Underlying differences in resting-state activity metrics related to sensitivity to punishment

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Short Title: ReHo, fALFF, and sensitivity to punishment

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Abstract

Reinforcement sensitivity theory (RST) of personality establishes the punishment sensitivity trait as a source of variation in defensive avoidance/approach behaviors. These individual differences reflect dissimilar sensitivity and reactivity of the fight-flight-freeze and behavioral inhibition systems (FFFS/BIS). The sensitivity to punishment (SP) scale has been widely used in personality research aimed at studying the activity of these systems. Structural and functional neuroimaging studies have confirmed the core biological correlates of FFFS/BIS in humans. Nonetheless, some brain functional features derived from resting-state blood-oxygen level-dependent (BOLD) activity and its association with the punishment sensitivity dimension remain unclear. This relationship would shed light on stable neural activity patterns linked to anxiety-like behaviors and anxiety predisposition. In this study, we analyzed functional activity metrics "at rest" [e.g., regional homogeneity (ReHo) and fractional amplitude of low-frequency fluctuation (fALFF)] and their relationship with SP in key FFFS/BIS regions (e.g., amygdala, hippocampus, and periaqueductal gray) in a sample of 127 healthy adults. Our results revealed a significant negative correlation between the fALFF within all these regions and the scores on SP. Our findings suggest aberrant neural activity (lower fALFF) within the brain's defense system in participants with high trait anxiety, which in turn could reflect lower FFFS/BIS activation thresholds. These neurally-located differences could lead to pathological fear/anxiety behaviors arising from the FFFS and BIS.

Keywords: sensitivity to punishment, anxiety, resting-state activity, amygdala, hippocampus, periaqueductal gray

1. Introduction

One of the most influential taxonomies of personality in contemporary personality psychology came hand in hand with reinforcement sensitivity theory (RST; Gray, 1982) and its revised version (rRST) in 2000 (Gray & McNaughton, 2000; McNaughton & Corr, 2008). Within the rRST, the behavioral and biological description of fear and anxiety behaviors was central. Based on the original RST, the revised version proposed two neurobehavioral systems in charge of the defense system: the fight-flight-freeze system (FFFS) and the behavioral inhibition system (BIS). The former would be responsible for mediating avoidance responses aroused by fearful stimuli, whereas the latter would be activated by conflict situations of approach-avoidance (and also by approach-approach or avoidance-avoidance situations; see McNaughton & Corr, 2004, 2008). This clear distinction of fear and anxiety in two separate dimensions established the most notorious difference between the RST and the rRST, since in the original theory they were conflated in a single anxiety domain. Of note, the behavioral approach system (BAS) would mediate responses toward appetitive, rewarding stimuli. Remarkably, the FFFS and BIS can also be distinguished in two ways: categorically and hierarchically. The category refers to the "defensive direction", that is, whether the behavioral action keeps the organism away from danger (FFFS) or moves it toward danger—this action would be mediated by the BIS by inhibiting behaviors and increasing risk assessment when both appetitive and aversive stimuli are present in the same direction and a conflict emerges between the FFFS and BAS. The hierarchy refers to the level of activation. This activation depends on the "defensive distance", that is, the perceived distance from a threatening stimulus (Corr & McNaughton, 2012; McNaughton & Corr, 2004, 2019). This hierarchy is represented by a neural top-down/bottom-up activation of interconnected regions. The FFFS is composed of the amygdala (fear perception) and the medial hypothalamus and periaqueductal gray (PAG; defensive avoidance behaviors), whereas the BIS relies on the hippocampus (defensive approach behaviors) and the amygdala (Adrián-Ventura, Costumero, Parcet, & Ávila, 2019a; McNaughton, DeYoung, & Corr, 2016).

Behaviorally, the activity of these systems is crucial for keeping organisms alive. Indeed, the behavioral responses elicited by potential threatening stimuli via FFFS or BIS are purely adaptive. In other words, these systems comprise "survival circuits" (McNaughton & Corr, 2018). There are two functioning modes of the FFFS/BIS circuits: checking mode and control mode. In the first case, the system acts as a comparator, monitoring all environmental information to detect possible aversive stimuli. The presence of an aversive stimulus activates the control mode, promoting response inhibition. Thus, individual differences in FFFS and BIS activity are associated with a cognitive pattern characterized by an attentional bias toward aversive stimuli (see Ávila & Torrubia, 2008, for a review). This pattern leads to more intense processing of threat-related stimuli (E. Fox, 1996; Mogg, Bradley, Williams, & Mathews, 1993), higher distractibility due to neutral and aversive peripheral stimuli (Broadbent, Broadbent, & Jones, 1986; E. Fox, 1994; Mathews, May, Mogg, & Eysenck, 1990; Poy, Eixarch, & Ávila, 2004), and enhanced vigilance for aversive stimuli, such as threatening faces or pictures (Bradley, Mogg, Falla, & Hamilton, 1998; Byrne & Eysenck, 1995; Mogg, Garner, & Bradley, 2007; Reinholdt-Dunne, Mogg, & Bradley, 2009; Yiend & Mathews, 2001). Therefore, in anxious persons, attentional mechanisms are more easily triggered by threat cues (Mathews, Yiend, & Lawrence, 2004; Mogg & Bradley, 2002), thus facilitating learning processes in aversive contexts (Avila, 2001; Avila, Moltó, & Segarra, 1995; Avila & Parcet, 2000). These differences can be captured by self-reported personality questionnaires, such as the BIS/BAS scales (Carver & White, 1994) or the Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ; Torrubia et al., 2001). In this regard, the BIS and SP scales have been extensively used in personality research to quantify the (hyper/hypo)activity of both the FFFS and BIS as a conflated dimension of "punishment sensitivity" (Corr, 2008; McNaughton & Corr, 2004), which serves as an index of underlying differences in the perceived defensive distance. Namely, individuals scoring high on these scales—largely associated with anxiety-related personality traits such as Neuroticism or Harm Avoidance—would perceive real distances as shorter, thus showing more intense and frequent defensive behaviors. Therefore, the hyperactivity/hypoactivity of these systems is observable on the psychopathological continuum. Previous studies have associated FFFS hyperactivation with

panic and phobic disorders (Barlow, 1988; Kimbrel, 2008; Pickering & Corr, 2008), and hyperactivation of the BIS with generalized anxiety disorders (Hundt, Nelson-Gray, Kimbrel, Mitchell, & Kwapil, 2007; Kimbrel, 2008; Maack, Tull, & Gratz, 2012; Sportel, Nauta, de Hullu, de Jong, & Hartman, 2011; Struijs et al., 2018; Vervoort et al., 2010). Likewise, BIS hypoactivity has been linked to psychopathic traits (Fowles, 1980; Kimbrel, Nelson-Gray, & Mitchell, 2007; Newman, MacCoon, Vaughn, & Sadeh, 2005; Ross, Benning, Patrick, Thompson, & Thurston, 2009; Ross et al., 2007). Thus, evidence from clinical contexts emphasizes the relationship between the punishment sensitivity dimension and internalizing (higher scores) and externalizing (lower scores) disorders (Bijttebier, Beck, Claes, & Vandereycken, 2009; Corr & McNaughton, 2015), a relationship that is also observed in children and adolescents (Slobodskaya, 2016).

