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Neural Signals of "Intensity" but not "Wanting" or "Liking" of Rewards may be Trait Markers for Depression.

Short title: Subjectitve reward and depression risk.

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Abstract

We have shown previously that particpants “at risk” of depression have decreased neural processing of reward suggesting this might be a neural biomarker for depression. However, how the neural signal related to subjective experiences of reward (wanting, liking, intensity) might differ as trait markers for depression, is as yet unknown.

Using SPM8 parametric modulation analysis the neural signal related to the subjective report of wanting, liking and intensity was compared between 25 young people with a biological parent with depression (FH) and 25 age/gender matched controls. In a second study the neural signal related to the subjective report of wanting, liking and intensity was compared between 13 unmedicated recovered depressed (RD) patients and 14 healthy age/gender matched controls.

The analysis revealed differences in the neural signal for wanting, liking and intensity ratings in the ventral striatum, dmPFC and caudate respectively in the RD group compared to controls . Despite no differences in the FH groups neural signal for wanting and liking there was a difference in the neural signal for intensity ratings in the dACC and anterior insula compared to controls.

These results suggest that the neural substrates tracking the intensity but not the wanting or liking for rewards and punishers might be a trait marker for depression.

Introduction:

Anhedonia has been suggested as an endophenotype of depression which may manifest in behavioural and neural outcome measures outside acute depressive episodes (Hasler et al., 2004). Further anhedonia has been suggested as a strong predictor of the onset of major depression (Dryman and Eaton, 1991) and in a group of patients with chronic depression followed up for a year, Schrader (1997) found that anhedonic symptoms remained fairly constant despite depression remission and that anhedonia scores correlated with the presence of depression in first-degree relatives, suggesting a genetic link between anhedonia and the risk of depression (Schrader, 1997).

We have examined this in our previous studies using a paradigm involving the sight and taste of chocolate to probe reward circuitry in unmedicated recovered depressed (RD) patients (McCabe et al., 2009) and in young people with a family history of depression (FH) (McCabe et al., 2012). We found that those "at risk" of depression have inconsistent processing of unpleasant taste and picture stimuli, with increases in the caudate (perhaps in line with the theory of increased negative biases in depression (McCabe et al., 2009; McCabe et al., 2012)) but also reduced responses to unpleasant stimuli in the anterior cingulate cortex and lateral orbitofrontal cortex, which might indicate an emotional blunting effect. Furthermore, we found reduced response to chocolate reward in RD participants in the anterior cingulate cortex, and consistently also in FH participants, suggesting that abnormalities in the neural basis of reward may be a trait marker of vulnerability to depression. Interestingly, we did not find impaired ventral striatal reward responses in the FH group which suggests that the latter abnormality might only develop through the course of recurrent depressive illness or its treatment (McCabe et al., 2009; McCabe et al., 2012). Although Gotlib et al did find impaired striatal responses to reward in young at-risk individuals using reward paradigms (Gotlib et al., 2010) their task demanded a higher level of incentive (wanting) responses compared to ours. This might then suggest that only certain aspects of reward responding, the "wanting", as opposed to the "liking/pleasantness" of the reward is a trait marker for depression. For example anhedonia is thought to consist of reward-processing components of 'wanting' and 'liking' also described as the diminished

incentive to pursue reward (appetitive, motivational processes: wanting) and the hedonic response to reward (consummatory processes; liking/pleasantness) (Berridge and Robinson, 1998a; Berridge and Robinson, 2003). How these sub components of reward might be affected in depression is of importance to the field, for knowing if it is the motivation (wanting) to gain reward or the actual experience (liking) of reward that is deficient and a trait marker for depression, could help us tailor both interventions and treatments more effectively (Simmons and Drevets, 2012). This may in part be due to the majority of behavioural experiments in depression focusing on the hedonics of reward whereas most neurobiological studies to date focus on the motivation and wanting for reward, as has been recently reviewed (Treadway and Zald, 2011). Even in our own studies of reward processing (described above) we have presented both pictures (appetitive/wanting) and tastes (consummatory/liking) of reward together which unfortunately then does not clearly differentiate the processes involved.

