Brain Imaging and Behavior (2019) 13:1554–1565
https://doi.org/10.1007/s11682-019-00081-z

ORIGINAL RESEARCH

# Fronto-striatal activity predicts anhedonia and positive empathy subtypes

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Published online: 13 March 2019


## Abstract

The dorsolateral prefrontal cortex, globus pallidus, and nucleus accumbens are important components of the reward circuit in the brain; and prior research suggests individuals with damage to these regions feel less pleasure (i.e., are anhedonic). However, little is known about how these brain regions relate to vicarious pleasure. Pilot fMRI data were collected from 20 participants ($M_{age} = 22$, SD = 7.0, 63% female) during a validated empathy induction paradigm that utilized video clips extracted from the television show "Extreme Makeover: Home Edition" to elicit empathic happiness (i.e. vicarious happiness) when targets display positive affect, and either empathic cheerfulness (i.e. the tendency to want to cheer someone up) or empathic concern (i.e. vicarious sadness) when targets display negative affect. Participants also completed the novel "Happy Faces" task—a behavioral measure of anhedonia—while fMRI was collected. fMRI data during task completion were used to predict trait empathy measured via self-report outside of the scanner, and accuracy on the "Happy Faces" task. Results indicate that globus pallidus activity during empathic concern-eliciting video clips significantly predicted self-reported trait empathic cheerfulness ($R^2 = 26\%$, p = 0.045). Furthermore, greater dorsolateral prefrontal cortex (DLPFC) activity during the Happy Faces task predicted accurate performance on the task ($R^2 = 34\%$, $p < .05$); and greater nucleus accumbens shell activity during the Happy Faces task predicted greater trait empathic happiness ($R^2 = 38\%$, $p < .05$). These results suggest that fronto-striatal circuitry contributes to our experience of anhedonia, empathic happiness, and empathic cheerfulness.

**Keywords** fMRI · Positive empathy · Anhedonia

Empathy can be defined as the ability to feel emotions vicariously and experience an other-oriented feeling of goodwill (Light et al. 2015). Consummatory anhedonia can be defined as the reduced ability to experience pleasure once a reward is obtained. Reduced empathy and elevated consummatory anhedonia can present together (or individually) in a variety of neuropsychiatric and neurological disorders, including Major Depressive Disorder (i.e., MDD), schizophrenia, Parkinson's disease, and even some forms of dementia (e.g., frontotemporal dementia).

Both anhedonia and reduced empathy may be caused by a partially overlapping functional disruption in fronto-striatal circuitry (Dichter et al. 2009; Lindquist et al. 2013). The fronto-striatal circuit associated with positive affect is—at minimum—composed of dorsolateral (DLPFC) and orbitofrontal (OFC) prefrontal cortex, as well as ventral striatum (Kringelbach and Berridge 2012). Overall, research indicates that the interaction between populations of neurons within fronto-striatal sub-regions (e.g., neurons within OFC vs. DLPFC; and/or nucleus accumbens shell vs. core) likely support normal positive affect (Kringelbach and Berridge 2012; Berridge and Kringelbach 2015; Dichter et al. 2009). However, despite our knowledge of the underlying neural circuitry involved, etiological mechanisms are still elusive, as there are no FDA-approved medications for treating syndromes characterized by either elevated anhedonia or by empathy deficits (or both), even though both deficits are likely related to malfunction in this fronto-striatal brain circuitry.

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Nevertheless, there are some treatments that may help relieve positive affect deficits. Specifically, one behavioral intervention—Behavioral Activation—has demonstrable efficacy equal to that of Selective Serotonin Reuptake Inhibitors (SSRI's) in treating MDD (Soucy Chartier and Provencher 2013), a disorder that frequently features anhedonia as a prominent symptom. Unfortunately, there is still a need for more refined and targeted treatments because current debate in the field exists regarding whether current SSRI's and/or current and popularly used psychological/behavioral therapies adequately address positive affect deficits, above and beyond their known effects on reducing negative affectivity. Thus, developing treatments specifically targeted at positive affect-related symptoms is important because, for example, low empathy is associated with conduct disorder in children (Blair et al. 2014) and psychopathy in adults (Seara-Cardoso and Viding 2014); which places a huge burden on society. Similarly, anhedonia relates to an increased risk of suicide—in comparison to individuals who have MDD without anhedonia (Treadway and Zald 2011). Thus, both elevated anhedonia and impaired empathy can confer increased risk for the manifestation of externalizing and internalizing disorders, and threaten the stability of our communities. In particular, improved treatment for anhedonia as it presents in MDD would directly reduce morbidity in this specific patient population.

This pilot study was designed to investigate—using functional magnetic resonance imaging (fMRI)—two novel positively-valenced empathy subtypes at a basic science level in healthy controls, with the intention of providing a foundation for new therapeutic approaches to be developed to treat consummatory anhedonia. The most widely-recognized form of empathy, termed "empathic concern," generally refers to vicarious sadness. However, there are at least two additional subtypes of empathy (Light et al. 2009, 2015; Morelli et al. 2015), namely, "empathic cheerfulness" (i.e. the tendency to desire and act on the desire to cheer someone up) and "empathic happiness" (i.e. vicarious happiness). These subtypes were compared and contrasted with empathic concern using a novel empathy induction paradigm while fMRI data pertaining to blood oxygenation levels in the brain was collected. Empathic cheerfulness is generally elicited as an alternative to empathic concern, in that both subtypes of empathy are generally elicited in the same types of (adverse) circumstances in which a target person is demonstrating negative affect. By contrast, empathic happiness is elicited in circumstances in which a target is exhibiting positive affect (e.g., Light et al. 2009, 2015).

Our main hypothesis for this pilot project centers on the idea that these two particular positive empathy subtypes (i.e., empathic cheerfulness and empathic happiness, but not empathic concern) have specific neural correlates in subcortical structures associated with pleasure; namely structures of the ventral striatum already well-elucidated at the rodent level (Berridge and Kringelbach 2015). Therefore, we aimed to replicate this rodent level work (that has implicated striatal structures in pleasure)—at the human level. The other aim of our study was to extend this work to include discussion of frontal regions, and to determine whether use of a fronto-striatal framework can help explain the constructs of empathic happiness and empathic cheerfulness. Namely, consistent with neural simulation theories of empathy (Singer et al. 2004) and smile decoding theory (Niedenthal et al. 2010), it is likely that the same brain regions that mediate our first-person (subjective) experience of positive affect will also play a role in any vicarious experience of positive affect. Therefore, we hypothesized that specific fronto-striatal structures involved in the first-hand experience of pleasure (described below) would also become active during a positive empathy induction.

