

Title: Reward network connectivity “at rest” is associated with reward sensitivity in healthy adults:
a resting-state fMRI study

Jesús Adrián-Ventura¹, Víctor Costumero^{1,2}, Maria Antònia Parcet¹, and César Ávila¹

¹ Department of Basic and Clinical Psychology and Psychobiology, Jaume I University, 12071 Castellón, Spain.

² Department of Methodology of the Behavioural Sciences, University of Valencia, 46010 Valencia, Spain.

Running title:

Personality and brain reward system at rest.

Corresponding author:

Jesús Adrián-Ventura (jadrian@uji.es)

+34964387664 / Fax +34 964729016

Basic and Clinical Psychology and Psychobiology, Jaume I University. Avda. Sos Baynat, s/n. E-12071 Castellón, Spain.

Abstract

The behavioral approach system (BAS), based on reinforcement sensitivity theory (RST), is a neurobehavioral system responsible for detecting and promoting motivated behaviors towards appetitive stimuli. Anatomically, the frontostriatal system has been proposed as the core of the BAS, mainly the ventral tegmental area and the ventral striatum and their dopaminergic connections with medial prefrontal structures. The RST also proposes the personality trait of reward sensitivity as a measurable construct of stable individual differences in BAS activity. However, the relationship between this trait and the brain connectivity “at rest” has been poorly studied, mainly because previous investigations have focused on studying brain activity under reward-related contingency paradigms. Here, we analyzed the influence of reward sensitivity on the resting-state functional connectivity (rs-FC) between BAS-related areas by correlating the BOLD time series with the scores on the Sensitivity to Reward (SR) scale in a sample of 89 healthy young adults. Rs-FC between ROIs were all significant. Results also revealed a positive association between SR scores and the rs-FC between the VTA and the ventromedial prefrontal cortex, and between the latter structure and the anterior cingulate cortex. These results suggest that reward sensitivity could be associated with different resting-state activity in the mesocortical pathway.

Keywords: Personality, reward, functional connectivity, basal ganglia, prefrontal cortex

Introduction

Reinforcement sensitivity theory (RST) describes a widely used taxonomy of personality at both behavioral and neuropsychological levels (Gray, 1982; Gray & McNaughton, 2000). This model proposes different brain systems responsible for promoting motivated behaviors to approach or avoid stimuli with a positive or negative emotional valence. In particular, the behavioral approach system (BAS) is responsible for detecting and initiating behaviors towards appetitive stimuli.

Anatomically, the BAS is associated with brain structures belonging to the mesolimbic and mesocortical dopaminergic pathways (Pickering & Gray, 1999, 2001). The key region is the ventral tegmental area (VTA), which is connected to the ventral striatum (VS; mesolimbic tract) and the medial prefrontal cortex (mesocortical tract), including the anterior cingulate (ACC) and the ventromedial prefrontal cortex (vmPFC). All these areas define the reward network, that is, the main structures involved in processing and responding to reward stimuli (see Haber & Knutson, 2010; Sescousse, Caldú, Segura, & Dreher, 2013).

According to the BAS description in the RST model, this system is involved not only in managing rewarding stimuli, but also in determining stable individual differences in the detection and response to appetitive stimuli. In other words, the model proposes that the reward sensitivity trait is associated with stable differences in BAS functioning, determining the probability of perceiving stimuli as rewarding and actively approaching them once detected (Ávila & Torrubia, 2008; Corr, 2004; Gray & McNaughton, 2000). To measure these differences, some psychometric measures have been developed, such as the Sensitivity to Reward (SR) scale included in the Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ; Torrubia, Ávila, Moltó, & Caseras, 2001) or the three BAS subscales included in the BIS/BAS questionnaire (Carver & White, 1994). Psychometric studies have shown that these measures are related to other personality traits such as extraversion, impulsivity, or sensation seeking (Caseras, Ávila, & Torrubia, 2003; Torrubia, Avila, & Caseras, 2008). BAS measures have also been found to be a good measure of proneness or vulnerability to some psychiatric pathologies. Higher reward sensitivity has been related to the presence of ADHD symptoms (Mitchell & Nelson-Gray, 2006), substance use and abuse (Boog et al., 2014; Franken, Muris, & Georgieva, 2006; Knyazev, 2004; Pardo, Aguilar, Molinuevo, & Torrubia, 2007; Yen et al., 2012), eating disorders (Glashouwer, Bloot, Veenstra, Franken, & de Jong, 2014; Matton, Goossens, Braet, & Vervaet, 2013; Matton, Goossens, Vervaet, & Braet, 2015), psychopathy (Newman, MacCoon, Vaughn, & Sadeh, 2005), and cluster B personality

disorders (Bijttebier, Beck, Claes, & Vandereycken, 2009; Pastor et al., 2007; Taylor, Reeves, James, & Bobadilla, 2006). Moreover, lower reward sensitivity has been associated with depressive disorders (Kasch, Rottenberg, Arnow, & Gotlib, 2002; Pinto-Meza et al., 2006).

Behavioral studies have consistently demonstrated that individuals with higher scores on these scales show better learning (i.e. conditioning) in appetitive situations than low scorers (i.e. those with lower reward sensitivity) (see Corr, 2004 for a review). On tasks requiring decision making, individuals with higher reward sensitivity focus their attention on rewarding stimuli (Derryberry & Reed, 1994), show faster responses to obtain rewards in the presence of possible aversive stimuli (Avila, 2001), prefer immediate rewards over delayed rewards (Avila, Parcet, Ortet, & Ibáñez-Ribes, 1999), and persevere in dominant responses for rewards (Avila, Moltó, & Segarra, 1995; Avila & Parcet, 2000; Newman, Widom, & Nathan, 1985), compared to individuals with lower reward sensitivity. This entire cognitive system oriented toward detecting reward cues and making approach responses to them is manifested in different social behaviors. As a result, individuals with higher reward sensitivity are more impulsive on multiple choice exams (Ávila & Torrubia, 2004), show more food cravings (Franken & Muris, 2006), have more sexual experiences (Aluja, 2004), exhibit early-stage entrepreneurial action (Lerner, Hatak, & Rauch, 2018), or initiate the use of drugs at a younger age (Pardo et al., 2007).

Behavioral studies have also shown that reward sensitivity determines differences on cognitive tasks with no specific reward contingencies. According to Aarts, van Holstein, & Cools (2011), individual differences in appetitive motivation appear to have parallel effects to those of increases in striatal dopamine, that is, the enhancement of cognitive flexibility, which may come, however, at the expense of reduced cognitive focusing (i.e. greater distractibility). There are different behavioral and fMRI studies showing that reward sensitivity determines differences in cognitive processing (Avila, 1995; Avila et al., 2012; Avila, Barrós, Ortet, Parcet, & Ibañez, 2003; Avila & Parcet, 1997; Avila & Parcet, 2002; Fuentes-Claramonte et al., 2015, 2016a, 2016b, Fuentes et al., 2014a, 2014b).

All this evidence is compatible with the idea that BAS-related traits should explain individual differences in cognition.