One way to begin to address these issues is to examine the neural signal elicited during the ratings of "pleasantness" and "wanting" during reward and aversion processing in our fMRI tasks. This will allow us to gain insight into how the neural correlates of the separate dimensions of the reward experience, consummatory (pleasantness) vs. appetitive (wanting) processing, might differ as trait abnormalities in those at risk of depression.

The present study therefore utilised the parametric modulation design matrix to examine how brain activity varies as a function of the subjective ratings "wanting" and "pleasantenss" in our RD and FH groups compared to age and gender matched controls (McCabe et al., 2009; McCabe et al., 2012). We and others have previously used parametric modulation analysis to examine correlations between brain responses and behavioural ratings in healthy controls (Grabenhorst et al., 2007; McCabe and Rolls, 2007; Rolls and McCabe, 2007). Parametric modulation simply means to examine how activity in a brain area is more (or less) sensitive to a given variable (rating).

Given the preclinical data eloquently demonstrating the dependency on dopamine rich striatal regions in the brain for "wanting" of rewards (Berridge and Robinson, 1998b) and the data illustrating the role of the opioid rich nucleus accumbens and medial prefrontal cortex, incorporating the orbitofrontal cortex and the anterior cingulate cortex in the hedonics of reward (Pecina et al., 2006) for review see (Treadway and Zald, 2011; Castro and Berridge, 2014), stronger correlations in these regions to the "wanting" and "liking" of the pleasant stimuli in the healthy control subjects vs. those "at risk" of depression were hypothesised. Further, studies also examining correlations between subjective ratings of pleasantness and wanting with brain activity have found prefrontal cortex and pregenual cingulate regions tracking pleasantness, whilst the anterior insula was found to track instead the "intensity" or sensory properties of experiences (Rolls et al., 2003; Rolls and McCabe, 2007; McCabe and Rolls, 2007; Grabenhorst et al., 2007; de Araujo et al., 2003; de Araujo et al., 2005; Anderson and Sobel, 2003).

Little work has been done on the intensity perception of taste rewards in depressed patients, some reports suggests sucrose is found less intense (Amsterdam et al., 1987) (Steiner et al., 1969) while more recently a study has found sucrose to be rated more intense in those with higher scores on depression questionnaires (Platte et al., 2013) whilst others have found no difference (Scinska et al., 2004). Although there is no data on the neural systems underlying taste intensity in depression, we hypothesised difference might be found in regions like the medial orbitofrontal cortex and anterior insula which we found to track intensity ratings in healthy volunteers using a similar design (Rolls and McCabe, 2007) and in studies examining the neural representation of the intensity of odors (Grabenhorst et al., 2007).

So the aim of the current study was to examine how brain activity relates to ratings of pleasantess, wanting and intensity of positive and negative taste stimuli (parametric modulation) in two "at risk" depression groups, those who have a family history (FH) of depression (no personal experience) and in those with a history of depression and now recovered (RD). This analysis will begin to uncover neural characteristics associated with being "at risk" before depression onset and after depression onset.

Methods:

The methods for collecting both RD and FH data sets have been previously published (McCabe et al., 2009; McCabe et al., 2012) but summarised again here. To be included in the recovered depressed group, the participants were required to meet criteria for at least one episode of major depression as a primary diagnosis using the structured clinical interview for DSM-IV (Spitzer et al., 2004). Recovery was determined in the same week as the study through clinical interview and with the Hamilton Depression Scale (HAM-D) (Hamilton, 1960) using a cut off score of 8. None of the participants took current medication apart from the contraceptive pill and the recovered depressed group had been free of antidepressant medication for a mean of 4.9 years (range=1.7-7years). Exclusion criteria for all subjects consisted of current or past history of alcohol or drug dependency, pregnancy and any contraindications to MRI e.g. pacemaker, mechanical heart valve, hip replacement, metal implants. Further the control group were determined to be free of current or past Axis-1 disorder on the structured clinical interview for DSM-IV (Spitzer et al., 2004).