Another aim of this pilot project was to investigate the neural correlates of positive empathy subtypes in relation to consummatory anhedonia (the reduced ability to experience pleasure in response to obtained rewards) utilizing an investigational behavioral task called the "Happy Faces" task. During the Happy Faces task, each participant was asked to look at various human faces evincing neutral or varying degrees of positive emotion (while in the scanner). The participant was instructed to make a decision as to the presence or absence of positive emotion on each of 92 faces via button press (faces were taken from the well validated Cohn-Kanade dataset, which includes hundreds of images of human faces expressing spontaneous neutral and varying degrees of spontaneous positive emotion). A subset of the faces display "low intensity" positive emotion (i.e., subtle smiles), and a subset display "high intensity" positive emotion (i.e., frank smiles). The main idea behind the task is that individuals who are prominently anhedonic will differentially perform worse when trying to identify low intensity happy faces relative to high intensity happy faces. Thus the main hypothesis was that activity in the same brain regions implicated in empathic happiness and/or empathic cheerfulness would relate to performance on this novel anhedonia task in a sample of healthy adults (because positive empathy is hypothesized to be antagonistic with anhedonia).

For the purposes of this paper, and given prior research looking at the role of fronto-striatal structures in pleasure capacity, we chose a priori to focus on three inter-related regions of the fronto-striatal reward circuitry to test our ideas: two subcortical structures—namely, the globus pallidus and nucleus accumbens (core and shell)—and one prefrontal region, the dorsolateral prefrontal cortex (DLPFC). To understand our interest in investigating the specific role that these particular regions play in positive empathy subtypes and anhedonia, an understanding of the brain reward circuit is needed. The fronto-striatal reward circuit of interest includes the ventral tegmental area, which projects to the nucleus accumbens and the globus pallidus (Miller et al. 2006). The nucleus accumbens also projects to the globus pallidus, which in turn projects back to the ventral tegmental area. Rewarding stimuli provoke firing in the nucleus accumbens and globus pallidus (Tindell et al. 2004), causing release of dopamine. Furthermore, the nucleus accumbens links the dorsolateral prefrontal cortex with the globus pallidus, allowing for higher-order reward-seeking and misery-fleeing behaviors (Anton et al. 2016). The nucleus accumbens has been linked to consummatory and anticipatory pleasure (anticipatory pleasure refers to pleasure derived from the pursuit of rewarding stimuli whereas consummatory pleasure refers to pleasure derived from the actual attainment of a reward), depending on whether describing the shell or core of the nucleus accumbens, respectively (Berridge and Kringelbach 2015). Consummatory pleasure is thought to relate to the release of opioids versus dopamine. Consistent with this, the nucleus accumbens is found to be active in relation to both basic rewards, such as sweet tastes (Castro and Berridge 2014), and more abstract rewards, such as money (Kringelbach and Berridge 2012), which generally requires co-activation in the prefrontal cortex. Dysfunction in nucleus accumbens—prefrontal cortex connectivity, and lateral prefrontal cortex have been found to relate to anhedonia, as seen in psychiatric disorders such as MDD (Heller et al. 2009; Light et al. 2011).

The globus pallidus has been linked to reward, initiative, and well-being (Bhatia and Marsden 1994). Selective damage to this region can lead to apathy, a syndrome characterized by a lack of feeling concern, interest, or happiness. This region becomes of interest in relation to empathy because we hypothesize that there is a certain motivational component involved when an individual takes the perspective of someone else and then chooses to take action on behalf of that person. As a case in point, a case study about a 44-year-old man with anoxic bilateral globus pallidus lesions suggested that the integrity of the globus pallidus may relate to the linkage between hedonic appreciation (a person's ability to judge the "pleasantness" of a stimulus) and motivated action, with lesions resulting in a reduced ability to generate positive emotion and/or convert the positive emotional states generated into action (Vijayaraghavan et al. 2008). Consistent with this hypothesis, Dillon et al. (2009) found that adults with a history of childhood maltreatment demonstrated anticipatory pleasure deficits during a rewarding behavioral task. Specifically, poorer performance on the anticipatory pleasure task related to concomitant reduction in left globus pallidus activation. Similarly, Adam et al. (2012) reported on a patient who had a lesion in the (dorsal) internal globus pallidus; which is thought to have made him lose interest in most daily activities in life. After an extended period of testing, Adam et al. (2012) found that augmentative dopamine treatment significantly reduced this patient's apathetic behavior and enabled him to feel interest again. Importantly, the dopamine treatment did not lead him to report feeling "happy" again per se; rather, it seemed to increase his motivation to seek pleasurable activities once more. Lastly, Zacharopoulos et al. (2016) studied the globus pallidus in a sample of healthy adults and found that the larger the area is, the greater the individual's level of "hedonism"—which is the pursuit of pleasurable experiences.

Overall, these studies suggest roles for both the dorsal and ventral globus pallidus in motivation. As such, we were interested in investigating whether this region as a whole related to positive empathy. Although Berridge and colleagues have largely focused on the nucleus accumbens in their work with animal models, our review of the human literature suggested that the globus pallidus may play an important, yet nuanced role in positive emotionality at the human level.

The dorsolateral prefrontal cortex (DLPFC) and the orbitofrontal prefrontal cortex (OFC) are important regions of interest because they are strongly linked to the nucleus accumbens and globus pallidus, and prior research suggests that they are—in their own right—places where "happiness" or positive affect can be generated, particularly more abstract forms of positive affect. Indeed, the dorsolateral prefrontal cortex has been found to become active when an individual is experiencing subjective positive emotion, as activity is detected within this region—using fMRI methodology—during subjectively rewarding experiences (e.g., when winning money, or winning a game; Heller et al. 2013). Similarly, activity in the orbitofrontal prefrontal cortex is thought to relate to hedonic value, or how stimuli come to possess the quality of differing reward intensities. However, in this study we chose to focus analyses on the dorsolateral prefrontal cortex rather than the OFC, given our more reliable ability to accurately detect signal from the DLPFC versus the OFC using fMRI methodology.

In summary, we first a priori hypothesized that we would observe (1a) greater activity in dorsolateral prefrontal cortex, nucleus accumbens, and/or globus pallidus—during an empathy induction paradigm in which empathic happiness-eliciting video clips were viewed relative to empathic concern-eliciting video clips. Should this hypothesis be borne out, it would suggest that empathic happiness and empathic concern are neurally dissociable, and such information would provide a neurally informed theoretical basis for ascertaining whether trait empathic happiness or trait empathic cheerfulness also relate to brain activity in those same fronto-striatal regions during the empathy induction (1b). Our second hypothesis related to anhedonia. We predicted that greater accuracy on low intensity happy face trials of the "Happy Faces" task (i.e., our novel behavioral measure of anhedonia) would selectively relate to greater DLPFC, nucleus accumbens, and/or globus pallidus activation during concomitant correct low intensity happy face trials. Finally, our third hypothesis was that brain activation during the low intensity trials of the "Happy Faces" task would relate to higher self-reported trait empathic happiness. More specifically we predicted that nucleus accumbens shell activity would relate to empathic happiness due to a greater linkage to consummatory pleasure.