RST is based on neuropsychological studies mainly conducted in animal research. The RST model predicts specific relationships between certain brain areas and the different personality dimensions. However, these proposals have been investigated less in the human brain. Previous morphometric studies have found associations between BAS scores and gray matter reductions in BAS-related areas, including the striatum, the anterior cingulate cortex, and prefrontal areas (Barrós-Loscertales et al., 2006; Holmes, Hollinshead, Roffman, Smoller, & Buckner, 2016). In addition, some fMRI studies have also linked BAS activation to brain activity in these basic structures. Specifically, task-based studies with different kinds of rewards (i.e. food and erotic stimuli, monetary incentives, etc.) have associated higher reward sensitivity with greater activation in brain areas involved in the mesolimbic and mesocortical pathways. Thus, a number of studies have found this association in mesolimbic areas, including the midbrain and ventral striatal regions (Beaver et al., 2006; Carter, MacInnes, Huettel, & Adcock, 2009; Costumero et al., 2016; Costumero et al., 2013a; Costumero et al., 2013b; Hahn et al., 2009; Mortensen, Lehn, Evensmoen, & Håberg, 2015; Simon et al., 2010), whereas others have also reported this correlation with ventromedial prefrontal regions of the mesocortical pathway (Barrós-Loscertales et al., 2010; Beaver et al., 2006; Costumero et al., 2013b; Hahn et al., 2009; Locke & Braver, 2008; Mortensen et al., 2015; Simon et al., 2010). Functional connectivity analysis revealed that BAS scores were also associated with relatively less connectivity between the VTA and vmPFC during the processing of high-incentive monetary cues (Costumero et al., 2013a). Thus, BAS scores in healthy participants correlated with greater activity in the brain areas involved in the mesolimbic and mesocortical pathways during the processing of reward cues. Importantly, other research has demonstrated that BAS scores determine different activity in mesolimbic and prefrontal areas during performance on executive tasks (Avila et al., 2012; Fuentes-Claramonte et al., 2016a, 2016b, 2015, Fuentes et al., 2014a, 2014b).

All this evidence suggests that reward sensitivity is related to a different general and stable functioning of reward-related areas involved in motivation and emotion: VTA, VS, ACC, and vmPFC. This variability in the functioning of these areas could be studied by measuring the functional connectivity (FC) between them using resting-state fMRI. As far as we know, only one previous study investigated the FC between striatal and cortical areas, including the prefrontal and cingulate cortex, based on a BAS measure (Angelides, Gupta, & Vickery, 2017). In this article, the authors reported a positive correlation between BAS-fun seeking and the FC between the middle OFC and the putamen, and a negative correlation between BAS-drive and the rs-FC between the middle cingulate cortex and the caudate. However, this study did not specifically investigate BAS relevant structures such as the VS or the VTA.

The aim of this study was to investigate the relationship between the reward sensitivity trait, measured with the SR scale from the SPSRQ, and the FC among key structures of the brain reward system (i.e. the VTA, VS, ACC, and vmPFC) in a sample of healthy adults. Based on previous reports, we hypothesize that the activity between all these structures will be positively associated, and that individuals with higher reward sensitivity would show a stronger FC between all these regions.

Methods

Participants

One hundred and twenty-eight participants took part in this study (63 women; age: mean=22.5, SD=4.8, range=18-37). All the participants were recruited from a community sample through local advertisements and word of mouth. Most of them were undergraduate students, given that our research group is integrated in a university campus. Following subject exclusion due to excessive head motion (see preprocessing section), the final sample for analyses included 89 participants (48 women; age: mean=22.4, SD=4.7, range=18-37). All the participants were right-handed, according

to the Edinburgh Handedness Inventory (Oldfield, 1971). No participant had a history of head injury with loss of consciousness, currently used psychoactive medications, or had ever been diagnosed with DSM-IV Axis I or II disorders or severe medical or neurological illnesses. Participants were informed of the nature of the research, and they provided written informed consent prior to their participation in the study. All the study procedures conformed to the Code of Ethics of the World Medical Association.

Personality assessment

All the participants completed the Sensitivity to Reward (SR) scale from the Sensitivity to Punishment and Sensitivity to Reward Questionnaire (Torrubia et al., 2001) as a measure of reward sensitivity. This questionnaire is a self-report measure with 48 dichotomous items that assess the reactivity and responsivity of the behavioral inhibition and activation systems described by Gray (1982; Gray & McNaughton, 2000). As our interest was reward sensitivity, only the SR scale was included in the study. The SR scale is a self-reported measure consisting of 24 yes-no items related to one's habitual behavior. In this particular case, the questions measure the proneness to approach behaviors towards appetitive stimuli. Different studies have shown the SR scale's convergent validity with other measures, as well as the association with disinhibitory and depressive pathologies (Torrubia et al., 2008). The mean score on the SR scale was 10.2 (SD = 4.7; range=1-21).

Image acquisition

Scan sessions consisted of an eyes-closed resting-state. Participants were instructed to simply rest with their eyes closed without sleeping or thinking about anything in particular. Images were acquired on a 1.5T scanner (Siemens Avanto; Erlangen, Germany). Participants were placed in a supine position in the MRI scanner, and their heads were immobilized with cushions to reduce motion artifacts. For the rs-fMRI, a total of 200 volumes were recorded using a gradient-echo T2*-

weighted echo-planar imaging sequence (TR, 2000 ms; TE, 48 ms; matrix, 64 x 64; voxel size, 3.5 x 3.5 mm; flip angle, 90°; slice thickness, 4 mm; slice gap, 0.8 mm). We acquired 24 interleaved axial slices parallel to the anterior–posterior commissure plane covering the entire brain. The total rs-fMRI scan length was 6:40 minutes. Prior to the rs-fMRI sequences, structural images were acquired using a high-resolution T1-weighted MPRAGE sequence with TR/TE = 2200/3.79 ms, flip angle 15°, voxel size = 1 × 1 × 1 mm, which facilitated the localization and co-registration of functional data.

Image preprocessing

We used the Data Processing Assistant for Resting-State (DPARSF, <http://rfmri.org/DPARSF>), which is a plug-in software within the Data Processing & Analysis for Brain Imaging (DPABI V2.0_151201, <http://rfmri.org/dpabi>; Yan, Wang, Zuo, & Zang, 2016), based on Statistical Parametric Mapping (SPM, <http://www.fil.ion.ucl.ac.uk/spm>), to carry out rs-fMRI data processing. Preprocessing included the following steps: 1) the first five volumes of each raw rs-fMRI dataset were discarded to allow for T1 equilibration; 2) slice timing correction for interleaved acquisitions (the middle slice was used as the reference point); 3) realignment using a six-parameter (rigid body) linear transformation with a two-pass procedure (registered to the first image and then registered to the mean of the images after the first realignment); 4) co-registration of the individual structural images (T1-weighted MPRAGE) to the mean functional image; 5) segmentation of structural images into gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) using the Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra (DARTEL) tool (Ashburner, 2007); 6) removal of spurious variance through linear regression: 24 parameters from the realignment step (6 head motion parameters, 6 head motion parameters one time point before, and the 12 corresponding squared items; Friston, Williams, Howard, Frackowiak, & Turner, 1996), scrubbing within regression (spike regression as well as 1 back and 2 forward neighbors; Yan, Craddock, He, & Milham, 2013) at framewise displacement of (FD)>0.2mm (Power, Barnes,

Snyder, Schlaggar, & Petersen, 2012), linear and quadratic trends, the WM signal (segmentation mask thresholded at 90% probability), and the CSF signal (segmentation mask thresholded at 70% probability); 7) spatial normalization to the Montreal Neurological Institute (MNI) space (voxel size $3 \times 3 \times 3 \text{ mm}^3$); 8) spatial smoothing with a 4 mm FWHM Gaussian Kernel; and 9) band-pass temporal filtering (0.01-0.1 Hz) to reduce the effect of low frequency drift and high frequency noise (Biswal, Zerrin Yetkin, Haughton, & Hyde, 1995; Lowe, Mock, & Sorenson, 1998).

Participants with more than 1 mm/degree of movement in any of the six directions or a large removal of data points during scrubbing regression (more than 50 volumes, ensuring at least 5 minutes of remaining data) were excluded from the analyses. In the final sample, descriptive statistics for the head motion metrics provided by DPARSFA were as follows: mean RMS (mean=0.11, SD=0.04, range=0.04-0.26), mean FD Power (mean=0.12, SD=0.03, range=0.05-0.20), mean FD Jenkinson (mean=0.06, SD=0.02, range=0.03-0.10), and mean FD Van Dijk (mean=0.03, SD=0.01, range=0.01-0.07).