For the FH study we recruited young people (age range 16–21 years) who had never personally suffered from major depression but who reported a biological parent with a history of major depression (FH). Potential participants were assessed on the structured clinical interview for DSM-IV (Spitzer et al., 2004) to exclude a personal current or previous history of major depression or any other Axis 1 disorder. The presence of major depression in a parent was assessed by the family history method using the participant as an informant (Andreasen et al., 1977). Parents were then approached directly with a standardised questionnaire. We included participants where a diagnosis of clinical depression had been made by a general practitioner and/ or psychiatrist and the symptoms described met criteria for major depression, together with the prescription of specific treatment, either psychotherapy or medication (all but one of the parents had received antidepressant medication at some stage of their illness). A history of bipolar disorder in a parent was an exclusion criterion. We also recruited controls (age range 16–21 years) who were determined by the same instruments to have no current or past history of major depression and no history of depression in a biological parent or

other first degree relative (HC). All participants were right handed, according to the Edinburgh Handedness Inventory (Oldfield, 1971) and had normal or corrected to normal vision. All subjects were rated on the following questionnaires: Beck Depression Inventory (BDI) (Beck et al., 1961) the Fawcett-Clarke Pleasure Scale (FCPS) (Fawcett et al., 1983), and the Snaith-Hamilton Pleasure Scale (SHAPS) (Snaith et al., 1995) approximately 1 week before scanning. The participants also completed a "chocolate questionnaire" to measure liking, craving and frequency of eating chocolate (Rolls and McCabe, 2007) and the body mass index (BMI) for each individual was also calculated. Ethical approval was provided by the Central Oxford Research Ethics Committee and written informed consent was obtained from all participants before screening and after the complete description of the study was given.

Overall design

The experimental design was the same for all groups. Each of the following six stimuli were applied nine times in a randomised order: chocolate in the mouth, chocolate picture, chocolate in the mouth with chocolate picture, medicinal-flavoured strawberry in the mouth, unpleasant strawberry picture (strawberries with mould on them), strawberry in the mouth with strawberry picture (for details see Table S1). Subjective effects of the stimuli were measured on a likert scale rating of "pleasantness", "intensity", and "wanting" made on every trial (36) by the subjects during the fMRI acquisition. The specific instructions were: "Please rate the pleasantness of what is in your mouth (please use the scale so that +2 is very pleasant, 0 is neutral, and -2 is very unpleasant). Please rate how much you want the taste (please use the scale so that +2 is that you want it very much, 0 is neutral, and -2 is that you very much do NOT want it.) Please rate the intensity of what was in your mouth (please use the scale so that 0 is not intense at all and +4 is very intense)". The participants were instructed not to eat chocolate for 24 hrs before the scan, and to eat only a small breakfast on the day of scanning. Mood state was recorded on the study day with the BDI.

Experimental procedure

If the trial involved an oral stimulus, this was delivered in a 0.5 ml aliquot to the subject's mouth at the same time as the corresponding image for 7 sec. The subject then rated the stimuli for pleasantness on that trial (with +2 being very pleasant and -2 very unpleasant), for intensity on that trial (0 to +4), and for current wanting for chocolate (+2 for wanting chocolate very much, 0 for neutral, and -2 for very much not wanting chocolate). After the last rating the grey visual stimulus indicated the delivery of the tasteless control solution that was also used as a rinse between stimuli (see (McCabe et al., 2009) for further details).

fMRI scan

All images were acquired with a 3.0-T VARIAN/SIEMENS whole-body scanner where T2* weighted EPI slices were acquired every 2 seconds (TR=2 with TE 30ms). Imaging parameters were selected to minimise susceptibility and distortion artefact in the orbitofrontal cortex (Wilson et al., 2002). Coronal slices with in-plane resolution of 3x3 mm and between plane spacing of 4 mm were obtained. The matrix size was 64 x 64 and the field of view was 192 x 192 mm. Acquisition was carried out during the task performance yielding 972 volumes in total. A whole brain T2* weighted EPI volume of the above dimensions, and an anatomical T1 weighted scan with coronal plane slice thickness 3 mm and in-plane resolution of 1.0 x 1.0 mm was also acquired.