At the neural level, a number of studies have also investigated the relationship between BIS/FFFS activity (measured by the BIS and SP scales) and the brain structure and function (Standen, Firth, Sumich, & Heym, 2022). Anatomically, research analyzing gray matter volume (GMV) in healthy young adults has found a positive relationship between SP and BIS scores and the GMVs of the amygdala and hippocampus (Adrián-Ventura et al., 2019a; Barrós-Loscertales et al., 2006; Cherbuin et al., 2008; Holmes et al., 2012; Levita et al., 2014). Functionally, different studies have also tested RST predictions in humans using functional MRI (fMRI) paradigms. By using different fMRI tasks, BIS scores have been positively related to blood-oxygen level-dependent (BOLD) activity in the anterior cingulate cortex and amygdala in fear-evoking conditions (Bunford, Roberts, Kennedy, & Klumpp, 2017; M Reuter et al., 2004), whereas the amygdala and the ventromedial prefrontal cortex are also positively correlated with BIS scores in the presence of appetitive stimuli (high-calorie food images vs low-calorie food images) in anxious, stressful contexts (Neseliler et al., 2017). Furthermore, two previous studies analyzed the functional connectivity (FC) between the amygdala and hippocampus in task-based fMRI paradigms (Hahn et al., 2010; Hahn, Heinzel, et al., 2013). Interestingly, by means of psychophysiological interaction (PPI) analyses, the authors found a positive association between the amygdala-hippocampus FC and SP during loss anticipation conditions (for reviews see Kennis et al., 2013;

Standen et al., 2022). Based on all this evidence, the amygdala and hippocampus seem to be RST hotspots in the human brain.

However, these previous fMRI studies (task-based) were primarily focused on the neural response to discrete emotional stimuli, whereas the sensitivity and capacity of the brain's defense system to detect threatening cues in the checking mode have been less explored. This predisposition could be studied by means of resting-state fMRI (rs-fMRI). Rs-fMRI provides useful information about stable brain patterns (Gratton et al., 2018; Sanchez-Alonso, Rosenberg, & Aslin, 2021), that is, how intrinsically the brain works "by default" (i.e., in the absence of stimuli). Only two investigations have tested resting-state metrics and their association with the SP personality trait. In a recent study, Costumero et al. (2021) found an association between the rs-FC of BIS/FFFS areas, such as the amygdala, hippocampus, and PAG, and the scores obtained on the SP scale. Nonetheless, the relationship between SP and the rs-FC patterns was observed in the eyes-open sample only. Specifically, the rs-FC between the PAG and the amygdalae and left hippocampus was negative, whereas the connectivity between the hippocampus and amygdala was positive in both hemispheres. In another study, Hahn, Dresler, et al. (2013) analyzed the local synchronization of resting-state BOLD activity. In this study, the authors examined the regional homogeneity (ReHo)—a connectivity measure between neighboring voxels (Aiello et al., 2015)—of both the amygdala and hippocampus, and its correlation with SP. Results showed a negative correlation between the ReHo within these regions and the SP scale. This negative association would reflect a local desynchronization (i.e., aberrant neural firing) within these regions in individuals who scored high on this personality trait (see Hahn, Dresler, et al., 2013). However, even though this latter research analyzed resting-state BOLD activity metrics and BIS/FFFS activity, other resting-state activity measures were not explored. Particularly, no previous investigation has examined the relationship between the fractional amplitude of low frequency fluctuations (fALFF; Zou et al., 2008) and punishment sensitivity. fALFF analyzes the amplitude within low-frequency bands relative to the entire frequency range (Zuo et al., 2010). Thus, fALFF quantifies slow fluctuations—characteristics in resting-state—in single voxels

independently, whereas ReHo depends on the synchronization ("connectivity") of near voxels (Aiello et al., 2015). Although previous studies have analyzed the ALFF in patients with medicated or treated generalized anxiety disorders, observing differences in core anxiety areas such as the hippocampus (e.g., Chen et al., 2020; Cui et al., 2020; Shen et al., 2020), research on its association with the punishment sensitivity trait in healthy adults is lacking. By analyzing this relationship, we could provide new predisposing factors for anxiety-like disorders from the RST framework.

Thus, the aim of this study was to analyze the relationship between BIS/FFFS activity, based on the scores obtained on the SP scale, and the ReHo and fALFF resting-state measures as proxies of neural activity and brain metabolism (Deng et al., 2022). We expected a different pattern of activity in key FFFS/BIS structures as a function of SP, reflecting the expected differences in the checking mode and predisposing these structures to different responses when detecting an aversive cue. Based on a previous study (Hahn, Dresler, et al., 2013) and the observed structural differences in these regions (Adrián-Ventura et al., 2019a), we expect to find differences in the ReHo of key areas within the defense system. In particular, we hypothesize a negative association between SP scores and ReHo within the amygdala, hippocampus, and PAG, whereas this relationship should be altered for fALFF in any direction, given that no previous research has explored this association.

2. Material and methods

2.1 Participants

A total of 136 participants were selected from different projects carried out by our research group. Part of this dataset was used in previous studies that investigated personality traits using RST and other structural (Adrián-Ventura et al., 2019a; Parcet, Adrián-Ventura, Costumero, & Ávila, 2020) and resting-state (e.g., functional connectivity; Adrián-Ventura et al., 2019a; Costumero et al., 2021) MRI metrics. All the participants were recruited through local advertisements. The vast

majority were undergraduate students (90%), given that our group is integrated in a university campus. After ruling out subjects with excessive head movement (see Image Preprocessing section), a final sample of 127 participants underwent data analysis (64 women; age: mean = 23.94, SD = 7.28, range = 18-49). All of them were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). No participant referred to a history of neurological, psychiatric, or severe medical disorders, none had traumatic brain injury with loss of consciousness, and none of them used psychoactive medications. Participants were informed of the nature of the research and provided written informed consent before inclusion. The research project was approved by the Ethical Committee of Jaume I University and was in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

2.2 Personality assessment

All participants completed the Sensitivity to Punishment (SP) scale from the Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ; Torrubia et al., 2001). The SP scale is a self-report measure consisting of 24 dichotomous ("Yes/No") items designed to assess the reactivity and responsivity of the BIS/FFFS by evaluating behavioral responses to potential aversive or conflicting situations. This scale has good content validity and strongly correlates with other anxiety-like personality traits, such as the BIS scale or Harm Avoidance, and with different punishment and anxiety scales (Caseras, Àvila, & Torrubia, 2003; Torrubia, Ávila, & Caseras, 2008). In our sample, the mean score on the SP scale was 9.99 (SD = 5.37; skewness = 0.23, kurtosis = -0.56), and the scale showed good internal consistency (Cronbach's α = 0.86).

2.3 Image acquisition

Images were all acquired on the same 1.5T scanner (Siemens Avanto; Erlangen, Germany). Participants were placed inside the MRI scanner in a supine position, and their heads were immobilized with pads in order to reduce head movement. During scan sessions, participants were

required to be in a resting state and instructed to keep their eyes closed without sleeping or thinking about anything in particular. After scanning, all the participants explicitly stated that they had not experienced any issues during the session. For the rs-fMRI scan, 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 a total of 24 interleaved axial slices parallel to the anterior–posterior commissure covering the whole brain. Prior to the resting state sequences, structural images were also acquired using a 3D T1-weighted MPRAGE sequence with TR = 2200 ms, TE = 3.79 ms, TI = 1090 ms, flip angle = 15°, voxel size = $1 \times 1 \times 1$ mm, matrix = 256 x 256, and bandwidth = 160 hz/px, which facilitated the localization and co-registration of the rs-fMRI data.

