume of medial temporal lobe limbic structures—namely, the amygdala and hippocampus. The amygdalo-hippocampal complex is an anatomically and functionally defined circuit associated with a variety of affective processes (McGaugh 2002; Pitkänen et al. 2006;

[2] For those interested in reading more about the relationship between sensation seeking, state euphoria, state anxiety, and cortisol reactivity to skydiving we refer you to our previous work assessing these variables (Mujica-Parodi et al. 2014; Carlson et al. 2012).

Phelps 2004; Phan et al. 2002). The amygdala has traditionally been associated with threat and stress reactivity (LeDoux 1996; McGaugh 2002; Davis 1992; Davis and Whalen 2001; Adolphs et al. 2005), but has also been found to be engaged by a number of other affective processes including positive emotions and reward processing (Berridge and Robinson 2003; Canli et al. 2002; Hamann et al. 2002; Hamann and Mao 2002; O'Doherty et al. 2002; Carlson et al. 2011; Greenberg et al. 2014). Meta-analysis of the functional neuroimaging research suggests that the amygdala and hippocampus are both involved in the emotions of fear and happiness (Phan et al. 2002). Although more research will be needed to clarify the precise role of the amygdalo-hippocampal complex in euphoric experience, our results suggest that the volumes of the left mOFC and amygdalo-hippocampal complex independently explain variability in euphoric experience in a parallel fashion such that when mOFC volumes are larger and amygdalo-hippocampal volumes are smaller euphoric experience is greater.

Our finding of increased euphoric experience in individuals with larger left mOFC volume complements volumetric research in MDD and schizophrenia. As mentioned in the introduction, both MDD and schizophrenia are characterized by anhedonia and both disorders are associated with reduced volume in the mOFC[3] (Rajkowska 2000; Liao et al. 2015; Baare et al. 1999; Gur et al. 2000; Grieve et al. 2013; Lorenzetti et al. 2009; Koolschijn et al. 2009; Kempton et al. 2011). The extent of volume reduction in the mOFC has been found to inversely correlate with symptoms of anhedonia (Rosso et al. 2010). Furthermore, bipolar disorder is characterized by fluctuating states of anhedonia and euphoric mania. Successful lithium-based treatment, alleviating depressive symptoms, in bipolar disorder is associated with increased mOFC gray matter post-treatment (Moore et al. 2009). It should be noted that on a functional level other structures such as the nucleus accumbens and anterior cingulate cortex show abnormal reward processing in relation to anhedonia in depressed individuals (Pizzagalli et al. 2009; Foti et al. 2014; Steele et al. 2007; Greenberg et al. 2015; Knutson et al. 2008; Keedwell et al. 2005; Wacker et al. 2009), which may in part be attributable to reduced mOFC volume in depression (Wagner et al. 2008). Our results add to this literature by indicating that not only is mOFC volume linked to the absence of pleasure, but also extreme pleasure. Collectively, these results suggest that the volume of the mOFC may represent an individual's capacity for joy or pleasure, which ranges from anhedonia to euphoria.

[3] In a subsample of our participants ($n = 20$) we collected Beck Depression scores, which were found to negatively correlate with left mOFC volume ($r = -0.45$, $P < 0.05$ in a partial correlation controlling for age, gender, handedness, and intra-cranial volume.

Our results suggest that in addition to mOFC volume being associated with the expression of positive affect (Welborn et al. 2009), it is also linked to the experience of euphoria. We found this to be true for the left, but not right, mOFC as well as the left amygdalo-hippocampal complex. The left lateralized nature of these findings was not hypothesized. Although typically associated with more dorsal prefrontal regions, traditional affective frontal asymmetries have linked the left hemisphere to positive emotions (Coan and Allen 2003; Davidson 1992; Sackeim et al. 1982; Gilbert et al. 2008). A more recent reconceptualization of frontal asymmetries suggests the left hemisphere is more associated with approach motivated emotive states including excitement (Harmon-Jones et al. 2010; Harmon-Jones and Allen 1998). While it is tempting to interpret this left mOFC effect in the context of the frontal asymmetry theory, further research is needed to test the robustness of this lateralized finding.

Although our study linked variability in left mOFC volume to skydive-induced euphoric experience, it should be noted that—given the nature of our euphoric induction—our sample size was relatively small, which limits the ability to detect more subtle brain-behavior relationships than that observed in the left mOFC. Thus, further research will be needed to both test the generalizability of this association to additional types of euphoric experiences and also assess, in a larger sample, the possibility of weaker associations in other brain regions. It should also be noted that the mOFC region identified here as correlating with euphoric experience is somewhat more ventral than that typically observed in fMRI-based reward-related tasks (Bartra et al. 2013). This apparent discrepancy between structure and function may in part be due to the well-known signal dropout affecting the most ventral aspects of the mOFC and ACC in gradient-echo fMRI. Finally, it should be noted that it is unclear if variability in left mOFC volume represents a predisposition for heightened euphoric experience or on the other hand, is the consequence of greater euphoric experiences across time. In either case, we show that subjective euphoric experience is linked to left mOFC volume, which may serve as a neural correlate of euphoria-related individual differences.

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