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Sensation-seeking is related to functional connectivities of the medial orbitofrontal cortex with the anterior cingulate cortex

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ABSTRACT

Sensation-seeking is a multifaceted personality trait with components that include experience-seeking, thrill and adventure seeking, disinhibition, and susceptibility to boredom, and is an aspect of impulsiveness. We analysed brain regions involved in sensation-seeking in a large-scale study with 414 participants and showed that the sensation-seeking score could be optimally predicted from the functional connectivity with typically (in different participants) 18 links between brain areas (measured in the resting state with fMRI) with correlation $r = 0.34$ ($p = 7.3 \times 10^{-13}$) between the predicted and actual sensation-seeking score across all participants. Interestingly, 8 of the 11 links that were common for all participants were between the medial orbitofrontal cortex and the anterior cingulate cortex and yielded a prediction accuracy $r = 0.30$ ($p = 4.8 \times 10^{-10}$). We propose that this important aspect of personality, sensation-seeking, reflects a strong effect of reward (in which the medial orbitofrontal cortex is implicated) on promoting actions to obtain rewards (in which the anterior cingulate cortex is implicated). Risk-taking was found to have a moderate correlation with sensation-seeking ($r = 0.49$, $p = 3.9 \times 10^{-26}$), and three of these functional connectivities were significantly correlated ($p < 0.05$) with the overall risk-taking score. This discovery helps to show how the medial orbitofrontal and anterior cingulate cortices influence behaviour and personality, and indicate that sensation-seeking can involve in part the medial orbitofrontal cortex reward system, which can thereby become associated with risk-taking and a type of impulsiveness.

1. Introduction

Sensation-seeking is a multifaceted personality trait with components that include experience-seeking, thrill and adventure seeking, disinhibition, and susceptibility to boredom (Zuckerman, 1994). High sensation seekers, compared to low sensation seekers, are more vulnerable to reckless driving (Jonah, 1997), physical risk sports (Ruedl et al., 2012), unprotected sexual activities (Hoyle et al., 2000), problem gambling (Harris et al., 2015), and substance use (Bardo et al., 1996). One critical issue is the mechanisms predisposing those high in sensation-seeking to such risky behaviours. Addressing this issue is of great importance not only in prevention programs aimed at reducing the occurrence of sensation-seeking behaviours where these may be dangerous (Sargent et al., 2010), but also in the development of risk-taking models (Schonberg et al., 2011).

Individuals with high sensation-seeking have a stronger orienting response and greater cortical arousal in response to intense visual or auditory stimuli. They also show a preference for, and have stronger skin conductance responses to, sexually explicit and violent stimuli (Smith et al., 1990). Taken together, this evidence suggests that high sensation seekers show hypersensitivity to intense and novel stimuli.

Previous research on brain processing related to sensation-seeking

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has typically involved activation studies with relatively low numbers of participants. In one study, activation in the ventral striatum in a delayed incentive task was related to individual differences in sensation-seeking and novelty seeking (Abler et al., 2006). In another study, reactivity to reward within the nucleus accumbens had different relations to sensation-seeking at different ages (Hawes et al., 2017). Joseph et al. (2009) found that high sensation seekers had larger responses in the posteromedial orbitofrontal cortex and insula to arousing pictures. In a gambling task, it was found that those with high scores for thrill and adventure-seeking had larger activations in the ventral striatum, insula, precuneus and superior frontal gyrus (Kruschwitz et al., 2012). In another gambling task, high sensation seekers had greater responses to Wins in the prefrontal cortex and insula (Cservenka et al., 2013). Activation of the ventrolateral prefrontal cortex to reward expectancy has also been related to impulsive sensation-seeking (Chase et al., 2017).