## Participants and methods

**Overview** Empathic cheerfulness, empathic happiness, and empathic concern were elicited utilizing a sample of 20 healthy adults by having them watch video clips extracted from a single episode of the television show "Extreme Makeover: Home Edition" while fMRI data were collected. The chosen video clips first show an underprivileged family that need their home remodeled, eliciting empathic concern and/or empathic cheerfulness. The second set of video clips show the family's happy reactions to the renovations made to their home, which tends to elicit empathic happiness. Trait empathy was measured via self-report using the Light-Moran Positive Empathy Scale (Light et al. 2015) outside of the scanner.

**Participant demographics and recruitment** Participants were recruited primarily using advertisements, which included a short study description and a brief listing of the eligibility criteria. Interested individuals were asked to contact the lab via an email address. Upon contacting the lab, potential participants were provided a detailed explanation of the study (i.e., they will undergo fMRI to study how the brain processes emotion while watching video clips and then they would complete a neuropsychological assessment to test their cognitive abilities) and informed about compensation at a rate of $25 per hour. A study eligibility screening form, medical history questionnaire, and MRI safety screening form were all completed over the phone. Participants were included in the study if they were 18 years or older, right-handed, had normal or corrected to normal vision, and were fluent in English. Individuals who were not free of neurological and psychiatric disorders and at risk for undergoing an MRI scan were excluded. All procedures were reviewed and approved by the Center for Advanced Brain Imaging (CABI) Institutional Review Board (IRB). A total of 20 individuals participated in the study. In this sample, the average age was 22 (SD = 7), and 63% were female. Ethnicity in the sample was 35% Caucasian, 30% African American/Black, 25% Hispanic, and 10% Asian.

**Study procedures** Participants completed all study procedures in one visit, lasting no longer than 3 h, at the Georgia State University/Georgia Institute of Technology Center for Advanced Brain Imaging (CABI). Upon arrival, a graduate student explained the study procedures and written informed consent was obtained. Participants were informed that the study was voluntary and they could withdraw at any time without penalty. Next, the participant underwent fMRI scanning while completing the "Empathy Task" and the "Happy Faces Task" (see descriptions below). Following the scan, participants were administered a battery of neuropsychological tests. Finally, they were debriefed and compensated.

**Empathy induction paradigm** This study utilized an ecologically valid empathy induction paradigm (Light et al. 2015) consisting of video clips from an episode of the television show Extreme Makeover: Home Edition. The episode that participants viewed depicts an African–American woman (Alice) and her family (living in Los Angeles, California) whose home was ruined by a devastating and rare flood. The beginning of the episode shows the viewer why the family needs a remodeled home. This first half of the episode elicits peak empathic concern. In the second portion of the show, the design team reveals the remodeled home to the family. This last half elicits peak empathic happiness.

This paradigm consisted of 18 video clips in total, three that elicit peak empathic concern/empathic cheerfulness (in the first half of the episode) and thirteen that elicit peak empathic happiness (in the second half of the episode), with two neutral clips embedded among the empathy-inducing clips. The average length of the video clips was 1 min, with a range of 0.18–6.26 min. All video clips were presented in sequential order to maintain the integrity of the story and make it ecologically valid. The paradigm was administered using Psychopy software, and neuroimaging data was collected using a Siemens 3 T MRI scanner. The paradigm consisted of 18 runs with each run starting with a fixation screen for 6 s, then the empathy inducing or neutral video clip, followed by another 6 s of fixation, then the state empathy rating scales (Light et al. 2015; Fig. 1).

**State empathy ratings** Participants were asked to rate their emotional reactivity immediately following each video clip to determine the subjective degree to which each video clip evoked an empathic emotional response exactly as in a previous study (Light et al. 2015). Participants were instructed to respond by pressing the corresponding button on an MRI-compatible button box. The participants rated the presence or absence of empathic concern and empathic happiness on a continuous scale from 1 to 4 with higher numbers indicating more empathy. Eleven of the thirteen questions asked if the participant felt interest, personal joy, personal contentment, alarmed, troubled, grieved, upset, worried, disturbed, perturbed or distressed. Each participant made a rating for each of these emotional states using a scale of 1 to 4, with 1 representing the absence of the emotion in question, 2 = somewhat, 3 = moderately, and 4 = extremely. Participants also had to rate how much positive empathy they felt on a 1 to 4 scale; with 1 = neutral/none of these emotions, 2 = contentment/happiness because I perceive the happiness/contentment of one or more of the people in the video clip, 3 = serene (i.e. a feeling of happiness or contentment marked by a feeling of being inspired or moved emotionally; mental tranquility), and 4 = I feel good because I can tell that one or more of the people in the video feel good, the positive mood of one or more of the people in the video clip has substantially impacted me