Resting-State Functional Connectivity analysis

A seed-based correlation approach between a priori regions of interest (ROIs) was performed to investigate the link between reward sensitivity and the rs-FC between the main areas of the brain reward system. In this method, FC relies on the correlation between the averaged BOLD signal of a ROI, also called the seed, and the BOLD signals of other parts of the brain (voxels or other ROIs). For this study, we defined seeds for four BAS-related areas involved in motivational and emotional processes (Haber & Knutson, 2010; McNaughton & Corr, 2008): the ventral tegmental area (VTA), the ventral striatum (VS), the anterior cingulate cortex (ACC), and the ventromedial prefrontal cortex (vmPFC). The seeds for the ACC and vmPFC (gyrus rectus plus medial orbital frontal cortex) were defined with the anatomical automatic labeling (AAL) template (Tzourio-Mazoyer et al., 2002). Unfortunately, this atlas does not include ROIs for VTA and VS. Thus, we used other atlases for these ROIs. For the VTA, we used a published probabilistic atlas provided by Murty et

al. (2014) at a probability threshold of 80%, whereas for the VS we used a published atlas provided by Tziortzi et al. (2014), taking the ventral striatal region defined within the “limbic network”. All the seeds were included bilaterally (see Figure 1).

After seed definition, the rs-FCs between the ROIs were investigated through pairwise correlations between the time-series of the seeds. After the correlations, Fisher's r-to-z transformation was performed to normalize the variance in correlation values.

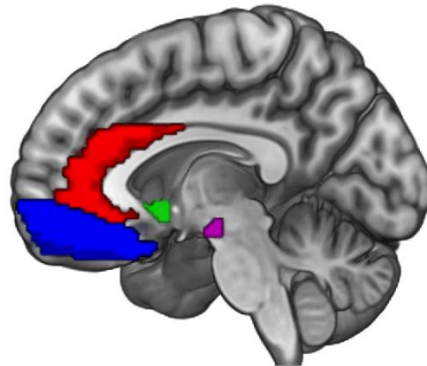


Figure 1. Seed ROIs included in the rs-FC analyses. Red: anterior cingulate cortex; Blue: ventromedial prefrontal cortex; Green: ventral striatum; Purple: ventral tegmental area.

Statistical analyses were performed using SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp.). First, we carried out a one-sample t test analysis on the framework of the general linear model using the z scores for each pair of ROIs as the dependent variable. Afterwards, in order to investigate how the connectivity between the a priori seeds was related to reward sensitivity, partial correlation analyses between the SR scores and the z scores were performed. Effects of age and gender were regressed out in all the analyses. The statistical significance threshold for all the analyses was set at $p < 0.05$ FDR-corrected (Benjamini & Hochberg, 1995) using a syntax script for SPSS (<http://www-01.ibm.com/support/docview.wss?uid=swg21476447>). Because we took four ROIs as seeds, six comparisons were carried out.

Results

Seed-based connectivity analyses

One-sample t test analyses revealed a significant FC between all the seed time series used in the study (Table 1), thus resulting in an interconnected network at rest ($p < .05$ FDR-corrected). All the FCs resulted in positive values, except for the vmPFC-VTA FC.

To investigate personality effects of the rs-FCs, partial correlations were carried out by taking rs-FCs between ROIs and scores on the SR scale. A significant effect was found in the rs-FC between the VTA-vmPFC ($p < .05$ FDR-corrected), showing an increase in the connectivity strength between the two structures. Furthermore, we also observed a stronger connectivity between the vmPFC-ACC ($p < .05$ FDR-corrected). Partial correlation analysis details are reported in Table 2 and Figure 2.

Moreover, because the ROIs selected as seeds differed considerably in size (mainly between cortical and subcortical regions), we performed further analyses to check that our results were not affected by different signal-to-noise levels (see details in Supplementary Material).

Table 1. Results from the one-sample t test (controlling for age and gender) on the Fisher's z correlation coefficients (as a measure of connectivity).

	t	Sig. (2-tailed)	Mean	Std. Deviation	Min.	Max.	95% Confidence Intervals	
							Inferior	Superior
ACC-vmPFC	17.06	.000*	.38	.21	-.24	.92	.34	.42
ACC-VS	14.75	.000*	.31	.20	-.16	.72	.27	.35
ACC-VTA	7.29	.000*	.11	.15	-.27	.44	.08	.14
VS-vmPFC	9.98	.000*	.23	.22	-.18	.88	.19	.28
VS-VTA	5.07	.000*	.10	.18	-.40	.63	.06	.13
vmPFC-VTA	-2.65	.010*	-.06	.20	-.60	.54	-.10	-.01

* FDR-corrected at $p < .05$; ACC=anterior cingulate cortex, vmPFC=ventromedial prefrontal cortex, VS=ventral striatum (bilateral), VTA=ventral tegmental area.

Table 2. Partial correlations (controlling for age and gender) between SR scores and Fisher's z correlation coefficients among seed time series.

		ACC-vmPFC	ACC-VS	ACC-VTA	VS-vmPFC	VS-VTA	vmPFC-VTA
SR	Corr.	.257	-.029	.086	-.117	.117	.257
	Sig.	.016*	.792	.427	.279	.281	.016*

* FDR-corrected at $p < .05$; ACC=anterior cingulate cortex, vmPFC=ventromedial prefrontal cortex, VS=ventral striatum (bilateral), VTA=ventral tegmental area.

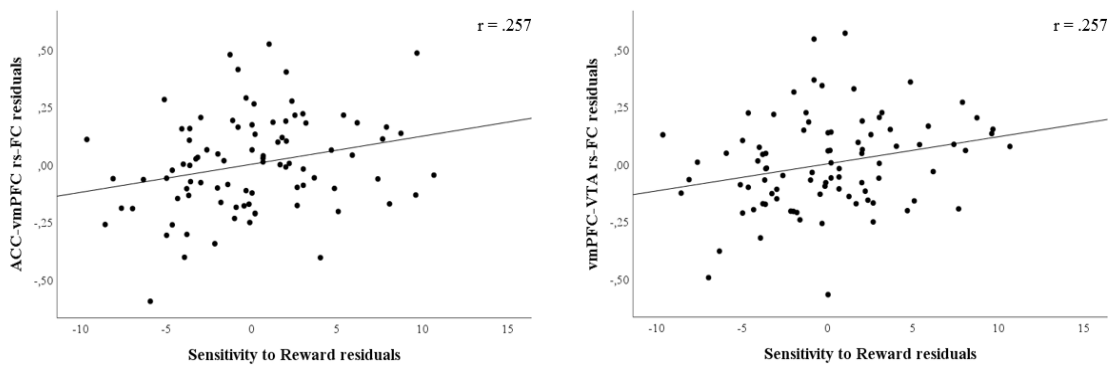


Figure 2. Scatterplots of residuals illustrating the partial correlations of ACC-vmPFC and vmPFC-VTA rs-FCs with SR scores after regressing out age and gender in each variable.

Discussion

In this study we analyzed the relationship between reward sensitivity, as a measure of BAS activity, and the rs-FC between key structures within the brain reward system in healthy adults. With one exception (the rs-FC between the vmPFC and VTA), our results showed a significant positive and moderate interconnectivity between all the areas included in the study, thus providing information about the neural coupling of BAS-related areas at rest. Furthermore, as expected, we observed a connection between the reward sensitivity trait and the rs-FC between areas of the BAS.

Specifically, we observed a positive correlation between the scores on the SR scale and the rs-FC between the ACC and vmPFC and the vmPFC and VTA. Thus, the individual differences in BAS activity were associated with a different, stable connectivity between the brain areas involved in reward detection and processing.