In the present study, we used a different approach with no task being performed, by analysing resting-state functional connectivity and relating this to sensation-seeking. A highlight of the investigation described here is the large number of participants involved (414). Another feature of the present investigation is the use and further development of methods in which, in addition to measuring correlations of sensation-seeking with functional connectivities, we also made predictions about sensation-seeking from the functional connectivities. The prediction approach provides another way to identify functional connectivity links related to sensation-seeking. The prediction method used was to identify relevant links by finding the links with which the optimal prediction could be made (Liu et al., 2018a). The predictions were made with an elastic net linear regression model because an elastic net operates reasonably when the features are correlated (Cui and Gong, 2018). We know of no other large-scale study of the relation between sensation-seeking and functional connectivity, although a small study did relate risk-taking to reduced functional connectivity between the mainly lateral orbitofrontal cortex and the amygdala (Crane et al., 2018). Because sensation-seeking may be related to some types of impulsivity, we also measured the correlations in this dataset between sensation-seeking and different types of impulsivity and further investigated whether the functional connectivities related to sensation-seeking were also related to impulsivity.

The hypotheses we investigated were: (1) Are some resting-state functional connectivities significantly related to sensation-seeking? (2) Can sensation-seeking be predicted from functional connectivities? (3) Are some of the functional connectivities related to sensation-seeking also related to impulsive behaviour? (4) Are functional connectivities in brain areas related to emotion such as the orbitofrontal cortex, amygdala, and anterior cingulate cortex (Rolls, 2014, 2019b) related to sensation-seeking? Although (4) was a hypothesis, we did not exclude any brain area from consideration and performed a whole-brain analysis.

2. Method

2.1. Participants, resting-state fMRI, and preprocessing

The data used in this study is provided by the enhanced Nathan Kline Institute-Rockland Sample (NKI-RS) dataset (Nooner et al., 2012). NKI-RS is an ongoing, institutionally centred endeavor aimed at creating a large-scale (N > 1000) community sample of participants across the lifespan, which was approved by the Ethics Committee of the Nathan Kline Institute and Montclair State University. Measures include a wide array of physiological and psychological assessments, genetic information, and advanced neuroimaging. Anonymised data are made available (fcon_1000.projects.nitrc.org/index/enhanced). 414 participants were involved in this prediction analysis, aged from 18 to 85. All of these participants have available resting-state fMRI data and the behaviour scores for sensation-seeking.

The resting-state fMRI data were acquired on a 3T Siemens Trio Scanner with a BOLD-weighted multiband EPI sequence (TR = 645 ms, voxel size = 3 mm, duration = 10 min), with the participants awake and looking at a fixation cross on the screen (Nooner et al., 2012).

2.1.1. Data preprocessing

Resting-state fMRI data were preprocessed using FSL (Jenkinson et al., 2012) and AFNI (Cox, 1996). For each individual, the preprocessing steps included: slice timing correction (FSL slicetimer), motion correction (FSL mcflirt), spatial smoothing by a 3D Gaussian kernel (FWHM = 6 mm), despiking motion artifacts using the Brain-Wavelet Toolbox (Patel et al., 2014), registering to a $3 \times 3 \times 3$ mm^3 standard space by first aligning the functional image to individual T1 structural images using boundary-based registration (BBR (Greve and Fischl, 2009)) and then to standard space using FSL's linear and non-linear registration tool (FSL flirt and fnirt), regressing out nuisance covariates including Friston's 24 head motion parameters (Friston et al., 1996), white matter signal, and the cerebrospinal fluid signal. No temporal filtering was used to ensure compatibility for possible analysis for effective connectivity. All the images were manually checked to ensure successful preprocessing. The resulting time courses were used for the construction and analysis of the brain functional connectivity networks. Global signals were not regressed out, for reasons described elsewhere (Cheng et al., 2016).

After preprocessing, the whole brain was parcellated to reduce the high dimensionality of the voxel-level data. In this study, 94 regions for the brain (excluding the cerebellum) were defined by the Automated Anatomical Labelling Atlas 2 because it has been tailored to include clear subdivisions of the orbitofrontal cortex (Rolls et al., 2015). The names of the brain areas are shown in Table S1. The time series were extracted for each region by averaging the signals of all voxels within that region.