fMRI analysis

The data were preprocessed and analysed with SPM (http://www.fil.ion.ucl.ac.uk/spm/). SPM realignment, reslicing with sinc interpolation, normalization to the Montreal Neurological Institute (MNI) coordinate system and spatial smoothing with a 6-mm full width at half maximum isotropic Gaussian kernel and global scaling was used (Collins et al. 1994). Time series nonsphericity at each voxel was estimated and corrected for (Friston et al. 2002), and a high-pass filter with a cut-off period of 128 s was applied. General linear models (GLMs) were applied to the time course of activation in which event onsets were modelled as single impulse response functions convolved with the canonical

hemodynamic response function. Further details of the simple main effects of condition with one-sample t-tests and the second level between group contrast analyses published in our previous papers (McCabe et al., 2009; McCabe et al., 2012). For this study we examined with correlation analyses the fMRI BOLD (blood oxygenation-level dependent) signal with a given parameter of interest (e.g. the pleasantness, wanting and intensity ratings). Parametric modulation as implemented in SPM8 was conducted in first level and group analyses were run using 2-sample t-test, this is similar to our analysis in a previous publication (Rolls and McCabe, 2007). Specifically this is done by entering individual subject's rating values of pleasantness, wanting and intensity for each trial (chocolate trial or strawberry trial) presented in fMRI as regressors in the design matrix. First, the correlation for each rating is calculated and then followed in a second step by direct comparison between the groups. Regions of interest in which we had *a priori* hypotheses, based on our previous studies using this task and other studies in, at risk, depression were as follows: medial orbitofrontal cortex [4 30 8] (Rolls and McCabe, 2007) anterior cingulate; [-4 54 10] [-4 24 38] (McCabe and Rolls, 2007) (Rolls and McCabe, 2007) ventral striatum [-4 16 -12; 10 8 -4] (Cowdrey et al., 2011; Rolls and McCabe, 2007) insula [50 14 -14] [42 20 -10] (Tudge et al., 2014) (Horder et al., 2010), and caudate [14 12 12] (Cowdrey et al., 2011) [14 4 8] (Tudge et al., 2014). Peaks within 15 mm of these a priori regions which also had a cluster threshold of at least thirty contiguous voxels (k=30), had small volume corrections (SVC) for multiple comparisons applied (Family wise error, FWE $p<0.05$). Thresholding at p=0.05 with a cluster threshold of k=30 was our attempt at reducing both Type 1 and Type 11 errors in our results. Given that we have ran this particular design in our previous studies we believe we are less likely to attribute real activation to noise (Type I errors are not likely to replicate across multiple studies) and more likely instead to miss effects by increasing the p threshold. Therefore we increase the cluster threshold to 30 in an attempt to rebalance the Type 1 and Type 11 error rate. We also think this is appropriate given that these are healthy human volunteers and so differences in reward subtype correlations might have relatively subtle effects (Lieberman and Cunningham, 2009). However an alternative analysis approach would be to not limit the cluster threshold and just correct for the no of ROIs predefined. From the main SPM analyses of significant differences in correlations between groups, we extracted the percent BOLD signal change on each trial (choc or starw) to plot

against the ratings for each individual, to allow a visualization of the underlying signal (Poldrack, 2007). The % BOLD was extracted for each trial, from the peak voxel of significant difference using SPM8 plots of Fitted Response (adjusted) against scans and then plotted against the actual subjective ratings made on each trial.

*R*esults:

Demographic details and mood ratings: Recovered Depressed (RD) vs. Controls (C).

The recovered depressed sample had controls that were matched for age, gender, BMI, and chocolate liking (Table 1). There were no differences between the control group and the recovered depressed group in the measures of anhedonia (SHAPS, FCPS) and the HAM-D. However, the recovered depressed group scored significantly higher on the BDI (Table 1)(McCabe et al., 2009).

Demographic details and mood ratings: Family History (FH) vs.Controls (C).

The FH sample had control participants matched for age, gender and BMI. There were no significant differences between the FH and the controls as determined by a one-way ANOVA for age, gender, BMI, chocolate craving, liking or frequency of eating chocolate (Table 2). There were no significant differences between the two groups as determined by one-way ANOVAs for measures of anhedonia (SHAPS, FCPS) or mood (BDI) all $p>0.09$ (Table 2)(McCabe et al., 2012).

Correlation analysis:

Using individual models for wanting, pleasantness and intensity regressors we found brain regions without overlap, suggesting that the subjective ratings engage different parts of the brain.

Recovered depressed sample vs. healthy controls: Neural response.

Correlation with Pleasantness Ratings.