In our study, we delimited four regions of interest related to the BAS associated with emotional and motivational processing: the VTA, the VS, the ACC, and the vmPFC. As expected, the results of this study corroborated that the activity of these areas during resting-state is moderately coupled. This is especially true between the last three ROIs, showing that the activity of the VS, vmPFC, and ACC is closely interrelated. Previous resting-state fMRI studies have shown a strong connectivity between the VS and the vmPFC and ACC (Cauda et al., 2011; Choi, Yeo, & Buckner, 2012; Di Martino et al., 2008), and animal and human studies have suggested that this relationship mediates the processing of rewards (Pujara, Philippi, Motzkin, Baskaya, & Koenigs, 2016; Richard & Berridge, 2013; Smith & Graybiel, 2013). In addition, the vmPFC and the ACC are functionally interrelated, as found in previous studies (Bzdok et al., 2013; Margulies et al., 2007), supporting the evaluation function of emotional and social stimuli (Bzdok et al., 2013). Although we obtained a strong interconnectivity between these areas, our results showed that the values of rs-FCs decreased when the VTA was involved (especially with ACC and vmPFC). The VTA is a small region that is of great relevance in processing reward stimuli (D'Ardenne, McClure, Nystrom, & Cohen, 2008; Düzel et al., 2009; Hayes, Duncan, Xu, & Northoff, 2014), but the cortical areas are bigger and receive influence from a large number of brain structures. Hence, this could be one of the reasons we observed a negative correlation between the VTA and vmPFC. Nonetheless, even in this negative correlation, the range of rs-FCs is wide. Therefore, some individuals presented a strong positive coupling between the VTA and cortical areas, whereas others presented negatively correlated activity between these two structures.

We also hypothesized that SR scores would be associated with the rs-FC between the BAS-related structures. According to this hypothesis, SR scores would be positively correlated with the rs-FC between the vmPFC (the medial segment of the OFC cortex) and the VTA, and between the vmPFC and the ACC. Both the vmPFC and VTA are connected via the mesocortical pathway, a dopaminergic branch responsible for initiating motivated reward-based approach behaviors (Arias-Carrión, Stamelou, Murillo-Rodríguez, Menéndez-González, & Pöppel, 2010; D'Ardenne et al., 2008; Haber & Knutson, 2010). The VTA has largely been described as the main component of the reward brain circuitry because the mesocortical and mesolimbic pathways arise from this structure (Arias-Carrión et al., 2010; Krebs, Schott, & Düzel, 2009). Furthermore, the dopamine cells in the VTA are involved in motivational salience and value (Bromberg-Martin, Matsumoto, & Hikosaka, 2010; Depue & Collins, 1999; Hayes et al., 2014), thus promoting reward approach and consumption, which is the “wanting” component of reward-based behaviors (Berridge, Robinson, & Aldridge, 2009). In addition to the VTA, the vmPFC is also a key region of the brain reward network and the principal projection from the VTA within the mesocortical pathway. Similarly to the VTA, the vmPFC has also been involved in reward processing, mainly in reward assessment and decision-making (Hayes et al., 2014; Rangel, Camerer, & Montague, 2008; Sescousse et al., 2013). Importantly, one of the factors that makes the vmPFC involved in reward-related decision-making stems from the modulatory effect on dopaminergic neurotransmission. Previous studies identified an inhibitory pathway between the medial prefrontal cortex and the VTA through glutamatergic activation of GABA interneurons in the VTA, thus reducing the levels of dopamine in the VS (mesolimbic pathway) (Carr & Sesack, 2000; Sesack, Carr, Omelchenko, & Pinto, 2003).

The results obtained are consistent with previous proposals relating reward sensitivity (Pickering & Gray, 2001) and extraversion (Depue & Collins, 1999; Pickering & Gray, 1999) to dopaminergic transmission from the VTA. Individual differences in the dopaminergic transmission from the VTA via the mesocortical pathway may be responsible for a different ability to detect and evaluate

rewarding stimuli. Interestingly, our results coincide with these previous reports, as we observed greater connectivity between the primary mesocortical areas during a resting-state condition (absence of stimuli), that is, during one's default basal activity. Therefore, the stronger rs-FC between the VTA and vmPFC may predispose the person to interpret more situations as rewarding. Importantly, the FC connectivity between the two areas is reversed when an incentive is detected (Costumero et al., 2013a). In the study by Costumero et al. (2013a), the authors compared the neural processing of low and high magnitude incentives as a function of reward sensitivity. Rewarding stimuli activated the VTA and VS significantly more in individuals with higher scores on the SR scale, but the connectivity between the VTA and vmPFC during high incentive stimuli was reduced in high SR individuals. Overall, these results may suggest that the reward sensitivity trait would be directly related to the connectivity between the VTA and vmPFC and, therefore, to the proneness to detecting (positive correlation under absence of stimuli) and responding (negative correlation under presence of stimuli) to rewarding stimuli. However, this hypothesis is speculative, and further studies are needed to investigate the relationship between BAS activity and VTA-vmPFC connectivity.

Our results also showed a positive correlation between SR scores and rs-FC between the ACC and vmPFC. Both are dopaminergic-innervated adjacent structures within the reward brain circuitry, and they are involved in evaluating, managing, and selecting rewarding situations. Global results showed a stronger rs-FC between them in the absence of a task, but previous literature has demonstrated this strong FC during reinforcement-guided decision making (Fatahi, Haghparast, Khani, & Kermani, 2018). The role of the two structures is different: whereas the ACC is relevant for reward prediction and prediction error encoding, the vmPFC is more involved in outcome evaluation, establishing stimulus-outcome associations and encoding rewarding features of a stimulus (Rushworth, Noonan, Boorman, Walton, & Behrens, 2011). The main dissociation is that the vmPFC encodes outcomes predicted by the ACC, but it also encodes unexpected rewarding

outcomes not predicted by the ACC (Vassena, Krebs, Silvetti, Fias, & Verguts, 2014). In relation to our results, we observed stronger connectivity at rest between these structures associated with SR, thus suggesting a tendency to predict contingencies associated with emotional stimuli. Thus, the increased rs-FC observed in participants with high SR scores may serve to establish more frequent predictions of positive outcomes when processing reward cues and evaluate these outcomes as more positive.

One of the relevant results of this study is that the influence of reward sensitivity on rs-FC within the reward network is more focused on the mesocortical pathway than on the mesolimbic pathway. Contrary to previous observations investigating reward processing as a function of reward sensitivity, where the mesolimbic and mesocortical pathways are relevant (Costumero et al., 2013a; Costumero et al., 2013b, for a review see Kennis, Rademaker, & Geuze, 2013), the absence of emotional stimuli seems to move the focus of attention to the mesocortical pathway. The results of a recent study are consistent with this pattern (Richter & Gruber, 2018). This study compared the brain areas involved in processing salient infrequent stimuli to those involved in processing salient rewarding stimuli. Results showed that both kinds of stimuli activated the VTA and the VS, but the PPI analysis revealed a different FC of the VTA: whereas reward stimuli only co-activated the VS, salient non-rewarding stimuli showed a FC of the VTA with both vmPFC and ACC. Similarly, our results revealed higher coupling of the VTA and vmPFC during a resting-state condition in participants with high reward sensitivity. Therefore, the reward sensitivity trait would be related to brain areas specialized in processing salient stimuli (and not only salient rewarding stimuli). Overall, this finding suggests that the mesocortical pathway is more involved in detecting salient stimuli, and the role of the vmPFC/ACC areas should be more related to regulating responses to these stimuli.

The present results are aligned with previous literature showing that reward sensitivity is associated with differences in cognitive processing. On different tasks, previous studies showed that reward

sensitivity was positively associated with more cognitive flexibility on tasks requiring fast, automatic processing (Avila et al., 2003; Avila & Parcet, 1997) and better cognitive focusing on tasks requiring slow, conscious processing (Avila, 1995; Ávila & Parcet, 2002). These tasks reflected differences in the capacity to process stimuli that, in fact, would determine a different capacity to detect rewarding stimuli. The results of the present study seem to suggest that these differences would be more related to the mesocortical pathway.

In sum, the present study adds to the extensive literature testing for neural differences associated with individual differences in BAS activity. All this literature has shown that reward sensitivity is associated with structural differences in frontostriatal areas and with enhanced responses to reward stimuli in the mesolimbic network. However, the RST model also predicts that a personality trait, such as reward sensitivity, would also determine a different functioning in detecting possible rewarding stimuli (Avila, Parcet, & Barrós-Loscertales, 2008; Derryberry & Reed, 1994). The present study has focused these differences on the mesocortical dopaminergic pathway, which could act as a global vigilance system prepared to detect reward stimuli.