2.4 Image preprocessing

The rs-fMRI data processing was performed with the Data Processing Assistant for Resting-State fMRI Advance Edition (DPARSFA, V5.1_201001; http://rfmri.org/DPARSF; Yan & Zang, 2010), a toolbox within the Data Processing and Analysis for Brain Imaging software (DPABI, V5.1_201201; http://rfmri.org/dpabi; Yan et al., 2016). This software was run under the Statistical Parametric Mapping (SPM12, v7771; https://www.fil.ion.ucl.ac.uk/spm/) package in a Matlab (R2018, v9.5; https://www.mathworks.com/) environment.

The preprocessing steps included: 1) removal of the first five volumes to rule out possible artifacts; 2) slice timing correction for interleaved acquisitions (the middle slice was used as the reference point); 3) head motion 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 T1-w structural images to the mean functional image; 5) segmentation of the structural images into gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) by "New Segment + DARTEL" (Ashburner, 2007); 6) removal of spurious variance (nuisance covariates) through linear

regression: 24 parameters from the head motion correction ("Friston 24"; Friston et al., 1996), scrubbing regression of volumes with framewise displacement of (FD) > 0.2 mm (Jenkinson), polynomial (linear and quadratic) trends, and the WM and CSF signals (segmentation masks thresholded at 99% probability) via "CompCor" (5 principal components; Behzadi et al., 2007); and 7) spatial normalization by DARTEL to the Montreal Neurological Institute (MNI) space (voxel size $3 \times 3 \times 3$ mm). The next preprocessing steps were differentially adapted to the ReHo and fALFF data (see sections below).

Participants with more than 1.0 mm or 1.0 degree of head motion in any of the six directions or less than 150 volumes with FD < 0.2 mm (ensuring at least 5 minutes of resting state data with low FD) were excluded for further analysis (9 participants).

2.5 Regional homogeneity (ReHo) analysis

The regional homogeneity (ReHo) maps were obtained to explore regional synchronization of fMRI time courses between neighboring voxels. After spatial normalization, a band-pass temporal filtering (0.01–0.1 Hz) was applied, and Kendall's coefficient of concordance was calculated between each voxel's BOLD time series and those of its 27 neighbors. The ReHo value of each voxel was divided by the global mean ReHo of the whole-brain mask, and the resulting ReHo maps were smoothed with a 4-mm FWHM Gaussian kernel (Yan & Zang, 2010).

2.6 Fractional amplitude of low-frequency fluctuations (fALFF) analysis

Differences in the amplitude of regional spontaneous activity were explored by analyzing the fractional amplitude of low-frequency fluctuations (fALFF). After spatial smoothing, the time series of each voxel was transformed into the frequency domain and band-pass filtered (0.01–0.1 Hz). Then, the square root was calculated at each frequency of the power spectrum, the averaged square root (i.e., ALFF) was obtained at each voxel, and a ratio between the total amplitude within

the low-frequency range and the total amplitude of the detectable frequency range was calculated (i.e., fALFF; Yan & Zang, 2010; Zuo et al., 2010). Another modification made in the data preprocessing pipeline was the omission of polynomial detrending, given that it has been shown to negatively impact fALFF maps (Woletz et al., 2019).

2.7 Statistical analysis

Once the ReHo and fALFF metrics had been obtained for each participant, the resulting standardized (z-scored) maps were analyzed at the SPM's 2nd level. Based on our hypotheses, region of interest (ROI) analyses were conducted by taking core FFFS/BIS regions (Gray & McNaughton, 2000). In particular, we selected the amygdala and the hippocampus from the Hammers atlas (http://brain-development.org/; Hammers et al., 2003). This atlas has two advantages over other available parcellations, that is, a primary focus on the temporal lobe and the removal of the hippocampus tail, which are especially relevant for our study (i.e., we are interested in the most anterior sections; see Bannerman et al., 2004; Fanselow & Dong, 2010). Moreover, we also included the PAG as a ROI. This mask was selected from the Harvard Ascending Arousal Network (AAN) Atlas (Edlow et al., 2012). Once extracted, the amygdala and hippocampus were added up for each hemisphere together with the bilateral PAG mask, thus resulting in a left (left amygdala and left hippocampus plus bilateral PAG) and right (right amygdala and right hippocampus plus bilateral PAG) ROI. The statistical inference for the ROI analyses was calculated via threshold-free cluster enhancement (TFCE, version r224; Smith & Nichols, 2009), a statistical toolbox freely distributed as an SPM extension. This method offers a non-parametric permutation approach that provides two advantages over traditional parametric approaches: better control of nonstationary smoothing and the avoidance of initial (arbitrary) cluster-forming thresholds (Li, Nickerson, Nichols, & Gao, 2017; Smith & Nichols, 2009). All the analyses included age and sex as covariates of no interest (i.e., nuisance regressors), whereas sex was also taken as a covariate of interest within an omnibus (interaction) model in order to explore differential effects by sex. All results were controlled for the false discovery rate (FDR)

at $p < 0.05$, whereas the number of permutations was set at 5000, and the cluster size was weighted on focal effects.

3. Results

Regarding fALFF, the ROI analysis yielded a significant result for the right hemisphere ROI (i.e., right amygdala + hippocampus). Specifically, a first negative correlation was observed between the scores on the SP scale and the ROI's fALFF ($k = 21$ voxels; pFDR-corrected = 0.008; TFCE = 43.05; local maxima at MNI x, y, z = 21, -18, -15, co-located within the hippocampus). Within the same cluster, a significant subpeak was also observed (pFDR-corrected = 0.023; TFCE = 28.04; local maxima at MNI x, y, z = 24, -6, -21, co-located within the amygdala). A second negative correlation within the right ROI was also observed in the PAG area ($k = 2$ voxels; pFDR-corrected = 0.008; TFCE = 25.28; local maxima at MNI x, y, z = -3, -33, -9). These results can be seen in Fig. 1. Additionally, sensitivity power analyses revealed that with our sample ($N = 127$) we could reliably detect effects of $r = -0.25$ with 80% power ($\alpha = 0.05$, two-tailed). Our correlation values ($r = -0.43$ and $r = -0.32$, see Fig. 1) reached this threshold, thus showing that our study was well-powered. The interaction (omnibus) model did not show significant differences by sex.