SPM parametric modulation analysis revealed differences between the RD sample and the C group correlations with the pleasantness ratings in the dmPFC ([4 46 24] $z=2.8$ $p=0.04$) (McCabe, 2014) (positive correlation in controls, negative correlation in RD). Further we extracted the % BOLD signal change data, for visualisation, from this region for the positive and negative conditions, for each group, on each trial. (Table 3, Fig1).

Correlation with Wanting Ratings.

SPM parametric modulation analysis revealed differences between the RD and the C groups correlations in the ventral striatum ([-4 6 -8] $z=2.2$ $p=0.01$ uncorrected, no correlation in controls,

negative correlation in RD). Further we extracted the % BOLD signal change data, for visualisation, from this region for the positive and negative conditions, for each group, on each trial. (Table 3, Fig2).

Correlation with Intensity Ratings.

SPM parametric modulation analysis revealed differences between the RD and the C groups correlations with the intensity ratings in the caudate ([18 18 8] z=3.09 p=0.03 positive correlation in controls, negative correlation in RD). Further we extracted the % BOLD signal change data, for visualisation, from this region for the positive and negative conditions, for each group, on each trial (Table 3).

Family History sample vs. healthy controls: Neural response.

There were no differences for pleasantness and wanting correlations with brain activity between the family history and control group.

Correlation with Intensity Ratings.

There were differences between the FH group and the control groups correlations with the intensity ratings in the anterior insula ([58 12 4] z=3.27 p<0.001 positive correlation in FH, no correlation in controls) and dACC ([-2 18 40] z=2.68 p=0.04 positive correlation in FH, no correlation in controls) but interestingly in the *opposite* direction to the recovered depressed group. Further we extracted the % BOLD signal change data, for visualisation, from this region for the positive and negative conditions, for each group, on each trial (Table 3, Fig 4).

Discussion:

The aim of the current study was to examine how brain activity changes as a function of the subjective experiences of "wanting", "liking" and "intensity" of pleasant and unpleasant food stimuli in those "at risk" of depression compared to controls using parametric modulation analyses. Although there is evidence for reward dysfunction in depressed individuals (Keedwell et al., 2005; Steele et al., 2007; Knutson et al., 2008) and also more recent data showing that this dysfunction is also present in those "at risk", (McCabe et al., 2009; McCabe et al., 2012) indicating a possible trait marker, there is no evidence as yet of how the neural tracking of different subjective experiences of rewarding and aversive stimuli (wanting, liking, intensity) might be different in those "at risk" of depression compared to controls.

We found differences in neural activations that tracked the subjective experiences. Specifically we found dmPFC increased in activity with increasing liking reports in healthy controls, as might be expected, however this was opposite to what was happening in the RD individuals (Fig 1). In fact, in RD individuals there was a negative correlation, in that as liking increased, brain activity in this region decreased. Reduced activity to reward in reward regions has been shown before in depressed patients (Kumar et al., 2008; Steele et al., 2007; Pizzagalli et al., 2009) however as can be seen from Fig 1 and Fig 2 perhaps this is not the whole story. In fact it seems that in the RD individuals compared to controls there is *more* activity in reward regions during the reporting of unpleasant and *not* wanted stimuli, suggesting that these regions are not just blunted but responding more when rating something as unpleasant or aversive. These results are thus an important addition to our previous contrast analyses which showed that regions within the cingulate gyrus for e.g. were less active for pleasant stimuli. These results are important for two reasons, 1. they show that both positive and negative stimuli can modulate the same brain regions and 2. that the activity to positive and negative stimuli in the same regions is opposite in those who are "at risk" of depression, due to a previous history, compared to control individuals. These analyses suggest that perhaps brain areas such as the dmPFC

are not specifically responding to "reward" but rather to what is the most relevant stimuli in the environment for that person, in this case for RD it might be negative information. Similarly there was a negative correlation with intensity in the RD group compared to controls in the caudate. The caudate as part of the dorsal striatum has been shown previously to respond during decision making (Grahn et al., 2009), emotional situations (Villablanca, 2010) and consistent with our result is found to have reduced activity in depression especially during consummatory processes (Pizzagalli et al., 2009).