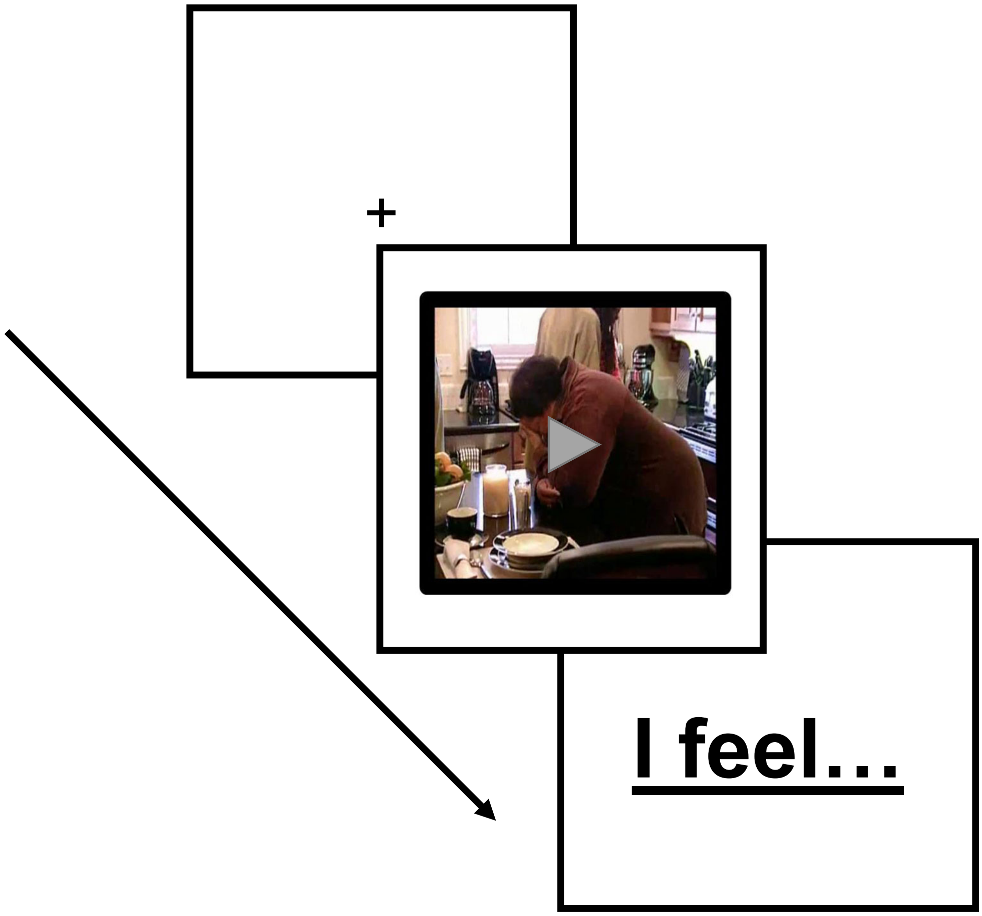


**Fig. 1** Schematic diagram of an experimental run of the empathy induction paradigm

mentally and/or emotionally. Finally the participant had to rate how much empathic concern they felt, with 1 = neutral/none of these emotions, 2 = sad, 3 = sad and concerned, and 4 = I feel bad because I can tell that one or more of the people in the video feel bad, are in pain, or are suffering emotionally, mentally, or physically, the negative mood of one or more of the people in the video clip has substantially impacted me mentally and/or emotionally. From their ratings, mean empathic concern and empathic happiness scores were derived. These scores were used as regressors at the individual level of fMRI data analysis. The empathy paradigm used in this study is weighted more heavily toward empathic happiness than concern or cheerfulness. In our prior study (Light et al. 2015), empathic cheerfulness was not reliably elicited by our video clips. However, in that study, the correlation between state empathic concern and state empathic cheerfulness was .61 ($p < .001$). Therefore, given the relatively good correlation between the two constructs, and the greater ease and accuracy of measuring empathic concern (and happiness) rather than adding an additional (third) scale to capture empathic cheerfulness, we opted not to measure it at the state level. Furthermore, the correlation between state empathic cheerfulness and state empathic happiness (measured by behavioral observation) in a child sample (Light et al. 2009) was .53 ($p < .01$). Again, taken together, these results suggested to us that the state measurement of empathic cheerfulness is much less reliable. Therefore, we chose to measure state empathic concern only given prior data suggesting that empathic cheerfulness reliably correlates with empathic concern.

**Measuring trait empathy** Participants completed the Light-Moran Positive Empathy Scale (Light et al. 2015) outside of the scanner. This 15-item self-report scale measures empathic happiness and empathic cheerfulness. Items are measured on a Likert-scale from 1 (not at all true) to 7 (extremely true). A sample from the empathic happiness subscale is: "I easily get excited when those around me are lively and happy." An example from the empathic cheerfulness subscale is: "I like making others see that they can turn lemons into lemonade." The inter-item reliability (Cronbach's alpha) for the total measure is .92 (Light et al. 2015). The 8-item empathic happiness subscale has a Cronbach's alpha of .87; and the 7-item empathic cheerfulness subscale has a Cronbach's alpha of .84. In an independent sample of 282 healthy adults, the correlation between trait empathic cheerfulness and trait empathic happiness was .76 ($p < .001$). Similarly, in the same study, the correlation between trait empathic concern and trait empathic cheerfulness was .54 ($p < .001$) (unpublished data).

**Measuring anhedonia** Participants also completed the "Happy Faces Task" while fMRI was collected. The "Happy Faces" task was designed as an initial and viable means by which to ascertain level of consummatory anhedonia in humans. During the Happy Faces task, participants were asked to look at human faces evincing either neutral or varying degrees of positive emotion. Previous work by others has focused on individuals' ability to correctly recognize/interpret the full set of discrete emotions, typically including sadness, anger, happiness, fear and sometimes neutral emotion. However, during the Happy Faces task, participants are simply instructed to make a decision as to the presence or absence of positive emotion only. Faces are taken from the well validated Cohn-Kanade dataset, which includes hundreds of images of human faces expressing spontaneous neutral and varying degrees of spontaneous positive emotion (Cohn et al. 1999; Ambadar et al. 2009). We used a large, natural (non-computer generated) range of smiling intensity, based on Ekman's FACS coding system, with a balance of gender (Fig. 2). Participants viewed neutral, "high intensity" positive faces, and "low intensity" positive faces, distinguishable based on FACS coding whereby low intensity faces only involved zygomaticus muscle movement, whereas "high intensity" happy faces required zygomaticus and orbicularis muscle involvement. Faces were presented in random order. We looked at "high intensity" versus "low intensity" faces relative to "neutral" faces in our analyses. Participants' performance on the task is hypothesized to be an indicator of their ability to detect, interpret, and appreciate different degrees of positive emotion via the face, and this ability is hypothesized to vary as a function of anhedonia; such that poorer performance on the task should relate to higher anhedonia. The "Happy Faces" task was initially validated on a separate sample of 19 clinically depressed adult patients using the Snaith-Hamilton Pleasure Scale (unpublished data). The Happy Faces task demonstrated good scale reliability with a Cronbach's alpha value equal to .83 within that sample of participants.

**Neuroimaging parameters** All MRI data were acquired on a Siemens 3 T Magnet Trio MRI scanner. A high-resolution T1 structural scan (3D MPRAGE, TI = 850 ms, field of view = 256 ms, flip angle = 9°, 1 mm isotropic resolution) was acquired before the start of the paradigm, and was used for anatomical registration. Functional images were obtained using a whole-brain echo-planar imaging sequence sensitive to blood oxygenation level-dependent (BOLD) signals (transverse orientation, TR = 2000 ms, TE = 30 ms, flip angle = 90°, field of view = 204 mm) of 37 interleaved slices with 3 mm isotropic resolution and a 17% gap.

**Preprocessing of fMRI data** fMRI data analysis was conducted using Analysis of Functional Neuroimages (AFNI) software from the National Institutes of Health (http://afni.nimh.nih.gov/afni). The following preprocessing steps were applied to the data using the Afni_proc.py program: (1) truncate spikes in each voxel's time series, (2) correct slice timing of the EPI images, (3) align EPI to the anatomical scan, 4) warp anatomy to MNI standard space, 5) spatial smoothing with a 6 mm full-width half-maximum three-dimensional Gaussian filter to account for small variations in signal due to movement and vascular effects (i.e., noise), (6) masking, (7) scaling, and (8) motion correction using six head motion parameters as nuisance regressors.

**Individual level processing of fMRI data** A general linear model (GLM) analysis was conducted on the data for each participant using AFNI's 3dDeconvolve tool. This included six head movement parameters and constant, linear, and quadratic trends as nuisance regressors. For each individual, a whole-brain map of beta coefficients was created associated with three contrasts of interest (e.g. Empathic Concern - Empathic Happiness; Correct Low Intensity Happy Face Trials – Neutral Face Trials; and Correct High Intensity Happy Face Trials – Neutral Face Trials). State empathy ratings were used as additional regressors in the empathy-related individual level model.