In relation to ReHo, no significant positive or negative results were found when analyzing the relationship between SP and ReHo within the ROIs. Likewise, no differential effects by sex were observed. Given that no results were obtained at the established threshold, we directly test the negative associations found in Hahn, Dresler, et al. (2013) and analyzed the left and right amygdala and hippocampus individually through partial correlations in IBM SPSS v.26. At the uncorrected level ($p < 0.10$), we only observed a negative association for the right amygdala ($p = 0.046$, one-tailed; $r = -0.15$) and right hippocampus ($p = 0.081$, one-tailed; $r = -0.13$) mean ReHo (controlling for age and sex). Still, these results did not survive the FDR correction, so they should be taken as a trend.
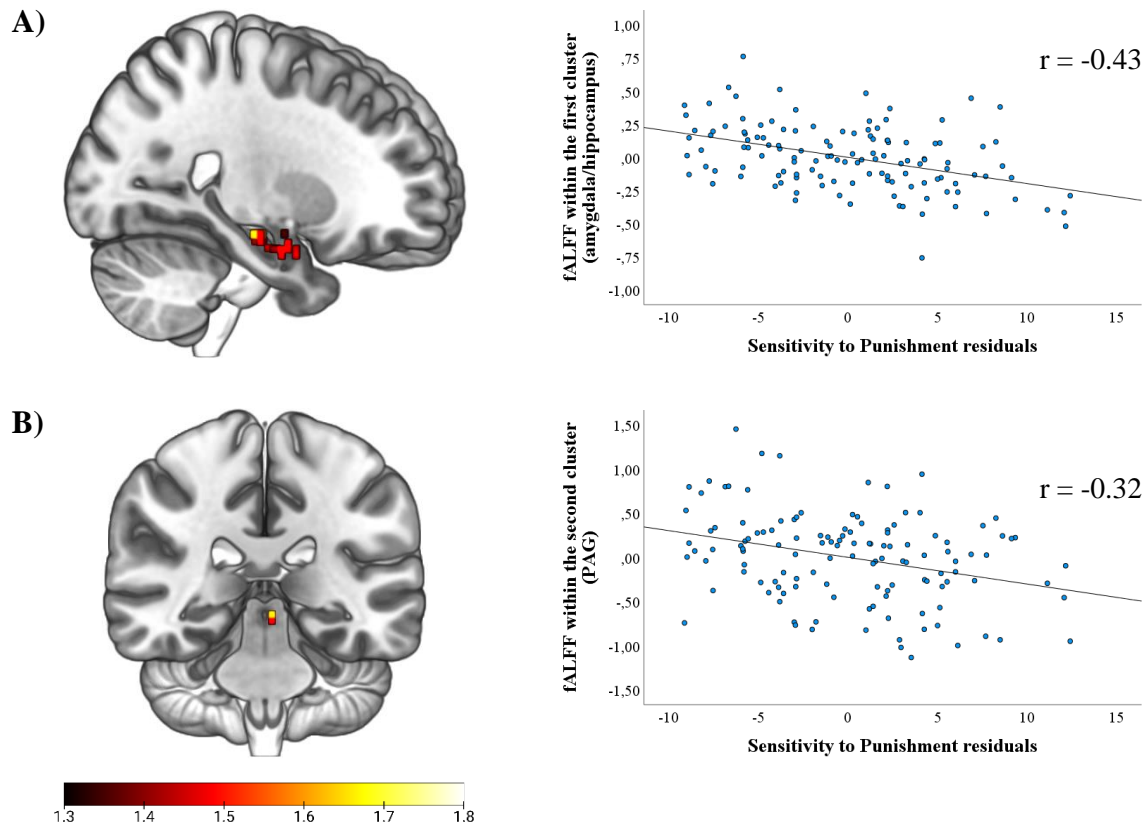
Fig. 1. Results from the TFCE-ROI analysis. A) A negative correlation was observed between the fALFF of the right ROI (co-located within the amygdala/hippocampus) and the scores on the sensitivity to punishment scale. B) Within the right ROI, a negative correlation was also observed in the PAG area. For visualization purposes, the scatterplots represent the correlation between the sensitivity to punishment scores (controlling for age and sex) and the average of the significant resulting voxels (first eigenvariate) from each cluster. The color bar represents log p-values (FDR-corrected). PAG: periaqueductal gray.

4. Discussion

In this study, we analyzed the relationship between the punishment sensitivity trait from RST and brain activity metrics at rest in a large sample of healthy young adults. Contrary to our hypothesis, our results showed no association between the SP scale—as an index of FFFS/BIS activity—and the brain's regional homogeneity within the defense system. Importantly, however, a negative correlation between the scores on this scale and the fALFF of core regions within the defense system (e.g., the amygdala, hippocampus, and PAG) was observed. Therefore,

avoidance/approach behaviors previously described in animal models can be biologically tracked in key brain regions and neural systems (namely, the FFFS and BIS) subject to underlying variances in their activation levels. Our study links anxious personality behaviors arising from these systems to abnormal spontaneous neural activity (i.e., lower fALFF) within the amygdala, hippocampus, and PAG, reflecting differences in the checking mode. These results provide new evidence supporting the biological foundations of RST in the human brain.

Regarding ReHo, we did not find any significant associations between SP and the ReHo of key FFFS/BIS areas. Although we found a tendency when replicating previous findings ($p < 0.10$), we were not able to find a link between the amygdala and hippocampus ReHo and SP (Hahn, Dresler, et al., 2013) and Neuroticism from the Zuckerman-Kuhlman Personality Questionnaire (ZKPQ; see Gentili et al., 2017). Some methodological issues could account for these differences. One of them could be related to the sample size, given that in the studies by Hahn, Dresler, et al. (2013) and Gentili et al. (2017), the samples consisted of 27 and 31 participants, respectively, which differ greatly from the sample size of the present investigation ($N = 127$). Indeed, in previous studies with larger samples, Tian et al. (2016) and Wei et al. (2011) found no association between trait anxiety from the State-Trait Anxiety Inventory (STAI) and Neuroticism from the Eysenck Personality Questionnaire (EPQ) and the amygdala and hippocampus ReHo. In the latter study, the authors only found a negative correlation between Neuroticism and a cluster located in the middle frontal gyrus, whereas in the former, a positive correlation was observed between trait anxiety scores and the ventromedial prefrontal cortex. Dissimilarities between studies could also stem from other methodological aspects, such as age distribution. Previous findings have shown effects of age on punishment sensitivity behaviors (Betts et al., 2020; Pagliaccio et al., 2016) and resting-state neural activity patterns (Hu, Chao, Zhang, Ide, & Li, 2014; Jiang & Zuo, 2016; Zhai & Li, 2019). In our study, the mean age was similar to the ones reported in the aforementioned studies, however, we displayed a larger standard deviation (i.e., a wider range). Furthermore, we included age as a covariate in our analyses. Thus, we cannot rule out age effects when comparing differences between studies. Another methodological issue would be associated with underlying

differences in self-reported instruments (i.e., SP, Neuroticism and trait anxiety). Thus, further research is needed to confirm the possible relationship between cerebral ReHo and anxiety-related personality traits.

When analyzing the low-frequency fluctuations, however, we did find a significant negative correlation between the SP scale and the fALFF within the amygdala, hippocampus, and PAG. The fALFF is defined as the sum of amplitudes within the low-frequency range (0.01–0.1 Hz) relative to the entire detectable frequency spectrum (Zou et al., 2008; Zuo et al., 2010). Thus, fALFF provides information on the intensity of spontaneous brain activity, which in turn may provide evidence about the activity patterns in discrete regions and, subsequently, in resting state networks (Buzsáki & Draguhn, 2004; Mennes et al., 2010; Zuo et al., 2010). This information is of particular interest in terms of behaviors arising from stable personality traits. Brain inter-individual activity during fMRI tasks is reflected in the brain's intrinsic functioning (i.e., at rest; Fox et al., 2007; Smith et al., 2009). In this line, a recent study linked the resting-state fALFF at the voxel-level to glucose metabolism, oxygen, blood flow, and blood volume through PET imaging (Deng et al., 2022). A lower fALFF, conversely, could also be reflecting a neurobehavioral compensation mechanism (Wang et al., 2018). That is, high trait anxiety could lead to lower FFFS/BIS activation thresholds. Hence, in the presence of aversive cues—or at larger defensive distances—, participants with higher SP would need less activation of the defense system areas than participants who score low on this trait. Thus, in relation to the RST framework, it would be plausible to link deviant behaviors arising from the BIS and FFFS to lower fALFF within core anxiety regions such as the amygdala, hippocampus, and PAG. From this perspective, these neural patterns at rest would define the extent to which the FFFS and BIS process and respond to potential aversive stimuli (for a similar interpretation, see Hahn, Dresler, et al., 2013).