Finally, our study presents some limitations. One of them is related to the rs-FC approach to the research question. Based on our a priori ROIs, we decided to use a seed-based (pairwise) correlation approach, as opposed to other useful methods for studying rs-FC, such as seed-based whole-brain FC or independent component analysis (ICA). Thus, although our method was more appropriate for testing specific hypotheses, these methods could provide further results not observed with our approach. Regarding our ROIs, another limitation would be related to their location, as the VTA and vmPFC are located at the ventral edge of the brain, making them vulnerable to the nuisance of susceptibility artefacts. However, this problem is inherent to all the fMRI, and new methods should be implemented to improve this aspect. Moreover, the sample selected for this study could also be a limitation. Although we recruited participants from a community sample, the majority of our participants were undergraduates, thus resulting in a relatively young sample (i.e. mean of 22.4 years). Even though this is not a problem in itself, it could impede the generalization of the results

to older populations. In addition, although the aim of this study was not to analyze sex differences in the rs-FC linked to reward sensitivity, future studies should investigate this subject because recent data have revealed differences in the rs-FC between males and females (Nostro et al., 2018).

Acknowledgements

This work was supported by grants from Generalitat Valenciana (PROMETEO/2017/109) and Ministerio de Economía y Competitividad (PSI2016-78805-R) to C.A. In addition, this work was supported by a pre-doctoral graduate program grant (National FPU to J.A.-V.) and a post-doctoral graduate program grant (Juan de la Cierva to V.C.).

References

- Aarts, E., van Holstein, M., & Cools, R. (2011). Striatal Dopamine and the Interface between Motivation and Cognition. *Frontiers in Psychology*, 2, 163. <https://doi.org/10.3389/fpsyg.2011.00163>
- Aluja, A. (2004). Sensitivity to punishment, sensitivity to reward and sexuality in females. *Personality and Individual Differences*, 36(1), 5–10. [https://doi.org/10.1016/S0191-8869\(02\)00219-2](https://doi.org/10.1016/S0191-8869(02)00219-2)
- Angelides, N. H., Gupta, J., & Vickery, T. J. (2017). Associating resting-state connectivity with trait impulsivity. *Social Cognitive and Affective Neuroscience*, 12(6), 1001–1008. <https://doi.org/10.1093/scan/nsx031>
- Arias-Carrión, O., Stamelou, M., Murillo-Rodríguez, E., Menéndez-González, M., & Pöppel, E. (2010). Dopaminergic reward system: a short integrative review. *International Archives of Medicine*, 3, 24. <https://doi.org/10.1186/1755-7682-3-24>

- Ashburner, J. (2007). A fast diffeomorphic image registration algorithm. *NeuroImage*, *38*(1), 95–113. <https://doi.org/10.1016/J.NEUROIMAGE.2007.07.007>
- Avila, C. (1995). Facilitation and inhibition of visual orienting as a function of personality. *Personality and Individual Differences*, *18*(4), 503–509. [https://doi.org/10.1016/0191-8869\(94\)00184-T](https://doi.org/10.1016/0191-8869(94)00184-T)
- Avila, C. (2001). Distinguishing BIS-mediated and BAS-mediated disinhibition mechanisms: a comparison of disinhibition models of Gray (1981, 1987) and of Patterson and Newman (1993). *Journal of Personality and Social Psychology*, *80*(2), 311–324. <http://dx.doi.org/10.1037/0022-3514.80.2.311>
- Avila, C., Barrós, A., Ortet, G., Antònia Parcet, M., & Ibañez, M. I. (2003). Set-shifting and sensitivity to reward: A possible dopamine mechanism for explaining disinhibitory disorders. *Cognition & Emotion*, *17*(6), 951–959. <https://doi.org/10.1080/02699930302314>
- Avila, C., Garbin, G., Sanjuán, A., Forn, C., Barrós-Loscertales, A., Bustamante, J. C., ... Parcet, M. A. (2012). Frontostriatal response to set switching is moderated by reward sensitivity. *Social Cognitive and Affective Neuroscience*, *7*(4), 423–430. <https://doi.org/10.1093/scan/nsr028>
- Avila, C., Moltó, J., & Segarra, P. (1995). Sensitivity to Conditioned or Unconditioned Stimuli: What Is the Mechanism Underlying Passive Avoidance Deficits in Extraverts? *Journal of Research in Personality*, *29*(4), 373–394. <https://doi.org/10.1006/JRPE.1995.1022>
- Avila, C., & Parcet, M. A. (1997). Impulsivity and anxiety differences in cognitive inhibition. *Personality and Individual Differences*, *23*(6), 1055–1064. [https://doi.org/10.1016/S0191-8869\(97\)00124-4](https://doi.org/10.1016/S0191-8869(97)00124-4)
- Avila, C., & Parcet, M. A. (2000). The role of Gray's impulsivity in anxiety-mediated differences in

resistance to extinction. *European Journal of Personality*, 14(3), 185–198.
[https://doi.org/10.1002/1099-0984\(200005/06\)14:3<185::AID-PER370>3.0.CO;2-U](https://doi.org/10.1002/1099-0984(200005/06)14:3<185::AID-PER370>3.0.CO;2-U)

Ávila, C., & Parcet, M. A. (2002). Individual differences in reward sensitivity and attentional focus. *Personality and Individual Differences*, 33(6), 979–996. [https://doi.org/10.1016/S0191-8869\(01\)00207-0](https://doi.org/10.1016/S0191-8869(01)00207-0)

Avila, C., Parcet, M. A., & Barrós-Loscertales, A. (2008). A cognitive neuroscience approach to individual differences in sensitivity to reward. *Neurotoxicity Research*, 14(2–3), 191–203.
<https://doi.org/10.1007/BF03033810>

Avila, C., Parcet, M. A., Ortet, G., & Ibáñez-Ribes, M. I. (1999). Anxiety and counter-conditioning: the role of the behavioral inhibition system in the ability to associate aversive stimuli with future rewards. *Personality and Individual Differences*, 27(6), 1167–1179.
[https://doi.org/10.1016/S0191-8869\(99\)00060-4](https://doi.org/10.1016/S0191-8869(99)00060-4)

Ávila, C., & Torrubia, R. (2004). Personality, expectations, and response strategies in multiple-choice question examinations in university students: a test of Gray's hypotheses. *European Journal of Personality*, 18(1), 45–59. <https://doi.org/10.1002/per.506>

Ávila, C., & Torrubia, R. (2008). Performance and conditioning studies. In P. J. Corr (Ed.), *The reinforcement sensitivity theory of personality* (pp. 228–260). New York: Cambridge University Press.

Barrós-Loscertales, A., Meseguer, V., Sanjuán, A., Belloch, V., Parcet, M. A., Torrubia, R., & Avila, C. (2006). Striatum gray matter reduction in males with an overactive behavioral activation system. *The European Journal of Neuroscience*, 24(7), 2071–2074.
<https://doi.org/10.1111/j.1460-9568.2006.05084.x>

Barrós-Loscertales, A., Ventura-Campos, N., Sanjuán-Tomás, A., Belloch, V., Parcet, M.-A., &