**Group level processing of fMRI data** Resulting beta-maps from particular contrasts (e.g. Empathic Concern - Empathic Happiness) from individual level analyses were subjected to second-level group analyses in the form of one-sample t-tests. The resulting t-maps were thresholded at a corrected family-wise error level of $p < .05$.

**Regions of interest analysis** Regions of interests (ROIs) were identified for the following regions: dorsolateral prefrontal

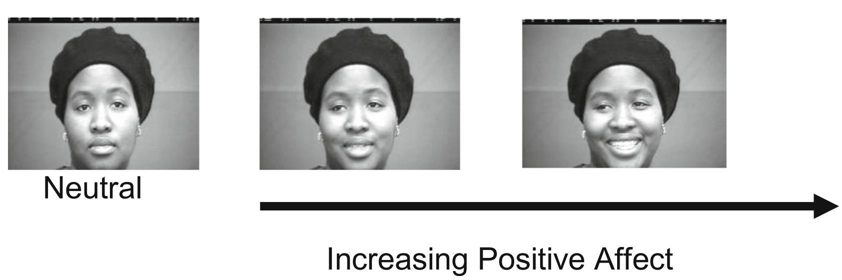


**Fig. 2** Sample range of emotions for the Happy Faces Task, it should be noted that participants did not view these faces in progressive order, the order was randomized

cortex (DLPFC), globus pallidus, and nucleus accumbens (core and shell), based on prior literature (Table 1). The globus pallidus ROI consisted of a sphere with a radius of 10 mm centered on the voxel of peak activity reported in Cauda et al. (2011). Masks for the nucleus accumbens core and shell ROIs were created to match the shapes originally reported in Baliki et al. (2013). Masks for the dorsolateral prefrontal cortex ROIs were created to match the shapes originally reported in Heller et al. (2013). Parameter estimates from these ROIs for the empathic concern and empathic happiness contrasts were extracted and analyzed using SPSS.

## Results

**Behavioral performance on the empathy task, Light-Moran PES scores, and the happy faces task** On the Empathy task, the average state empathic concern rating across empathic concern-eliciting video clips was 1.67 (SD = .489), and the average state empathic happiness rating across empathic happiness-eliciting video clips was 2.68 (SD = .69). In the current sample, the correlation between trait empathic cheerfulness and trait empathic happiness (as measured by the Light-Moran PES) was .812 ($p < .001$). On the Happy Faces task, participants performed better at recognizing faces exhibiting high positive affect ($M_{Accuracy} = 88.1\%$, SD = 13.5401) compared to low positive affect ($M_{Accuracy} = 37.6\%$, SD = 23.4052), $p < .001$.

**Hypothesis 1a: On average, greater fronto-striatal activity (in any of the following regions: DLPFC, nucleus accumbens, and/or globus pallidus) will occur during empathic happiness eliciting video clips relative to empathic concern eliciting video clips.** A whole-brain GLM comparing activity during empathic concern-eliciting video clips minus activity during empathic happiness-eliciting video clips (corrected at $p < .05$) revealed that empathic concern was associated with increased activity in medial frontal and anterior cingulate cortex, whereas empathic happiness was associated with increased activity in lateral prefrontal cortex (Fig. 3). **Hypothesis 1b:** We then looked to see whether activity in subcortical nodes of this fronto-striatal network during the empathy induction related to trait empathic happiness and/or trait empathic cheerfulness. Results revealed that greater activity in the globus pallidus during empathic concern-eliciting video clips predicted trait empathic cheerfulness score ($R^2 = 26\%$, $p < .05$; Fig. 4).

**Hypothesis 2: Fronto-striatal activity during "low intensity" trials of the Happy Faces task will selectively relate to accuracy on those corresponding low intensity trials of the Happy Faces task.** A whole-brain GLM comparing activity during correct low intensity happy face trials versus correct neutral trials, revealed that correctly recognizing low intensity positive affect versus correctly identifying neutral affect during the Happy Faces Task was associated with increased activation in the dorsolateral prefrontal cortex ($R^2 = 34\%$, $p < .05$; Fig. 5). A whole-brain GLM comparing activity during correct high intensity happy face trials versus correct neutral trials, revealed that recognizing high intensity positive affect versus neutral affect during the Happy Faces Task was not associated with any significant regions of activation.

**Hypothesis 3: Brain activation in fronto-striatal regions during correct low intensity "Happy Faces" trials will predict higher self-reported trait empathic happiness score.** Using the ROI method—as predicted—greater activity in the nucleus accumbens shell during low intensity happy face trials relative to neutral trials predicted greater empathic happiness trait score (as measured using the Light-Moran PES Empathic Happiness subscale) ($R^2 = 38\%$, $p < .05$; Fig. 6). Analyses using the ROI method did not reveal any significant effects with high intensity happy faces.

**Table 1** A priori brain regions of interest

| Region of interest | MNI coordinates | | | Reference |
|---|---|---|---|---|
| | x | y | z | |
| Globus Pallidus | 23 | −8 | −3 | (Cauda et al. 2011) |
| Nucleus Accumbens Core | 10 | 14 | −8 | (Baliki et al. 2013) |
| Nucleus Accumbens Shell | 10 | 8 | −8 | (Baliki et al. 2013) |
| Dorsolateral Prefrontal Cortex | −40 | 42 | 34 | (Heller et al. 2013) |

## Discussion

Overall we found support for our a priori hypothesis that nodes of the fronto-striatal reward circuitry differentially related to empathic happiness versus empathic concern. Medial prefrontal cortex related to empathic concern, whereas lateral prefrontal cortex (e.g., DLPFC) differentially related to empathic happiness. This supports prior evidence collected at the behavioral level of analysis (Light et al. 2015) that empathic