The implications of our results align with the foundations of RST. The amygdala, hippocampus, and PAG play a central role in the FFFS/BIS, thus driving a repertoire of behavioral responses associated with fear and anxiety (Gray & McNaughton, 2000; LeDoux, 1994). Whereas previous structural and (task-based) functional studies have confirmed the RST basis in humans (see

Standen et al., 2022 for a recent review), our results also highlight individual differences at rest—particularly in fALFF. These findings complement the results by Hahn, Dresler, et al. (2013), in relation to ReHo, and studies analyzing the connectivity between these regions and its relationship with SP, showing significant correlations at rest (in the eyes-open condition, see Costumero et al. 2021) or during loss anticipation (Hahn et al., 2010). Moreover, the negative correlation between trait anxiety and fALFF within the hippocampus was previously reported (Xue, Lee, & Guo, 2018). Other studies did not find a relationship between anxiety personality traits and fALFF in any of these regions. In particular, using the Neuroticism scale from the ZKPQ and the NEO Five Factor Inventory (NEO-FFI), only a negative correlation was co-located within the precuneus (Gentili et al., 2017; Kunisato et al., 2011). All this evidence suggests that individual differences in amygdala, hippocampus, and PAG activity can be tracked specifically in the context of RST. Therefore, a lower fALFF within these regions plus a larger volume (Adrián-Ventura et al., 2019a) could represent a biological vulnerability trait to anxiety-related disorders. Indeed, in the clinical context, higher ALFF values within the hippocampus have been reported in patients with generalized anxiety disorder (GAD) under medication or in remission, in contrast to healthy controls (Chen et al., 2020; Cui et al., 2020; Shen et al., 2020). These studies would establish a higher ALFF within the hippocampus as a marker of recovery from anxiety disorders. Note, however, that the latter studies analyzed ALFF (but not fALFF) measures, and so our interpretation is speculative.

To the best of our knowledge, this is the first study to analyze the relationship between the punishment sensitivity personality trait and fALFF using rs-fMRI. The reported results add new evidence about the neurobiological correlates of RST in humans in terms of stable brain patterns at rest. However, our research has some limitations. On the one hand, we used the SP scale as a conflated measure of FFFS/BIS activity. Although this approach would be in line with the original RST framework (Gray, 1982), the rRST suggest that individual differences in FFFS/BIS activity are explained by separate dimensions of fear and anxiety (Corr & Cooper, 2016). Along these lines, new scales have been specifically designed for the assessment of rRST systems, which

could be helpful in future rRST studies. Among these new instruments we found the Jackson-5 (Jackson, 2009), the Reinforcement Sensitivity Questionnaire (RSQ; Smederevac, Mitrović, Čolović, & Nikolašević, 2014), the revised Reinforcement Sensitivity Theory Questionnaire (rRST-Q; Reuter, Cooper, Smillie, Markett, & Montag, 2015), and the Reinforcement Sensitivity Theory of Personality Questionnaire (RST-PQ; Corr & Cooper, 2016). So, by using these scales, the personality dimensions raising from the anxiety and fear systems would be more accurately evaluated. Still, the SP trait provides a valid index to study individual differences within the defense system as a source of variation in defensive approach/avoidance behaviors. On the other hand, we utilized a 1.5T scanner to collect the rs-fMRI scans. Currently, however, higher magnetic field scanners (i.e., 3T) are the gold standard, even though 1.5T scanners are still common. Thus, although these methodological issues do not compromise our results, they should be taken into account in future research.

CRediT

Jesús Adrián Ventura: Conceptualization, Methodology, Formal analysis, Writing - Original Draft. **Jaime Fabregat-Nabás**: Methodology, Formal analysis, Data Curation, Writing - Original Draft. **Víctor Costumero**: Conceptualization, Methodology, Writing - Review & Editing. **César Ávila**: Conceptualization, Resources, Writing - Review & Editing, Funding acquisition.

Conflict of interest

The authors declare that they have no conflict of interest.

References

Adrián-Ventura, J., Costumero, V., Parcet, M. A., & Ávila, C. (2019a). Linking personality and brain anatomy: a structural MRI approach to Reinforcement Sensitivity Theory. *Social Cognitive and Affective Neuroscience*, *14*(3), 329–338. https://doi.org/10.1093/scan/nsz011

Adrián-Ventura, J., Costumero, V., Parcet, M. A., & Ávila, C. (2019b). Reward network connectivity "at rest" is associated with reward sensitivity in healthy adults: A resting-state fMRI study. *Cognitive, Affective, & Behavioral Neuroscience*, *19*, 726–736. https://doi.org/10.3758/s13415-019-00688-1

Aiello, M., Salvatore, E., Cachia, A., Pappatà, S., Cavaliere, C., Prinster, A., … Quarantelli, M. (2015). Relationship between simultaneously acquired resting-state regional cerebral glucose metabolism and functional MRI: A PET/MR hybrid scanner study. *NeuroImage*, *113*, 111–121. https://doi.org/10.1016/J.NEUROIMAGE.2015.03.017

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. (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. https://doi.org/10.1037/0022-3514.80.2.311

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. (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

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.

Bannerman, D. M., Rawlins, J. N. P., McHugh, S. B., Deacon, R. M. J., Yee, B. K., Bast, T., … Feldon, J. (2004). Regional dissociations within the hippocampus--memory and anxiety. *Neuroscience and Biobehavioral Reviews*, *28*(3), 273–283. https://doi.org/10.1016/j.neubiorev.2004.03.004

Barlow, D. H. (1988). *Anxiety and its disorders: the nature and treatment of anxiety disorder*. New York: Guilford.

Barrós-Loscertales, A., Meseguer, V., Sanjuán, A., Belloch, V., Parcet, M. A., Torrubia, R., & Avila, C. (2006). Behavioral Inhibition System activity is associated with increased amygdala and hippocampal gray matter volume: A voxel-based morphometry study. *NeuroImage*, *33*(3), 1011–1015. https://doi.org/10.1016/j.neuroimage.2006.07.025

Behzadi, Y., Restom, K., Liau, J., & Liu, T. T. (2007). A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *NeuroImage*, *37*(1), 90–101. https://doi.org/10.1016/J.NEUROIMAGE.2007.04.042

Betts, M. J., Richter, A., de Boer, L., Tegelbeckers, J., Perosa, V., Baumann, V., … Krauel, K. (2020). Learning in anticipation of reward and punishment: perspectives across the human lifespan. *Neurobiology of Aging*, *96*, 49–57. https://doi.org/10.1016/J.NEUROBIOLAGING.2020.08.011

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

Bradley, B. P., Mogg, K., Falla, S. J., & Hamilton, L. R. (1998). Attentional Bias for Threatening Facial Expressions in Anxiety: Manipulation of Stimulus Duration. *Cognition and Emotion*, *12*(6), 737–753. https://doi.org/10.1080/026999398379411

Broadbent, D. E., Broadbent, M. H. P., & Jones, J. L. (1986). Performance correlates of self-reported cognitive failure and of obsessionality. *British Journal of Clinical Psychology*, *25*(4), 285–299. https://doi.org/10.1111/j.2044-8260.1986.tb00708.x

Bunford, N., Roberts, J., Kennedy, A. E., & Klumpp, H. (2017). Neurofunctional correlates of behavioral inhibition system sensitivity during attentional control are modulated by perceptual load. *Biological Psychology*, *127*, 10–17. https://doi.org/10.1016/J.BIOPSYCHO.2017.04.015

Buzsáki, G., & Draguhn, A. (2004). Neuronal olscillations in cortical networks. *Science*, *304*(5679), 1926–1929. https://doi.org/10.1126/science.1099745

Byrne, A., & Eysenck, M. W. (1995). Trait Anxiety, Anxious Mood, and Threat Detection. *Cognition and Emotion*, *9*(6), 549–562. https://doi.org/10.1080/02699939508408982

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

Chen, Y., Wu, Y., Mu, J., Qiu, B., Wang, K., & Tian, Y. (2020). Abnormal fear circuits activities correlated to physical symptoms in somatic anxiety patients. *Journal of Affective Disorders*, *274*, 54–58. https://doi.org/10.1016/J.JAD.2020.05.036

Cherbuin, N., Windsor, T. D., Anstey, K. J., Maller, J. J., Meslin, C., & Sachdev, P. S. (2008). Hippocampal volume is positively associated with behavioural inhibition (BIS) in a large community-based sample of mid-life adults: the PATH through life study. *Social Cognitive*

and Affective Neuroscience, *3*(3), 262–269. https://doi.org/10.1093/scan/nsn018

Corr, P. J. (2008). Reinforcement Sensitivity Theory (RST): introduction. In P. J. Corr (Ed.), *The reinforcement sensitivity theory of personality* (pp. 1–43). Cambridge: Cambridge University Press.