For the FH group compared to controls there were no differences in pleasantness and wanting correlations with the brain data. However there were differences in correlations with intensity ratings in the FH group compared to the controls but intriguingly in the *opposite* way to the RD sample. So unlike the negative correlations with intensity in the RD group the FH group had positive correlations with intensity in the anterior insula and the dorsal anterior cingulate cortex (dACC). The anterior insula has been found previously to respond specifically to intensity and not pleasant or wanting ratings (Grabenhorst et al., 2008) and previously in our studies to respond to chocolate tase and strawberry taste (McCabe et al., 2009). In this current study positive correlations were present in both regions for both the pleasant chocolate stimuli and the unpleasant strawberry stimuli. Could this then reflect differences in state vs trait markers? That is, could the decreased responses to pleasant, wanted and intense stimuli in the RD group be scars from having experienced depression in the past and not in fact trait markers?. Further it is tantalising to suggest that the increased neural response to increasingly unpleasant stimuli in the dmPFC, ventral striatum and caudate (we find in our RD sample) is only something that happens *after* having experienced depressive episodes.

In our previous paper using contrast analyses (McCabe et al., 2012) we reported blunted brain activity to tastes and sights of pleasant and unpleasant stimuli in a similar part of the dACC in the FH group. However from these new analyses with subjective experiences we can see that this area is actually more active for increasing "intensity" of both positive and negative stimuli in the FH group, opposite to the response seen in the C group. This suggests that this part of the brain is tracking the "intensity" of experiences rather than the valence in the FH group. Further we found the anterior insula more

active for increasing "intensity" of both positive and negative stimuli in the FH group, opposite to the response seen in the C group. The insula has been shown to respond to the intensity rather than the pleasantness of warm and cold stimulation (Rolls et al., 2009; Rolls et al., 2008) and in some studies the insula also tracked subjective *unpleasantness* (Grabenhorst and Rolls, 2009). Experiencing situations as more "intense", before depression onset, might thus be a vulnerability marker for depression. For example if one experiences negative life events as more *intense* this might increase risk for depression.

Conclusion: These results suggest that the differences in neural correlates of subjective "wanting" and "liking" for reward and aversion might be due to having had a depression history whereas the neural response to the "intensity" of pleasant and unpleasant stimuli might be a trait marker for depression. Further studies with larger sample sizes and directly comparing at risk depression groups with more in depth analysis of the neural correlates of subjective experiences are needed to clarify this. Further examining recovered patients with and without a medication history may also help clarify state from trait markers. In future studies it will be important to know if the neurobiology of subjective experiences such as pleasantness, wanting and intensity can predict the onset of anhedonia in those at risk, which may in turn be before the onset of clinical depression. This information could therefore help guide prevention and intervention strategies.

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Figure Legends:

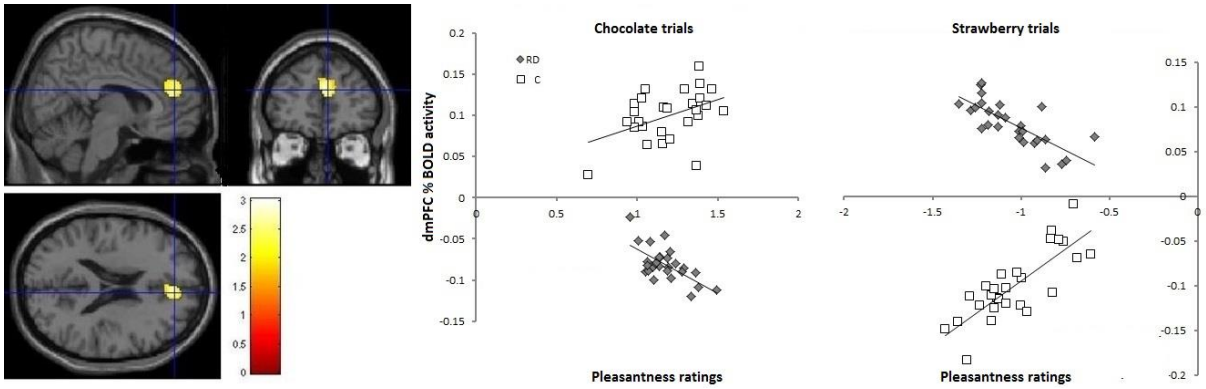

Fig 1a. Shows dmPFC. b. Each data point represents the average % BOLD signal change per group, per trial, plotted as a function of pleasantness ratings in recovered depressed RD and controls C for chocolate and strawberry separately.