- Avila, C. (2010). Behavioral activation system modulation on brain activation during appetitive and aversive stimulus processing. *Social Cognitive and Affective Neuroscience*, 5(1), 18–28. <https://doi.org/10.1093/scan/nsq012>
- Beaver, J. D., Lawrence, A. D., van Ditzhuijzen, J., Davis, M. H., Woods, A., & Calder, A. J. (2006). Individual differences in reward drive predict neural responses to images of food. *The Journal of Neuroscience*, 26(19), 5160–5166. <https://doi.org/10.1523/JNEUROSCI.0350-06.2006>
- Benjamini, Y., & Hochberg, Y. (1995). Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society. Series B (Methodological)*, 57(1), 289–300. <https://doi.org/10.2307/2346101>
- Berridge, K. C., Robinson, T. E., & Aldridge, J. W. (2009). Dissecting components of reward: “liking”, “wanting”, and learning. *Current Opinion in Pharmacology*, 9(1), 65–73. <https://doi.org/10.1016/j.coph.2008.12.014>
- Bijttebier, P., Beck, I., Claes, L., & Vandereycken, W. (2009). Gray’s Reinforcement Sensitivity Theory as a framework for research on personality-psychopathology associations. *Clinical Psychology Review*, 29(5), 421–430. <https://doi.org/10.1016/j.cpr.2009.04.002>
- Biswal, B., Zerrin Yetkin, F., Haughton, V. M., & Hyde, J. S. (1995). Functional connectivity in the motor cortex of resting human brain using echo-planar mri. *Magnetic Resonance in Medicine*, 34(4), 537–541. <https://doi.org/10.1002/mrm.1910340409>
- Boog, M., Goudriaan, A. E., Wetering, B. J. M. v. d., Polak, M., Deuss, H., & Franken, I. H. A. (2014). Rash Impulsiveness and Reward Sensitivity as predictors of treatment outcome in male substance dependent patients. *Addictive Behaviors*, 39(11), 1670–1675. <https://doi.org/10.1016/J.ADDBEH.2014.02.020>

- Bromberg-Martin, E. S., Matsumoto, M., & Hikosaka, O. (2010). Dopamine in Motivational Control: Rewarding, Aversive, and Alerting. *Neuron*, 68(5), 815–834. <https://doi.org/10.1016/J.NEURON.2010.11.022>
- Bzdok, D., Langner, R., Schilbach, L., Engemann, D. A., Laird, A. R., Fox, P. T., & Eickhoff, S. B. (2013). Segregation of the human medial prefrontal cortex in social cognition. *Frontiers in Human Neuroscience*, 7, 232. <https://doi.org/10.3389/fnhum.2013.00232>
- Carr, D. B., & Sesack, S. R. (2000). Projections from the rat prefrontal cortex to the ventral tegmental area: target specificity in the synaptic associations with mesoaccumbens and mesocortical neurons. *The Journal of Neuroscience*, 20(10), 3864–3873. <https://doi.org/10.1523/JNEUROSCI.20-10-03864.2000>
- Carter, R. M., Macinnes, J. J., Huettel, S. A., & Adcock, R. A. (2009). Activation in the VTA and nucleus accumbens increases in anticipation of both gains and losses. *Frontiers in Behavioral Neuroscience*, 3, 21. <https://doi.org/10.3389/neuro.08.021.2009>
- Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS Scales. *Journal of Personality and Social Psychology*, 67(2), 319–333. <https://doi.org/10.1037/0022-3514.67.2.319>
- Caseras, X., Àvila, C., & Torrubia, R. (2003). The measurement of individual differences in Behavioural Inhibition and Behavioural Activation Systems: a comparison of personality scales. *Personality and Individual Differences*, 34(6), 999–1013. [https://doi.org/10.1016/S0191-8869\(02\)00084-3](https://doi.org/10.1016/S0191-8869(02)00084-3)
- Cauda, F., Cavanna, A. E., D'agata, F., Sacco, K., Duca, S., & Geminiani, G. C. (2011). Functional Connectivity and Coactivation of the Nucleus Accumbens: A Combined Functional Connectivity and Structure-Based Meta-analysis. *Journal of Cognitive Neuroscience*, 23(10), 2864–2877. <https://doi.org/10.1162/jocn.2011.21624>

- Choi, E. Y., Yeo, B. T. T., & Buckner, R. L. (2012). The organization of the human striatum estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, *108*(8), 2242–2263. <https://doi.org/10.1152/jn.00270.2012>
- Corr, P. J. (2004). Reinforcement sensitivity theory and personality. *Neuroscience and Biobehavioral Reviews*, *28*(3), 317–332. <https://doi.org/10.1016/j.neubiorev.2004.01.005>
- Costumero, V., Barrós-Loscertales, A., Bustamante, J. C., Ventura-Campos, N., Fuentes, P., & Ávila, C. (2013a). Reward sensitivity modulates connectivity among reward brain areas during processing of anticipatory reward cues. *The European Journal of Neuroscience*, *38*(3), 2399–2407. <https://doi.org/10.1111/ejn.12234>
- Costumero, V., Barrós-Loscertales, A., Bustamante, J. C., Ventura-Campos, N., Fuentes, P., Rosell-Negre, P., & Ávila, C. (2013b). Reward sensitivity is associated with brain activity during erotic stimulus processing. *PloS One*, *8*(6), e66940. <https://doi.org/10.1371/journal.pone.0066940>
- Costumero, V., Barrós-Loscertales, A., Fuentes, P., Rosell-Negre, P., Bustamante, J. C., & Ávila, C. (2016). BAS-drive trait modulates dorsomedial striatum activity during reward response-outcome associations. *Brain Imaging and Behavior*, *10*(3), 869–879. <https://doi.org/10.1007/s11682-015-9466-5>
- D'Ardenne, K., McClure, S. M., Nystrom, L. E., & Cohen, J. D. (2008). BOLD responses reflecting dopaminergic signals in the human ventral tegmental area. *Science*, *319*(5867), 1264–1267. <https://doi.org/10.1126/science.1150605>
- Depue, R. A., & Collins, P. F. (1999). Neurobiology of the structure of personality: dopamine, facilitation of incentive motivation, and extraversion. *Behavioral and Brain Sciences*, *22*(3), 491–569. <http://dx.doi.org/10.1017/S0140525X99002046>

- Derryberry, D., & Reed, M. A. (1994). Temperament and attention: orienting toward and away from positive and negative signals. *Journal of Personality and Social Psychology*, 66(6), 1128–1139. <http://dx.doi.org/10.1037/0022-3514.66.6.1128>
- Di Martino, A., Scheres, A., Margulies, D. S., Kelly, A. M. C., Uddin, L. Q., Shehzad, Z., ... Milham, M. P. (2008). Functional Connectivity of Human Striatum: A Resting State fMRI Study. *Cerebral Cortex*, 18(12), 2735–2747. <https://doi.org/10.1093/cercor/bhn041>
- Düzel, E., Bunzeck, N., Guitart-Masip, M., Wittmann, B., Schott, B. H., & Tobler, P. N. (2009). Functional imaging of the human dopaminergic midbrain. *Trends in Neurosciences*, 32(6), 321–328. <https://doi.org/10.1016/J.TINS.2009.02.005>
- Fatahi, Z., Haghparast, A., Khani, A., & Kermani, M. (2018). Functional connectivity between anterior cingulate cortex and orbitofrontal cortex during value-based decision making. *Neurobiology of Learning and Memory*, 147, 74–78. <https://doi.org/10.1016/J.NLM.2017.11.014>
- Franken, I. H. A., & Muris, P. (2006). BIS/BAS personality characteristics and college students' substance use. *Personality and Individual Differences*, 40(7), 1497–1503. <https://doi.org/10.1016/j.paid.2005.12.005>
- Franken, I. H. A., Muris, P., & Georgieva, I. (2006). Gray's model of personality and addiction. *Addictive Behaviors*, 31(3), 399–403. <https://doi.org/10.1016/j.addbeh.2005.05.022>
- Friston, K. J., Williams, S., Howard, R., Frackowiak, R. S. J., & Turner, R. (1996). Movement-Related effects in fMRI time-series. *Magnetic Resonance in Medicine*, 35(3), 346–355. <https://doi.org/10.1002/mrm.1910350312>
- Fuentes-Claramonte, P., Ávila, C., Rodríguez-Pujadas, A., Costumero, V., Ventura-Campos, N., Bustamante, J. C., ... Barrós-Loscertales, A. (2016a). Characterizing individual differences in

reward sensitivity from the brain networks involved in response inhibition. *NeuroImage*, 124(Pt A), 287–299. <https://doi.org/10.1016/j.neuroimage.2015.08.067>