Corr, P. J., & Cooper, A. J. (2016). The Reinforcement Sensitivity Theory of Personality Questionnaire (RST-PQ): Development and Validation. *Psychological Assessment*, *28*(11), 1427–1440. https://doi.org/10.1037/pas0000273

Corr, P. J., & McNaughton, N. (2012). Neuroscience and approach/avoidance personality traits: A two stage (valuation–motivation) approach. *Neuroscience & Biobehavioral Reviews*, *36*(10), 2339–2354. https://doi.org/10.1016/j.neubiorev.2012.09.013

Corr, P. J., & McNaughton, N. (2015). Neural Mechanisms of Low Trait Anxiety and Risk for Externalizing Behavior. In T. P. Beauchaine & S. P. Hinshaw (Eds.), *The Oxford Handbook of Externalizing Spectrum Disorders* (pp. 220–238). New York: Oxford University Press. https://doi.org/10.1093/oxfordhb/9780199324675.013.1

Costumero, V., Adrián-Ventura, J., Bueichekú, E., Miró-Padilla, A., Palomar-García, M. Á., Marin-Marin, L., … Ávila, C. (2021). The manifestation of individual differences in sensitivity to punishment during resting state is modulated by eye state. *Cognitive, Affective and Behavioral Neuroscience*, *21*(1), 144–155. https://doi.org/10.3758/s13415-020-00856-8

Cui, Q., Sheng, W., Chen, Y., Pang, Y., Lu, F., Tang, Q., … Chen, H. (2020). Dynamic changes of amplitude of low-frequency fluctuations in patients with generalized anxiety disorder. *Human Brain Mapping*, *41*(6), 1667–1676. https://doi.org/10.1002/HBM.24902

Deng, S., Franklin, C. G., O'Boyle, M., Zhang, W., Heyl, B. L., Jerabek, P. A., … Fox, P. T. (2022). Hemodynamic and metabolic correspondence of resting-state voxel-based physiological metrics in healthy adults. *NeuroImage*, *250*, 118923.

https://doi.org/10.1016/J.NEUROIMAGE.2022.118923

Edlow, B. L., Takahashi, E., Wu, O., Benner, T., Dai, G., Bu, L., … Folkerth, R. D. (2012). Neuroanatomic connectivity of the human ascending arousal system critical to consciousness and its disorders. *Journal of Neuropathology and Experimental Neurology*, *71*(6), 531–546. https://doi.org/10.1097/NEN.0b013e3182588293

Fanselow, M. S., & Dong, H.-W. (2010). Are the Dorsal and Ventral Hippocampus Functionally Distinct Structures? *Neuron*, *65*(1), 7–19. https://doi.org/10.1016/J.NEURON.2009.11.031

Fowles, D. C. (1980). The Three Arousal Model: Implications of Gray's Two-Factor Learning Theory for Heart Rate, Electrodermal Activity, and Psychopathy. *Psychophysiology*, *17*(2), 87–104. https://doi.org/10.1111/j.1469-8986.1980.tb00117.x

Fox, E. (1994). Attentional Bias in Anxiety: A Defective Inhibition Hypothesis. *Cognition and Emotion*, *8*(2), 165–195. https://doi.org/10.1080/02699939408408934

Fox, E. (1996). Selective processing of threatening words in anxiety: The role of awareness. *Cognition and Emotion*, *10*(5), 449–480. https://doi.org/10.1080/026999396380114

Fox, M. D., Snyder, A. Z., Vincent, J. L., & Raichle, M. E. (2007). Intrinsic Fluctuations within Cortical Systems Account for Intertrial Variability in Human Behavior. *Neuron*, *56*(1), 171–184. https://doi.org/10.1016/J.NEURON.2007.08.023

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

Gentili, C., Cristea, I. A., Ricciardi, E., Vanello, N., Popita, C., David, D., & Pietrini, P. (2017). Not in one metric: Neuroticism modulates different resting state metrics within distinctive brain regions. *Behavioural Brain Research*, *327*, 34–43. https://doi.org/10.1016/j.bbr.2017.03.031

Gratton, C., Laumann, T. O., Nielsen, A. N., Greene, D. J., Gordon, E. M., Gilmore, A. W., …

Petersen, S. E. (2018). Functional Brain Networks Are Dominated by Stable Group and Individual Factors, Not Cognitive or Daily Variation. *Neuron*, *98*(2), 439-452.e5. https://doi.org/10.1016/j.neuron.2018.03.035

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. (2000). *The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system* (2nd ed.). Oxford: Oxford University Press.

Hahn, T., Dresler, T., Plichta, M. M., Ehlis, A.-C., Ernst, L. H., Markulin, F., … Fallgatter, A. J. (2010). Functional amygdala-hippocampus connectivity during anticipation of aversive events is associated with Gray's trait "sensitivity to punishment". *Biological Psychiatry*, *68*(5), 459–464. https://doi.org/10.1016/j.biopsych.2010.04.033

Hahn, T., Dresler, T., Pyka, M., Notebaert, K., & Fallgatter, A. J. (2013). Local Synchronization of Resting-State Dynamics Encodes Gray's Trait Anxiety. *PLOS ONE*, *8*(3), e58336. https://doi.org/10.1371/JOURNAL.PONE.0058336

Hahn, T., Heinzel, S., Notebaert, K., Dresler, T., Reif, A., Lesch, K.-P., … Fallgatter, A. J. (2013). The tricks of the trait: Neural implementation of personality varies with genotype-dependent serotonin levels. *NeuroImage*, *81*, 393–399. https://doi.org/10.1016/J.NEUROIMAGE.2013.05.037

Hammers, A., Allom, R., Koepp, M. J., Free, S. L., Myers, R., Lemieux, L., … Duncan, J. S. (2003). Three-dimensional maximum probability atlas of the human brain, with particular reference to the temporal lobe. *Human Brain Mapping*, *19*(4), 224–247. https://doi.org/10.1002/HBM.10123

Holmes, A. J., Lee, P. H., Hollinshead, M. O., Bakst, L., Roffman, J. L., Smoller, J. W., & Buckner, R. L. (2012). Individual differences in amygdala-medial prefrontal anatomy link negative affect, impaired social functioning, and polygenic depression risk. *The Journal of*

Neuroscience, *32*(50), 18087–18100. https://doi.org/10.1523/JNEUROSCI.2531-12.2012

Hu, S., Chao, H. H. A., Zhang, S., Ide, J. S., & Li, C. S. R. (2014). Changes in cerebral morphometry and amplitude of low-frequency fluctuations of BOLD signals during healthy aging: correlation with inhibitory control. *Brain Structure & Function*, *219*(3), 983–994. https://doi.org/10.1007/S00429-013-0548-0