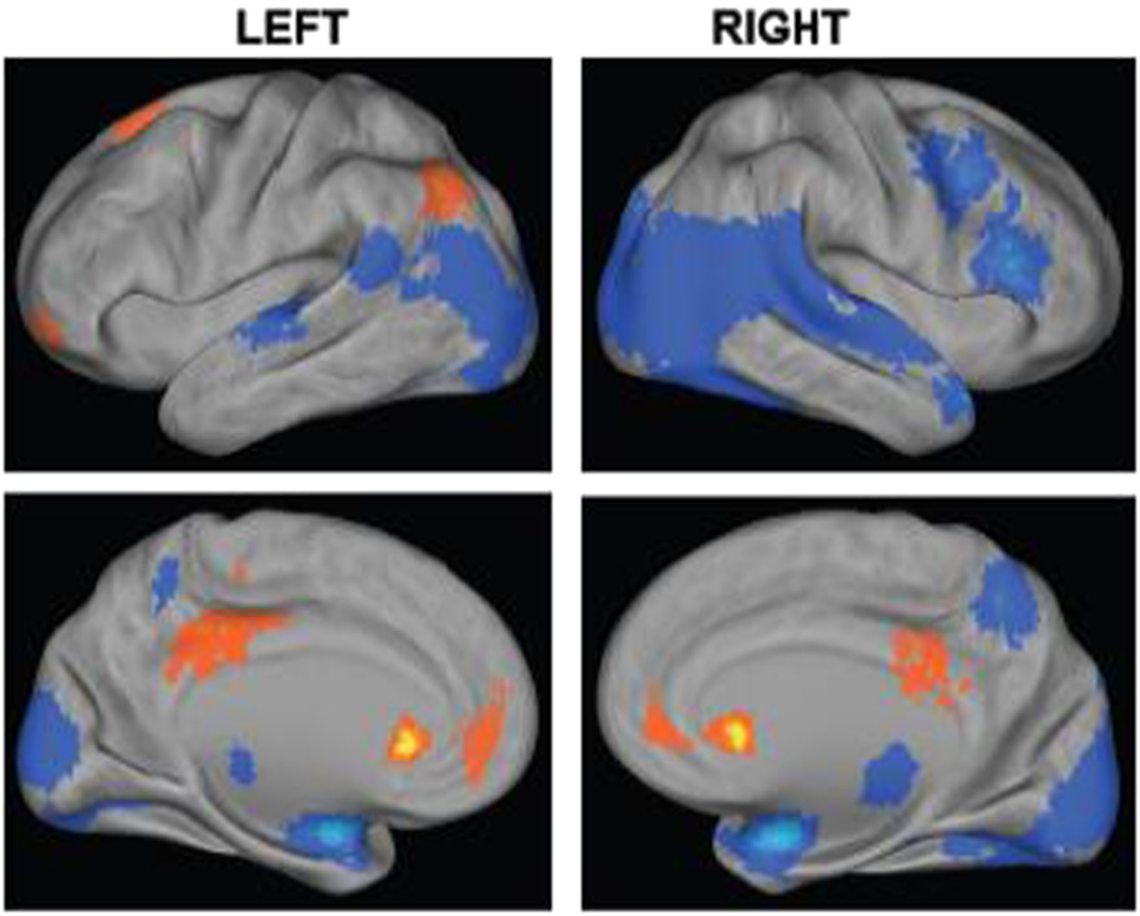


**Fig. 3** Whole-Brain Analysis. Orange represents areas more active during empathic concern (e.g., medial prefrontal cortex and anterior cingulate), and blue areas represent areas more active during empathic happiness (e.g., dorsolateral and ventrolateral prefrontal cortex)

concern and empathic happiness are distinct constructs (Hypothesis 1a). Furthermore, our analysis revealed that increased activity in the globus pallidus during empathic concern-eliciting video clips specifically related to higher levels of trait empathic cheerfulness (Hypothesis 1b). This replicates the previously reported correlation between empathic concern and empathic cheerfulness in children (Light et al. 2009) in an adult sample, and suggests that there is a positive linear relationship between situations that evoke empathic concern and the tendency to experience trait empathic cheerfulness.

Nevertheless, we did not observe a direct link between activity in nucleus accumbens (i.e., nucleus accumbens shell in particular) during the empathy induction and trait empathic happiness, as hypothesized. This suggests that the relationship between empathic happiness and subcortical activity may be more nuanced. In support of this, our hypothesis regarding the intersection between anhedonia and empathic happiness was supported; as activity in the nucleus accumbens shell during correct low intensity trials of the Happy Faces Task predicted higher trait empathic happiness (Hypothesis 3). Thus, there appears to be an indirect relationship between nucleus accumbens activity and empathic happiness such that nucleus accumbens activity promotes the accurate identification of subtle positive emotion in others, and this identification relates to trait empathic happiness.

Finally, we found that greater activity in the dorsolateral prefrontal cortex (DLPFC) during low-intensity happy face trials was associated with increased accuracy on those trials; providing preliminary evidence that performance on the Happy Faces task does map onto the functioning of at least one brain region known to be prominently involved in positive emotionality (Hypothesis 2).

The literature has shown that damage to the prefrontal cortex can be linked to changes in emotionality/personality. Specifically, when there is damage to the dorsolateral prefrontal cortex (DLPFC), people lose their will to act, and with this, their ability to differentiate/experience positive emotions and detect subtle positive emotions in others may selectively deteriorate as well (Szczepanski and Knight 2014; Anderson et al. 2006).