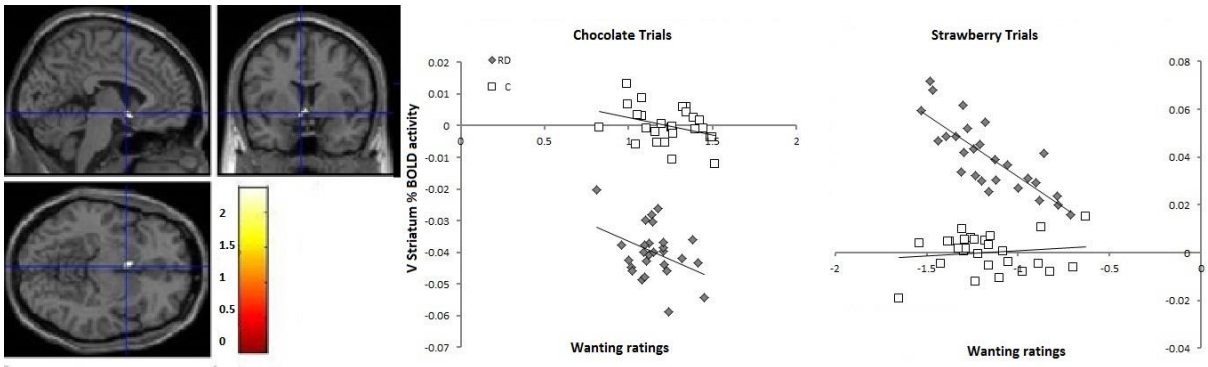

Fig 2a. Shows ventral striatum. d. Each data point represents the average % BOLD signal change per group, per trial, plotted as a function of wanting ratings in recovered depressed RD and controls C for strawberry.

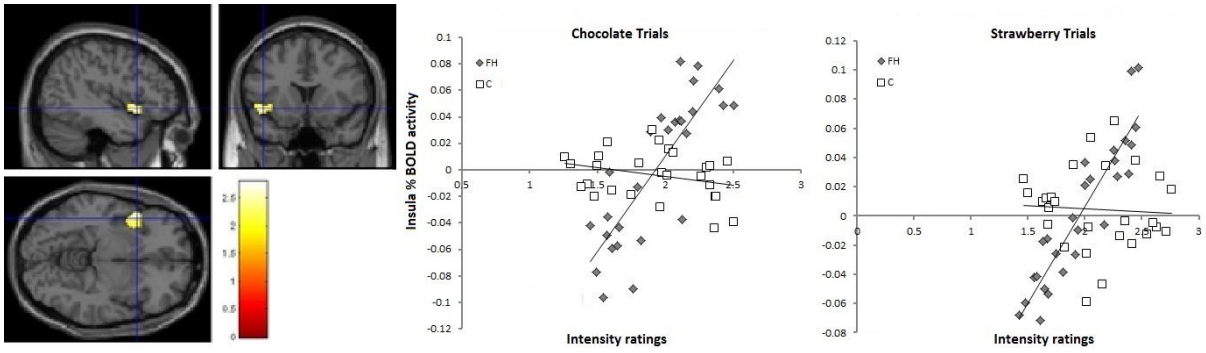

Fig 3a. Shows Anterior Insula. b. Each data point represents the average % BOLD signal change per group, per trial, plotted as a function of intensity ratings in FH and controls C for chocolate and strawberry separately.