Hundt, N. E., Nelson-Gray, R. O., Kimbrel, N. A., Mitchell, J. T., & Kwapil, T. R. (2007). The interaction of reinforcement sensitivity and life events in the prediction of anhedonic depression and mixed anxiety-depression symptoms. *Personality and Individual Differences*, *43*(5), 1001–1012. https://doi.org/10.1016/j.paid.2007.02.021

Jackson, C. J. (2009). Jackson-5 scales of revised Reinforcement Sensitivity Theory (r-RST) and their application to dysfunctional real world outcomes. *Journal of Research in Personality*, *43*(4), 556–569. https://doi.org/10.1016/j.jrp.2009.02.007

Jiang, L., & Zuo, X. N. (2016). Regional Homogeneity: A Multimodal, Multiscale Neuroimaging Marker of the Human Connectome. *Neuroscientist*, *22*(5), 486–505. https://doi.org/10.1177/1073858415595004

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

Kimbrel, N. A. (2008). A model of the development and maintenance of generalized social phobia. *Clinical Psychology Review*, *28*(4), 592–612. https://doi.org/10.1016/j.cpr.2007.08.003

Kimbrel, N. A., Nelson-Gray, R. O., & Mitchell, J. T. (2007). Reinforcement sensitivity and maternal style as predictors of psychopathology. *Personality and Individual Differences*, *42*(6), 1139–1149. https://doi.org/10.1016/j.paid.2006.06.028

Kunisato, Y., Okamoto, Y., Okada, G., Aoyama, S., Nishiyama, Y., Onoda, K., & Yamawaki, S.

(2011). Personality traits and the amplitude of spontaneous low-frequency oscillations during resting state. *Neuroscience Letters*, *492*(2), 109–113. https://doi.org/10.1016/j.neulet.2011.01.067

LeDoux, J. E. (1994). Emotion, memory and the brain. *Scientific American*, *270*(6), 50–57. https://doi.org/10.1038/scientificamerican0694-50

Levita, L., Bois, C., Healey, A., Smyllie, E., Papakonstantinou, E., Hartley, T., & Lever, C. (2014). The Behavioural Inhibition System, anxiety and hippocampal volume in a non-clinical population. *Biology of Mood & Anxiety Disorders*, *4*(1), 4. https://doi.org/10.1186/2045-5380-4-4

Li, H., Nickerson, L. D., Nichols, T. E., & Gao, J.-H. (2017). Comparison of a non-stationary voxelation-corrected cluster-size test with TFCE for group-Level MRI inference. *Human Brain Mapping*, *38*(3), 1269–1280. https://doi.org/10.1002/hbm.23453

Maack, D. J., Tull, M. T., & Gratz, K. L. (2012). Examining the incremental contribution of behavioral inhibition to generalized anxiety disorder relative to other Axis I disorders and cognitive-emotional vulnerabilities. *Journal of Anxiety Disorders*, *26*(6), 689–695. https://doi.org/10.1016/j.janxdis.2012.05.005

Mathews, A., May, J., Mogg, K., & Eysenck, M. (1990). Attentional bias in anxiety: Selective search or defective filtering? *Journal of Abnormal Psychology*, *99*(2), 166–173. https://doi.org/10.1037/0021-843X.99.2.166

Mathews, A., Yiend, J., & Lawrence, A. D. (2004). Individual differences in the modulation of fear-related brain activation by attentional control. *Journal of Cognitive Neuroscience*, *16*(10), 1683–1694. https://doi.org/10.1162/0898929042947810

McNaughton, N., & Corr, P. J. (2004). A two-dimensional neuropsychology of defense: fear/anxiety and defensive distance. *Neuroscience and Biobehavioral Reviews*, *28*(3), 285–305. https://doi.org/10.1016/j.neubiorev.2004.03.005

McNaughton, N., & Corr, P. J. (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.

McNaughton, N., & Corr, P. J. (2018). Survival circuits and risk assessment. *Current Opinion in Behavioral Sciences*, *24*, 14–20. https://doi.org/10.1016/j.cobeha.2018.01.018

McNaughton, N., & Corr, P. J. (2019). Hierarchical Levels of Control: The State-Trait Distinction. *Psychological Inquiry*, *30*(3), 158–164. https://doi.org/10.1080/1047840X.2019.1646058

McNaughton, N., DeYoung, C. G., & Corr, P. J. (2016). Approach/Avoidance. In J. R. Absher & J. Cloutier (Eds.), *Neuroimaging Personality, Social Cognition, and Character* (pp. 25–49). Elsevier Inc. https://doi.org/10.1016/B978-0-12-800935-2.00002-6

Mennes, M., Kelly, C., Zuo, X. N., Di Martino, A., Biswal, B. B., Castellanos, F. X., & Milham, M. P. (2010). Inter-individual differences in resting-state functional connectivity predict task-induced BOLD activity. *NeuroImage*, *50*(4), 1690–1701. https://doi.org/10.1016/J.NEUROIMAGE.2010.01.002

Mogg, K., & Bradley, B. P. (2002). Selective orienting of attention to masked threat faces in social anxiety. *Behaviour Research and Therapy*, *40*(12), 1403–1414. https://doi.org/10.1016/S0005-7967(02)00017-7

Mogg, K., Bradley, B. P., Williams, R., & Mathews, A. (1993). Subliminal processing of emotional information in anxiety and depression. *Journal of Abnormal Psychology*, *102*(2), 304–311. https://doi.org/10.1037/0021-843X.102.2.304

Mogg, K., Garner, M., & Bradley, B. P. (2007). Anxiety and orienting of gaze to angry and fearful faces. *Biological Psychology*, *76*(3), 163–169. https://doi.org/10.1016/j.biopsycho.2007.07.005

Neseliler, S., Tannenbaum, B., Zacchia, M., Larcher, K., Coulter, K., Lamarche, M., … Dagher,

A. (2017). Academic stress and personality interact to increase the neural response to high-calorie food cues. *Appetite*, *116*, 306–314. https://doi.org/10.1016/j.appet.2017.05.016

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

Oldfield, R. C. 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

Pagliaccio, D., Luking, K. R., Anokhin, A. P., Gotlib, I. H., Hayden, E. P., Olino, T. M., … Barch, D. M. (2016). Revising the BIS/BAS to Study Development: Measurement Invariance and Normative Effects of Age and Sex from Childhood through Adulthood. *Psychological Assessment*, *28*(4), 429–442. https://doi.org/10.1037/PAS0000186

Parcet, M. A., Adrián-Ventura, J., Costumero, V., & Ávila, C. (2020). Individual Differences in Hippocampal Volume as a Function of BMI and Reward Sensitivity. *Frontiers in Behavioral Neuroscience*, *14*, 53. https://doi.org/10.3389/fnbeh.2020.00053

Pickering, A. D., & Corr, P. J. (2008). J.A. Gray's reinforcement sensitivity theory (RST) of personality. In G. J. Boyle, G. Matthews, & D. H. Saklofske (Eds.), *The SAGE handbook of personality theory and assessment, Vol 2: Personality measurement and testing.* (pp. 239–256). Thousand Oaks, CA: Sage Publications, Inc. https://doi.org/10.4135/9781849200462.n11

Poy, R., Eixarch, M. del C., & Ávila, C. (2004). On the relationship between attention and personality: Covert visual orienting of attention in anxiety and impulsivity. *Personality and Individual Differences*, *36*(6), 1471–1481. https://doi.org/10.1016/S0191-8869(03)00242-3