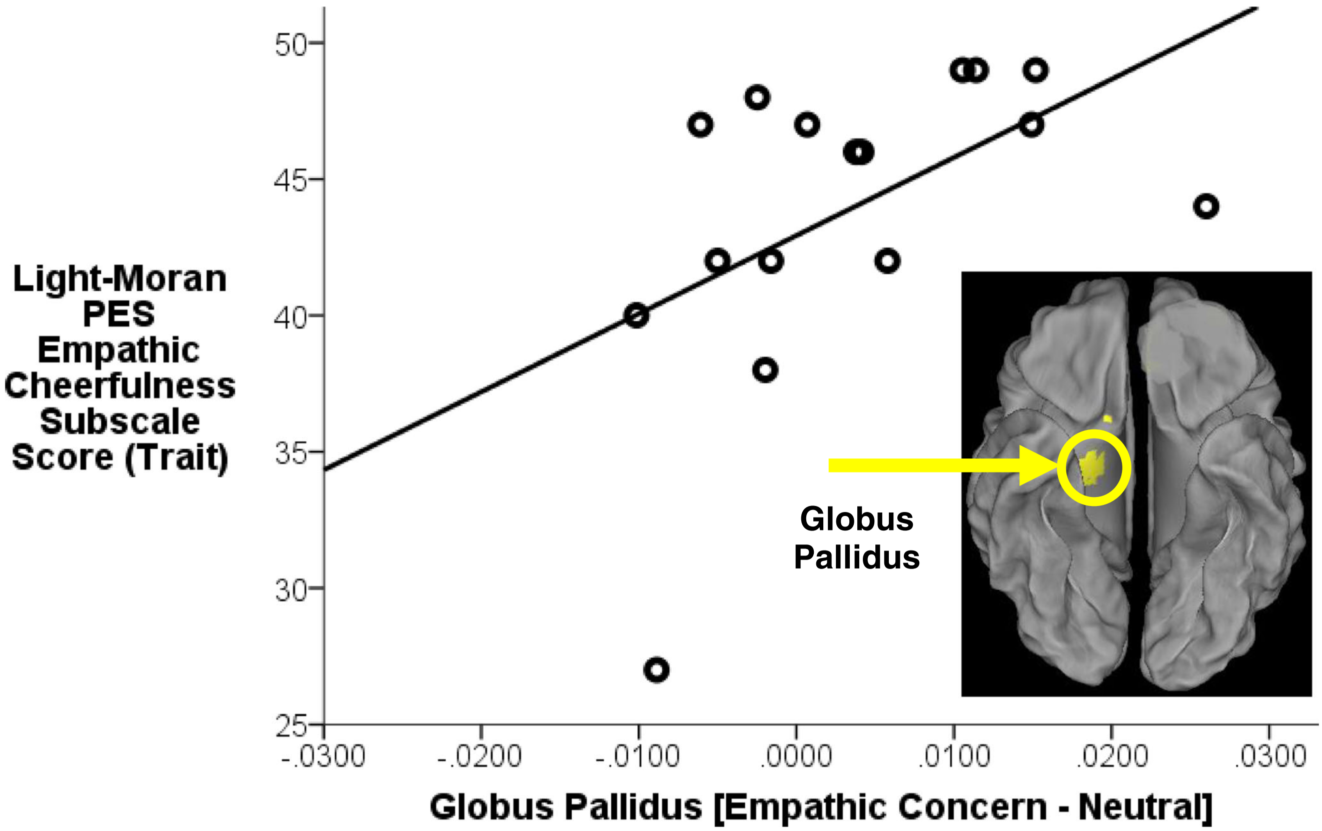


**Fig. 4** As activity in the globus pallidus increases during empathic concern inducing video clips, the greater the trait empathic cheerfulness score ($R^2 = 26\%$, $p < .05$)

Consistent with this, our findings related to the dorsolateral prefrontal cortex (DLPFC) suggest that the more active this region is, the more easily we are able to detect and interpret subtly positive stimuli (e.g., a subtle smile on the face of a peer). The ability to "see" even the slightest positive affect in others is probably beneficial from a psychological and general health standpoint. This ability likely buffers against anhedonia and leads to greater subjective (personal) happiness/joy. Specifically, it may be that activity in this region plays an important role in the mental representation of the positive emotion of someone else, and may also then play a role in transforming that perception into an actual experience of positive emotion in the observer.

Research has shown that damage to the globus pallidus can result in apathy. Our results indicate that increased activity in this region of the brain while viewing empathic concern-eliciting video clips relates to higher levels of trait empathic cheerfulness. Activity in this region may provide a platform upon which an ingrained "urge" to act in a positive manner is initiated and helps activate a motor program in the DLPFC when faced with the suffering of someone else; in an effort to increase the other person's comfort and happiness.

These findings may have implications for targeted treatment development. The discovery of a drug that specifically hones these rich opioid and dopaminergic regions to help combat the symptom of low empathy is needed. The current findings shed new insight by illuminating not only regions of the brain that could be targeted, but providing some basic information about how these systems may cooperate together. For example, although past research has shown that the globus pallidus is essential for effective decision making (Clark et al. 2004), the present results add to our knowledge by implicating this region in vicarious positive emotionality and empathic decision-making. In particular, our findings suggest that, in keeping with this region's known role in motivated behavior, activity here relates to the subtype of empathy that has a notably action-oriented component. Further research is needed to determine whether activity in this region directly kick-starts the actual motor program in DLPFC. It may be that dysfunction in the globus pallidus signals not only little or no motivation to engage in rewarding activities, but also an inability to engage in social behaviors that would increase personal (subjective) positive affect. Therefore, developing treatments that target this region

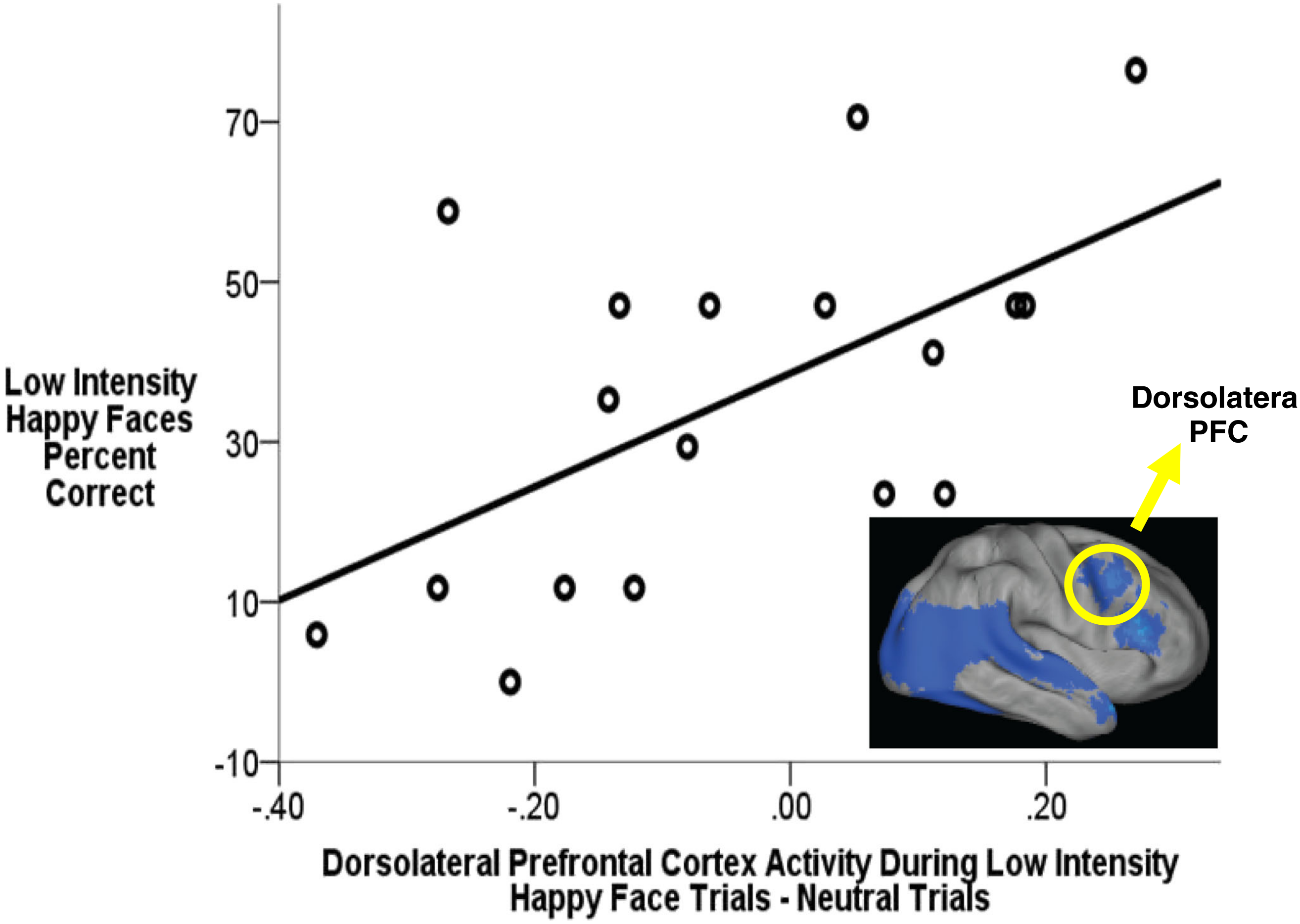


**Fig. 5** The more active the dorsolateral prefrontal cortex was during correct low intensity happy face trials (relative to correct neutral trials), the greater the percentage of low intensity happy face trials the participant identified correctly ($R^2 = 34\%$, $p < .05$)

and the DLPFC could potentially allow patients to achieve the necessary motivation to make decisions and perform actions that will increase their subjective positive affect.