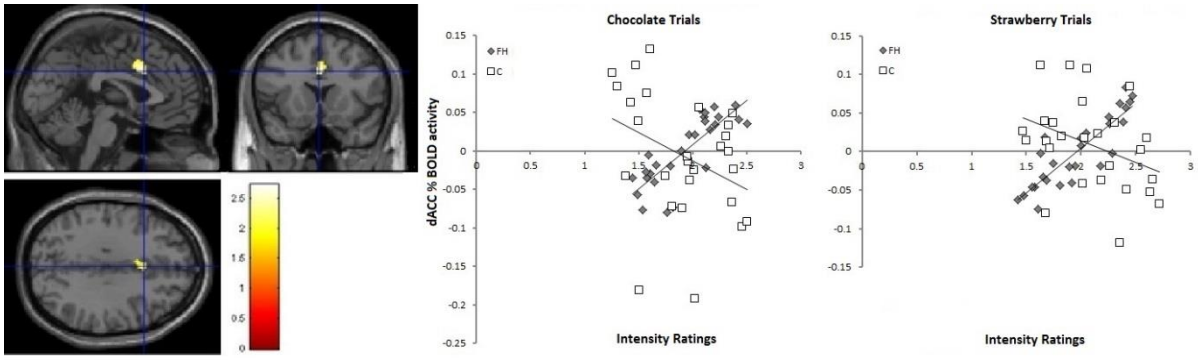

Fig 4. Shows significant difference in dACC. b. Each data point represents the average % BOLD signal change per group, per trial, plotted as a function of intensity ratings in FH and controls C for chocolate and strawberry separately.

TABLE 1: GROUP demographic and psychosocial measures: Recovered Depressed.

Measure	Recovered Depressed (n=13) Mean (s.d.)	Controls (n=14) Mean(s.d.)
Age, years	27.8 (6.6)	28.5 (6.3)
Gender	Male=3/13	Male=5/14
BDI	5.5 (6.3)	0.8 (1.3) *
HAM-D	2.3 (2.9)	0.5 (1.1)
FCPS	118 (33.7)	118 (33.5)
SHAPS	23 (6)	19.25 (6)
BMI	22.1 (2.5)	22.2 (5.14)
Choc Craving	6.1 (2.4)	6.8 (2.1)
Choc Liking	7.9(1.7)	8.0 (1.7)
Choc Freq Eat	5.0 (3.2)	5.0 (3.1)

BDI, Beck Depression Inventory; HAM-D, Hamilton Depression Score; FCPS, Fawcett Clarke Pleasure Scale; SHAPS, Snaith-Hamilton Pleasure Scale; BMI, Body Mass Index. One-way ANOVA * P=0.01 (all other p>0.1).

TABLE 2: GROUP demographic and psychosocial measures: Family History.

Measure	Family History (n=25) Mean (s.d.)	Controls (n=25) Mean(s.d.)
Age, years	18.6 (1.6)	19.2 (1.2)
Gender	F=16 M=9	F=16 M=9
BDI	3.6 (3.4)	2.5 (2.5)
FCPS	134 (15)	134 (12)
SHAPS	21.8 (4.17)	20.6 (4.26)
BMI	22 (2.4)	22 (2)
Choc Craving	6.5 (1.8)	6.3 (2)
Choc Liking	7.5 (1.5)	8.3 (1)
Choc Freq Eat	2 (1)	2.2 (1)

BDI, Beck Depression Inventory; FCPS, Fawcett Clarke Pleasure Scale; SHAPS, Snaith-Hamilton Pleasure Scale; BMI, Body Mass Index. One-way ANOVA all $p>0.09$.

Table 3.
Parametric modulation analysis in SPM8 revealed regions of significant difference between groups, RD: recovered depressed, FH: Family history, C: Controls.

Main analysis: Parametric modulation: Pleasantness ratings and brain activity, RD vs. HC					
Brain Region	*x*	*y*	*z*	*Z score*	*P value*
dmPFC	4	46	24	3.0	=0.03
Main analysis: Parametric modulation: Wanting ratings and brain activity, RD vs. HC					
Brain Region	*x*	*y*	*z*	*Z score*	*P value*
Ventral Striatum	-4	6	-8	2.2	0.01 unc
Main analysis: Parametric modulation: Intensity ratings and brain activity, RD vs. HC.					
Brain Region	*x*	*y*	*z*	*Z score*	*P value*
Caudate	18	18	8	3.09	=0.03
Main analysis: Parametric modulation: Intenisty ratings and brain activity, FH vs. HC.					
Brain Region	*x*	*y*	*z*	*Z score*	*P value*
Anterior Insula	58	12	4	3.27	<0.001*
dACC	-2	18	40	2.68	=0.04

Threshold p=0.05 uncorrected; P values, FWE-small volume corrected for multiple comparisons; *, whole brain corrected and also survives correction for no of ROIs.

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