Reinholdt-Dunne, M. L., Mogg, K., & Bradley, B. P. (2009). Effects of anxiety and attention control on processing pictorial and linguistic emotional information. *Behaviour Research*

and Therapy, *47*(5), 410–417. https://doi.org/10.1016/j.brat.2009.01.012

Reuter, M, Stark, R., Hennig, J., Walter, B., Kirsch, P., Schienle, A., & Vaitl, D. (2004). Personality and emotion: test of Gray's personality theory by means of an fMRI study. *Behavioral Neuroscience*, *118*(3), 462–469. https://doi.org/10.1037/0735-7044.118.3.462

Reuter, Martin, Cooper, A. J., Smillie, L. D., Markett, S., & Montag, C. (2015). A new measure for the revised reinforcement sensitivity theory: psychometric criteria and genetic validation. *Frontiers in Systems Neuroscience*, *9*, 38. https://doi.org/10.3389/fnsys.2015.00038

Ross, S. R., Benning, S. D., Patrick, C. J., Thompson, A., & Thurston, A. (2009). Factors of the Psychopathic Personality Inventory. *Assessment*, *16*(1), 71–87. https://doi.org/10.1177/1073191108322207

Ross, S. R., Moltó, J., Poy, R., Segarra, P., Pastor, M. C., & Montañés, S. (2007). Gray's model and psychopathy: BIS but not BAS differentiates primary from secondary psychopathy in noninstitutionalized young adults. *Personality and Individual Differences*, *43*(7), 1644–1655. https://doi.org/10.1016/j.paid.2007.04.020

Sanchez-Alonso, S., Rosenberg, M. D., & Aslin, R. N. (2021). Functional connectivity patterns predict naturalistic viewing versus rest across development. *NeuroImage*, *229*, 117630. https://doi.org/10.1016/J.NEUROIMAGE.2020.117630

Shen, Z., Zhu, J., Ren, L., Qian, M., Shao, Y., Yuan, Y., & Shen, X. (2020). Aberrant amplitude low-frequency fluctuation (ALFF) and regional homogeneity (ReHo) in generalized anxiety disorder (GAD) and their roles in predicting treatment remission. *Annals of Translational Medicine*, *8*(20), 1319–1319. https://doi.org/10.21037/ATM-20-6448

Slobodskaya, H. R. (2016). The contribution of reinforcement sensitivity to the personality-psychopathology hierarchical structure in childhood and adolescence. *Journal of Abnormal Psychology*, *125*(8), 1067–1078. https://doi.org/10.1037/abn0000179

Smederevac, S., Mitrović, D., Čolović, P., & Nikolašević, Ž. (2014). Validation of the measure of revised reinforcement sensitivity theory constructs. *Journal of Individual Differences*, *35*(1), 12–21. https://doi.org/10.1027/1614-0001/a000121

Smith, S. M., Fox, P. M. T., Miller, K. L., Glahn, D. C., Fox, P. M. T., Mackay, C. E., … Beckmann, C. F. (2009). Correspondence of the brain's functional architecture during activation and rest. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(31), 13040–13045. https://doi.org/10.1073/pnas.0905267106

Smith, S. M., & Nichols, T. E. (2009). Threshold-free cluster enhancement: Addressing problems of smoothing, threshold dependence and localisation in cluster inference. *NeuroImage*, *44*(1), 83–98. https://doi.org/10.1016/j.neuroimage.2008.03.061

Sportel, B. E., Nauta, M. H., de Hullu, E., de Jong, P. J., & Hartman, C. A. (2011). Behavioral Inhibition and Attentional Control in Adolescents: Robust Relationships with Anxiety and Depression. *Journal of Child and Family Studies*, *20*(2), 149–156. https://doi.org/10.1007/s10826-010-9435-y

Standen, B., Firth, J., Sumich, A., & Heym, N. (2022). The neural correlates of reinforcement sensitivity theory: A systematic review of the (f)MRI literature. *Psychology & Neuroscience*. https://doi.org/10.1037/PNE0000284

Struijs, S. Y., Lamers, F., Rinck, M., Roelofs, K., Spinhoven, P., & Penninx, B. W. J. H. (2018). The predictive value of Approach and Avoidance tendencies on the onset and course of depression and anxiety disorders. *Depression and Anxiety*, *35*(6), 551–559. https://doi.org/10.1002/da.22760

Tian, X., Wei, D., Du, X., Wang, K., Yang, J., Liu, W., … Qiu, J. (2016). Assessment of trait anxiety and prediction of changes in state anxiety using functional brain imaging: A test-retest study. *NeuroImage*, *133*, 408–416. https://doi.org/10.1016/J.NEUROIMAGE.2016.03.024

Torrubia, R., Ávila, 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

Vervoort, L., Wolters, L. H., Hogendoorn, S. M., de Haan, E., Boer, F., & Prins, P. J. M. (2010). Sensitivity of Gray's Behavioral Inhibition System in clinically anxious and non-anxious children and adolescents. *Personality and Individual Differences*, *48*(5), 629–633. https://doi.org/10.1016/j.paid.2009.12.021

Wang, S., Zhao, Y., Cheng, B., Wang, X., Yang, X., Chen, T., … Gong, Q. (2018). The optimistic brain: Trait optimism mediates the influence of resting-state brain activity and connectivity on anxiety in late adolescence. *Human Brain Mapping*, *39*(10), 3943–3955. https://doi.org/10.1002/HBM.24222

Wei, L., Duan, X., Yang, Y., Liao, W., Gao, Q., Ding, J., … Chen, H. (2011). The synchronization of spontaneous BOLD activity predicts extraversion and neuroticism. *Brain Research*, *1419*, 68–75. https://doi.org/10.1016/j.brainres.2011.08.060

Woletz, M., Hoffmann, A., Tik, M., Sladky, R., Lanzenberger, R., Robinson, S., & Windischberger, C. (2019). Beware detrending: Optimal preprocessing pipeline for low-frequency fluctuation analysis. *Human Brain Mapping*, *40*(5), 1571–1582. https://doi.org/10.1002/hbm.24468

Xue, S., Lee, T., & Guo, Y. (2018). Spontaneous activity in medial orbitofrontal cortex correlates with trait anxiety in healthy male adults. *Journal of Zhejiang University. Science. B*, *19*(8), 643–653. https://doi.org/10.1631/JZUS.B1700481

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

Yan, C.-G., & Zang, Y.-F. (2010). DPARSF: A MATLAB Toolbox for "Pipeline" Data Analysis of Resting-State fMRI. *Frontiers in Systems Neuroscience*, *4*. https://doi.org/10.3389/FNSYS.2010.00013

Yiend, J., & Mathews, A. (2001). Anxiety and attention to threatening pictures. *The Quarterly Journal of Experimental Psychology Section A*, *54*(3), 665–681. https://doi.org/10.1080/713755991

Zhai, J., & Li, K. (2019). Predicting brain age based on spatial and temporal features of human brain functional networks. *Frontiers in Human Neuroscience*, *13*, 62. https://doi.org/10.3389/fnhum.2019.00062

Zou, Q. H., Zhu, C. Z., Yang, Y., Zuo, X. N., Long, X. Y., Cao, Q. J., … Zang, Y. F. (2008). An improved approach to detection of amplitude of low-frequency fluctuation (ALFF) for resting-state fMRI: Fractional ALFF. *Journal of Neuroscience Methods*, *172*(1), 137–141. https://doi.org/10.1016/j.jneumeth.2008.04.012

Zuo, X. N., Di Martino, A., Kelly, C., Shehzad, Z. E., Gee, D. G., Klein, D. F., … Milham, M. P. (2010). The oscillating brain: complex and reliable. *NeuroImage*, *49*(2), 1432–1445. https://doi.org/10.1016/J.NEUROIMAGE.2009.09.037