The nucleus accumbens shell was active during the correct processing of low intensity happy faces, and this activity predicted increased trait empathic happiness. The nucleus accumbens shell is generally thought to relate to consummatory pleasure, which occurs in the moment when a reward is obtained. This finding thus suggests that vicarious joy is in the "consummatory pleasure" family, and this may have implications for how we think about "hedonic hotspots" (Berridge and Kringelbach 2015) at the human level. In particular, future research will need to focus on whether the induction of empathic happiness enables us to actually feel supra-levels of happiness. If this hypothesis pans out, empathic happiness may be utilized as an intervention to achieve higher levels of happiness. We predict that this may become one of the front-runners in treating the symptom of anhedonia, because such a treatment likely would not pose the risk of addiction that certain pharmacological treatments often do.

Overall, these findings lay a foundation for better understanding how key positive affect constructs relate to underlying neural mechanisms. Research to date shows that the ventral striatum in general, and the nucleus accumbens in particular, is rich in dopaminergic and opioid neurotransmitters, which likely mediate this region's role in reward processes (Berridge and Kringelbach 2015). However, little attention has been paid to the globus pallidus specifically; or how the globus pallidus, nucleus accumbens, and dorsolateral prefrontal cortex may work together in subjective happiness and positive empathy. Here we have provided preliminary evidence for these regions' role in anhedonia, vicarious happiness, and empathic cheerfulness.

In conclusion, it will be important to conduct more research in this area with medical populations rather than the small healthy control population used in this study. We do understand and want to acknowledge that our study was underpowered to detect small effects. For

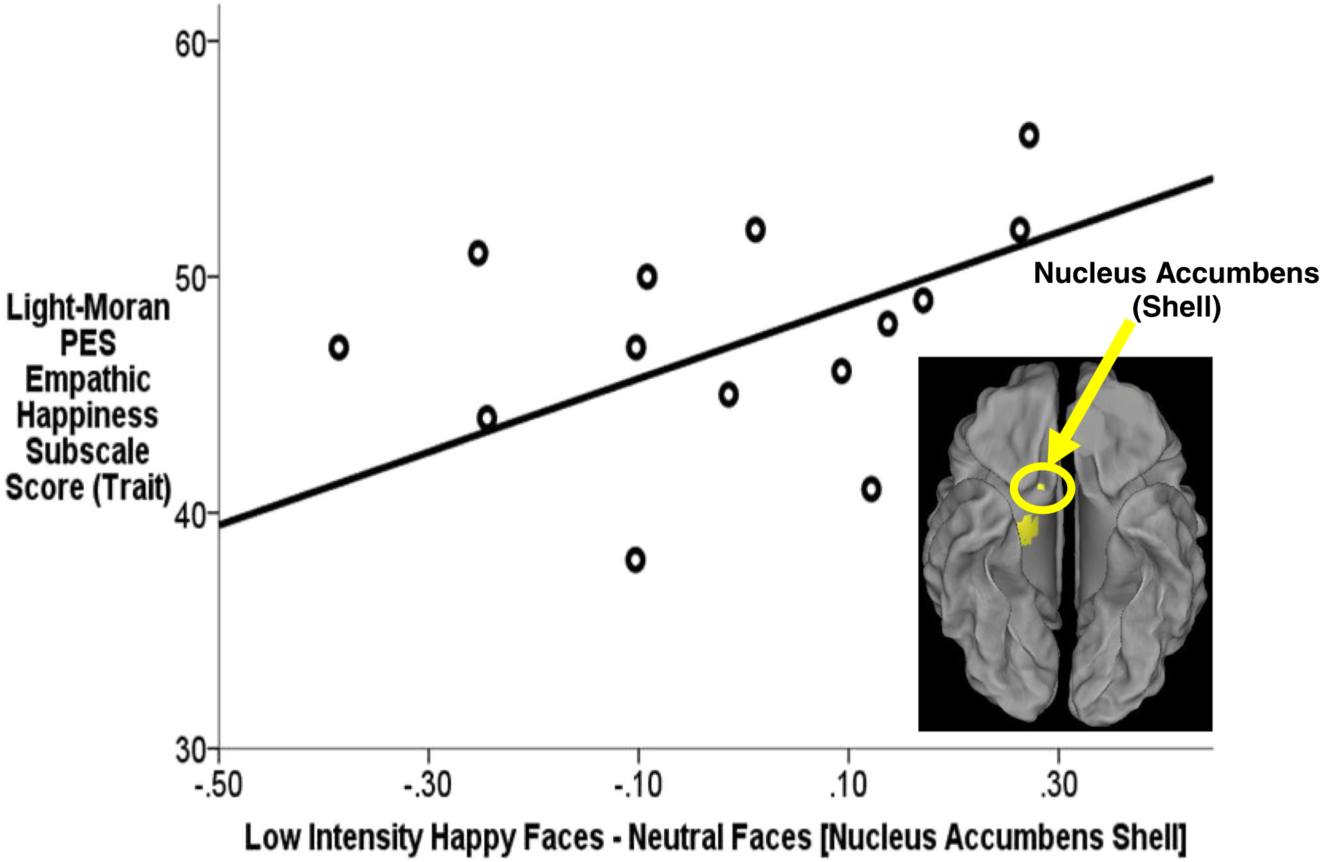


**Fig. 6** Greater activity in the nucleus accumbens shell during low intensity happy face trials relative to neutral trials predicted greater trait empathic happiness score ($R^2 = 38\%$, $p < .05$)

example, high intensity happy face trials may yield useful information in a larger sample. Thus, replication of this research is necessary with a larger sample size. Ultimately, we want to further understand these regions' role in positive emotionality so that researchers can pinpoint just how best to manipulate activity in these identified brain areas for treatment purposes; whether that be through techniques such as deep brain stimulation, rTMS, or behavioral treatments.

**Funding** This study was funded by a 2015–2016 Seed grant from the Joint Georgia State University/Georgia Tech Center for Advanced Brain Imaging (CABI).

## Compliance with ethical standards

**Conflict of interest** Grazia Mirabito declares that she has no conflict of interest. Zinat Taiwo declares that she has no conflict of interest. Dr. Matt Bezdek declares that he has no conflict of interest. Dr. Sharee N. Light declares that she has no conflict of interest.

**Ethical approval** All procedures performed were in accordance with the ethical standards of the Center for Advanced Brain Imaging Institutional Review Board (IRB) and with the 1964 Helsinki declaration and its later amendments. Informed consent was obtained from all individual participants included in the study.

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