Fuentes-Claramonte, P., Ávila, C., Rodríguez-Pujadas, A., Costumero, V., Ventura-Campos, N., Bustamante, J. C., ... Barrós-Loscertales, A. (2016b). Inferior frontal cortex activity is modulated by reward sensitivity and performance variability. *Biological Psychology*, 114, 127–137. <https://doi.org/10.1016/j.biopsycho.2016.01.001>

Fuentes-Claramonte, P., Ávila, C., Rodríguez-Pujadas, A., Ventura-Campos, N., Bustamante, J. C., Costumero, V., ... Barrós-Loscertales, A. (2015). Reward Sensitivity Modulates Brain Activity in the Prefrontal Cortex, ACC and Striatum during Task Switching. *PLoS One*, 10(4), e0123073. <https://doi.org/10.1371/journal.pone.0123073>

Fuentes, P., Barrós-Loscertales, A., Rodríguez-Pujadas, A., Ventura-Campos, N., Bustamante, J. C., Costumero, V., ... Ávila, C. (2014a). Behavioral Activation System modulation of brain activity during task switching. *Personality and Individual Differences*, 60, S52. <https://doi.org/10.1016/J.PAID.2013.07.212>

Fuentes, P., Barrós-Loscertales, A., Rodríguez-Pujadas, A., Ventura-Campos, N., Bustamante, J. C., Costumero, V., ... Ávila, C. (2014b). Reward sensitivity modulation of brain activity during response inhibition. *Personality and Individual Differences*, 60, S69. <https://doi.org/10.1016/J.PAID.2013.07.303>

Glashouwer, K. A., Bloot, L., Veenstra, E. M., Franken, I. H. A., & de Jong, P. J. (2014). Heightened sensitivity to punishment and reward in anorexia nervosa. *Appetite*, 75, 97–102. <https://doi.org/10.1016/j.appet.2013.12.019>

Gray, J. A. (1982). *The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system*. Oxford: Oxford University Press.

- Gray, J. A., & McNaughton, N. J. (2000). *The neuropsychology of anxiety: An inquiry into the functions of the septo-hippocampal system* (2nd ed). Oxford: Oxford University Press.
- Haber, S. N., & Knutson, B. (2010). The reward circuit: linking primate anatomy and human imaging. *Neuropsychopharmacology*, *35*(1), 4–26. <https://doi.org/10.1038/npp.2009.129>
- Hahn, T., Dresler, T., Ehlis, A.-C., Plichta, M. M., Heinzl, S., Polak, T., ... Fallgatter, A. J. (2009). Neural response to reward anticipation is modulated by Gray's impulsivity. *NeuroImage*, *46*(4), 1148–1153. <https://doi.org/10.1016/j.neuroimage.2009.03.038>
- Hayes, D. J., Duncan, N. W., Xu, J., & Northoff, G. (2014). A comparison of neural responses to appetitive and aversive stimuli in humans and other mammals. *Neuroscience and Biobehavioral Reviews*, *45*, 350–368. <https://doi.org/10.1016/j.neubiorev.2014.06.018>
- Holmes, A. J., Hollinshead, M. O., Roffman, J. L., Smoller, J. W., & Buckner, R. L. (2016). Individual Differences in Cognitive Control Circuit Anatomy Link Sensation Seeking, Impulsivity, and Substance Use. *The Journal of Neuroscience*, *36*(14), 4038–4049. <https://doi.org/10.1523/JNEUROSCI.3206-15.2016>
- Kasch, K. L., Rottenberg, J., Arnow, B. A., & Gotlib, I. H. (2002). Behavioral activation and inhibition systems and the severity and course of depression. *Journal of Abnormal Psychology*, *111*(4), 589–597. <http://dx.doi.org/10.1037/0021-843X.111.4.589>
- Kennis, M., Rademaker, A. R., & Geuze, E. (2013). Neural correlates of personality: an integrative review. *Neuroscience and Biobehavioral Reviews*, *37*(1), 73–95. <https://doi.org/10.1016/j.neubiorev.2012.10.012>
- Knyazev, G. G. (2004). Behavioural activation as predictor of substance use: mediating and moderating role of attitudes and social relationships. *Drug and Alcohol Dependence*, *75*(3), 309–321. <https://doi.org/10.1016/j.drugalcdep.2004.03.007>

- Krebs, R. M., Schott, B. H., & Düzel, E. (2009). Personality traits are differentially associated with patterns of reward and novelty processing in the human substantia nigra/ventral tegmental area. *Biological Psychiatry*, *65*(2), 103–110. <https://doi.org/10.1016/j.biopsych.2008.08.019>
- Lerner, D. A., Hatak, I., & Rauch, A. (2018). Deep roots? Behavioral Inhibition and Behavioral Activation System (BIS/BAS) sensitivity and entrepreneurship. *Journal of Business Venturing Insights*, *9*, 107–115. <https://doi.org/10.1016/J.JBVI.2018.02.005>
- Locke, H. S., & Braver, T. S. (2008). Motivational influences on cognitive control: behavior, brain activation, and individual differences. *Cognitive, Affective & Behavioral Neuroscience*, *8*(1), 99–112. <https://doi.org/10.3758/CABN.8.1.99>
- Lowe, M. J., Mock, B. J., & Sorenson, J. A. (1998). Functional Connectivity in Single and Multislice Echoplanar Imaging Using Resting-State Fluctuations. *NeuroImage*, *7*(2), 119–132. <https://doi.org/10.1006/NIMG.1997.0315>
- Margulies, D. S., Kelly, A. M. C., Uddin, L. Q., Biswal, B. B., Castellanos, F. X., & Milham, M. P. (2007). Mapping the functional connectivity of anterior cingulate cortex. *NeuroImage*, *37*(2), 579–588. <https://doi.org/10.1016/j.neuroimage.2007.05.019>
- Matton, A., Goossens, L., Braet, C., & Vervaet, M. (2013). Punishment and Reward Sensitivity: Are Naturally Occurring Clusters in These Traits Related to Eating and Weight Problems in Adolescents? *European Eating Disorders Review*, *21*(3), 184–194. <https://doi.org/10.1002/erv.2226>
- Matton, A., Goossens, L., Vervaet, M., & Braet, C. (2015). Temperamental differences between adolescents and young adults with or without an eating disorder. *Comprehensive Psychiatry*, *56*, 229–238. <https://doi.org/10.1016/J.COMPPSYCH.2014.09.005>
- McNaughton, N., & Corr, P. (2008). The neuropsychology of fear and anxiety: a foundation for

- Reinforcement Sensitivity Theory. In P. J. Corr (Ed.), *The reinforcement sensitivity theory of personality* (pp. 44–94). Cambridge: Cambridge University Press.
- Mitchell, J. T., & Nelson-Gray, R. O. (2006). Attention-Deficit/Hyperactivity Disorder symptoms in adults: Relationship to Gray's Behavioral Approach System. *Personality and Individual Differences, 40*(4), 749–760. <https://doi.org/10.1016/j.paid.2005.08.011>
- Mortensen, J. A., Lehn, H., Evensmoen, H. R., & Håberg, A. K. (2015). Evidence for an antagonistic interaction between reward and punishment sensitivity on striatal activity: A verification of the Joint Subsystems Hypothesis. *Personality and Individual Differences, 74*, 214–219. <https://doi.org/10.1016/J.PAID.2014.10.023>
- Murty, V. P., Shermohammed, M., Smith, D. V., Carter, R. M., Huettel, S. A., & Adcock, R. A. (2014). Resting state networks distinguish human ventral tegmental area from substantia nigra. *NeuroImage, 100*, 580–589. <https://doi.org/10.1016/J.NEUROIMAGE.2014.06.047>
- Newman, J. P., MacCoon, D. G., Vaughn, L. J., & Sadeh, N. (2005). Validating a distinction between primary and secondary psychopathy with measures of Gray's BIS and BAS constructs. *Journal of Abnormal Psychology, 114*(2), 319–323. <https://doi.org/10.1037/0021-843X.114.2.319>
- Newman, J. P., Widom, C. S., & Nathan, S. (1985). Passive avoidance in syndromes of disinhibition: psychopathy and extraversion. *Journal of Personality and Social Psychology, 48*(5), 1316–1327. <http://dx.doi.org/10.1037/0022-3514.48.5.1316>
- Nostro, A. D., Müller, V. I., Varikuti, D. P., Pläschke, R. N., Hoffstaedter, F., Langner, R., ... Eickhoff, S. B. (2018). Predicting personality from network-based resting-state functional connectivity. *Brain Structure and Function, 223*(6), 2699–2719. <https://doi.org/10.1007/s00429-018-1651-z>

- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, 9(1), 97–113. [https://doi.org/10.1016/0028-3932\(71\)90067-4](https://doi.org/10.1016/0028-3932(71)90067-4)
- Pardo, Y., Aguilar, R., Molinuevo, B., & Torrubia, R. (2007). Alcohol use as a behavioural sign of disinhibition: evidence from J.A. Gray's model of personality. *Addictive Behaviors*, 32(10), 2398–2403. <https://doi.org/10.1016/j.addbeh.2007.02.010>
- Pastor, M. C., Ross, S. R., Segarra, P., Montañés, S., Poy, R., & Moltó, J. (2007). Behavioral inhibition and activation dimensions: Relationship to MMPI-2 indices of personality disorder. *Personality and Individual Differences*, 42(2), 235–245. <https://doi.org/10.1016/J.PAID.2006.06.015>
- Pickering, A. D., & Gray, J. A. (1999). The neuroscience of personality. In L. A. Pervin & O. P. John (Eds.), *Handbook of personality: Theory and research (2nd edition)* (pp. 277–299). New York: Guilford Press.
- Pickering, A. D., & Gray, J. A. (2001). Dopamine, appetitive reinforcement, and the neuropsychology of human learning: An individual differences approach. In A. Elias & A. Angleitner (Eds.), *Advances in individual differences research* (pp. 113–149). Lengerich: PABST Science Publishers.
- Pinto-Meza, A., Caseras, X., Soler, J., Puigdemont, D., Pérez, V., & Torrubia, R. (2006). Behavioural Inhibition and Behavioural Activation Systems in current and recovered major depression participants. *Personality and Individual Differences*, 40(2), 215–226. <https://doi.org/10.1016/j.paid.2005.06.021>
- Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage*, 59(3), 2142–2154. <https://doi.org/10.1016/J.NEUROIMAGE.2011.10.018>

- Pujara, M. S., Philippi, C. L., Motzkin, J. C., Baskaya, M. K., & Koenigs, M. (2016). Ventromedial Prefrontal Cortex Damage Is Associated with Decreased Ventral Striatum Volume and Response to Reward. *The Journal of Neuroscience*, *36*(18), 5047–5054. <https://doi.org/10.1523/JNEUROSCI.4236-15.2016>
- Rangel, A., Camerer, C., & Montague, P. R. (2008). A framework for studying the neurobiology of value-based decision making. *Nature Reviews. Neuroscience*, *9*(7), 545–556. <https://doi.org/10.1038/nrn2357>
- Richard, J. M., & Berridge, K. C. (2013). Prefrontal Cortex Modulates Desire and Dread Generated by Nucleus Accumbens Glutamate Disruption. *Biological Psychiatry*, *73*(4), 360–370. <https://doi.org/10.1016/J.BIOPSYCH.2012.08.009>
- Richter, A., & Gruber, O. (2018). Influence of ventral tegmental area input on cortico-subcortical networks underlying action control and decision making. *Human Brain Mapping*, *39*(2), 1004–1014. <https://doi.org/10.1002/hbm.23899>
- Rushworth, M. F. S., Noonan, M. P., Boorman, E. D., Walton, M. E., & Behrens, T. E. (2011). Frontal Cortex and Reward-Guided Learning and Decision-Making. *Neuron*, *70*(6), 1054–1069. <https://doi.org/10.1016/J.NEURON.2011.05.014>
- Sesack, S. R., Carr, D. B., Omelchenko, N., & Pinto, A. (2003). Anatomical substrates for glutamate-dopamine interactions: evidence for specificity of connections and extrasynaptic actions. *Annals of the New York Academy of Sciences*, *1003*, 36–52. <https://doi.org/10.1196/annals.1300.066>
- Sescousse, G., Caldú, X., Segura, B., & Dreher, J.-C. (2013). Processing of primary and secondary rewards: a quantitative meta-analysis and review of human functional neuroimaging studies. *Neuroscience and Biobehavioral Reviews*, *37*(4), 681–696. <https://doi.org/10.1016/j.neubiorev.2013.02.002>

- Simon, J. J., Walther, S., Fiebach, C. J., Friederich, H.-C., Stippich, C., Weisbrod, M., & Kaiser, S. (2010). Neural reward processing is modulated by approach- and avoidance-related personality traits. *NeuroImage*, *49*(2), 1868–1874. <https://doi.org/10.1016/J.NEUROIMAGE.2009.09.016>
- Smith, K. S., & Graybiel, A. M. (2013). A Dual Operator View of Habitual Behavior Reflecting Cortical and Striatal Dynamics. *Neuron*, *79*(2), 361–374. <https://doi.org/10.1016/J.NEURON.2013.05.038>
- Taylor, J., Reeves, M., James, L., & Bobadilla, L. (2006). Disinhibitory trait profile and its relation to Cluster B personality disorder features and substance use problems. *European Journal of Personality*, *20*(4), 271–284. <https://doi.org/10.1002/per.585>
- Torrubia, R., Avila, C., & Caseras, X. (2008). Reinforcement sensitivity scales. In P. J. Corr (Ed.), *The reinforcement sensitivity theory of personality* (pp. 188–226). New York: Cambridge University Press.
- Torrubia, R., Ávila, C., Moltó, J., & Caseras, X. (2001). The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ) as a measure of Gray's anxiety and impulsivity dimensions. *Personality and Individual Differences*, *31*(6), 837–862. [https://doi.org/10.1016/S0191-8869\(00\)00183-5](https://doi.org/10.1016/S0191-8869(00)00183-5)
- Tziortzi, A. C., Haber, S. N., Searle, G. E., Tsoumpas, C., Long, C. J., Shotbolt, P., ... Gunn, R. N. (2014). Connectivity-Based Functional Analysis of Dopamine Release in the Striatum Using Diffusion-Weighted MRI and Positron Emission Tomography. *Cerebral Cortex*, *24*(5), 1165–1177. <https://doi.org/10.1093/cercor/bhs397>
- Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., ... Joliot, M. (2002). Automated Anatomical Labeling of Activations in SPM Using a Macroscopic Anatomical Parcellation of the MNI MRI Single-Subject Brain. *NeuroImage*,

15(1), 273–289. <https://doi.org/10.1006/nimg.2001.0978>

Vassena, E., Krebs, R. M., Silvetti, M., Fias, W., & Verguts, T. (2014). Dissociating contributions of ACC and vmPFC in reward prediction, outcome, and choice. *Neuropsychologia*, *59*, 112–123. <https://doi.org/10.1016/J.NEUROPSYCHOLOGIA.2014.04.019>

Yan, C.-G., Craddock, R. C., He, Y., & Milham, M. P. (2013). Addressing head motion dependencies for small-world topologies in functional connectomics. *Frontiers in Human Neuroscience*, *7*, 910. <https://doi.org/10.3389/fnhum.2013.00910>

Yan, C.-G., Wang, X.-D., Zuo, X.-N., & Zang, Y.-F. (2016). DPABI: Data Processing & Analysis for (Resting-State) Brain Imaging. *Neuroinformatics*, *14*(3), 339–351. <https://doi.org/10.1007/s12021-016-9299-4>

Yen, J.-Y., Cheng-Fang, Y., Chen, C.-S., Chang, Y.-H., Yeh, Y.-C., & Ko, C.-H. (2012). The bidirectional interactions between addiction, behaviour approach and behaviour inhibition systems among adolescents in a prospective study. *Psychiatry Research*, *200*(2–3), 588–592. <https://doi.org/10.1016/J.PSYCHRES.2012.03.015>