2.2. Construction of the whole-brain functional network

Functional connectivity is defined as the correlation of the BOLD signal averaged across time between pairs of brain regions or voxels (Biswal et al., 1995). For each pair of brain regions, the Pearson correlation was calculated from the BOLD signal across the time series for that pair of brain regions, to provide the measure of functional connectivity between the 94×94 brain regions for each participant. Fisher's r-to-z transformation was then implemented to improve the normality of the correlation coefficients, resulting in a 94 by 94 symmetric matrix that represented the links between every pair of brain regions.

2.3. Correlation of the functional connectivities with sensation-seeking

Interest in sensation-seeking as a measure was developed by Zuckerman (1994) and came to be included in the UPPS as a result of a factor analysis (Whiteside and Lynam, 2001). The UPPS-P is a 59-item self-report inventory in its revised version (originally UPPS) that quantifies five different aspects of impulsive behaviour (Lynam et al., 2006): (i) negative urgency, which refers to the tendency to experience strong impulses under conditions of negative affect; (ii) lack of perseverance that reflects the experience of having problems with remaining focused on a task that might be boring or too difficult; (iii) lack of premeditation that describes the tendency to engage in an act without reflecting the consequences of that act beforehand; (iv) sensation-seeking that further comprises two aspects: (a) the propensity to enjoy and chase exciting activities; (b) an openness to engage in new experiences that might be dangerous; and (v) positive urgency that involves the tendency towards rash actions in response to very positive mood. Each item can be scored on a four-point Likert scale, ranging from 1 (strongly agree) to 4 (strongly disagree). Reversed items are recoded afterwards so that higher scores indicate a more pronounced level of self-reported trait impulsivity. The questions used to produce the sensation-seeking score are available (Whiteside and Lynam, 2001) and are shown in the Supplementary Material, and included: “I generally seek new and exciting experiences and sensations”, “I welcome new and exciting experiences and sensations, even if they are a little frightening and unconventional", and "I quite enjoy taking risks".

After the functional connectivity matrices of all participants had been calculated, correlations between the functional connectivities and the sensation-seeking scores across all participants were calculated to investigate which brain regions have connectivities related with sensation-seeking. In more detail, a partial correlation was performed between the functional connectivities and the sensation-seeking scores with age, sex, ethnicity, race and head motion regressed out. In this study, FDR correction ($p < 0.05$) for multiple comparisons (Benjamini and Hochberg, 1995) for the functional connectivity between any pair of AAL2 brain regions was used.

2.4. *Prediction of the sensation-seeking scores from the functional connectivities*

A schematic overview of the method used in this study is shown in Fig. 1A. The method used was developed from methods described by Liu et al. (2018a) and Cui and Gong (2018) in which the links optimal in making the prediction were found (see 2.5), and an elastic net linear

A

Step 1. Calculate the 94*94 functional connectivity matrix for each individual.

Step 2. Use leave-one-out (or k-fold) for cross-validation:

Perform a partial correlation between the functional connectivities and the NKI sensation-seeking scores across all individuals in the training set.

This provides a 94*94 correlation matrix between the functional connectivities and the sensation-seeking scores.

Threshold this correlation matrix at a set of p values (0.0001 to 0.05 in the step of 0.0001) to obtain a subset of the most significant links and perform elastic net regression to obtain the predicted sensation-seeking score of each individual from the subset of functional connectivities.

The optimal λ value and α value of the elastic net regression model, and the p threshold of selecting the most significant links, were obtained by cross-validation within the training dataset of each leave-one-out loop.

Step 3. Perform a permutation test to test the significance of the best prediction of the sensation-seeking score.

Step 4. Analyze the functional connectivity links selected that provide the best prediction.

B

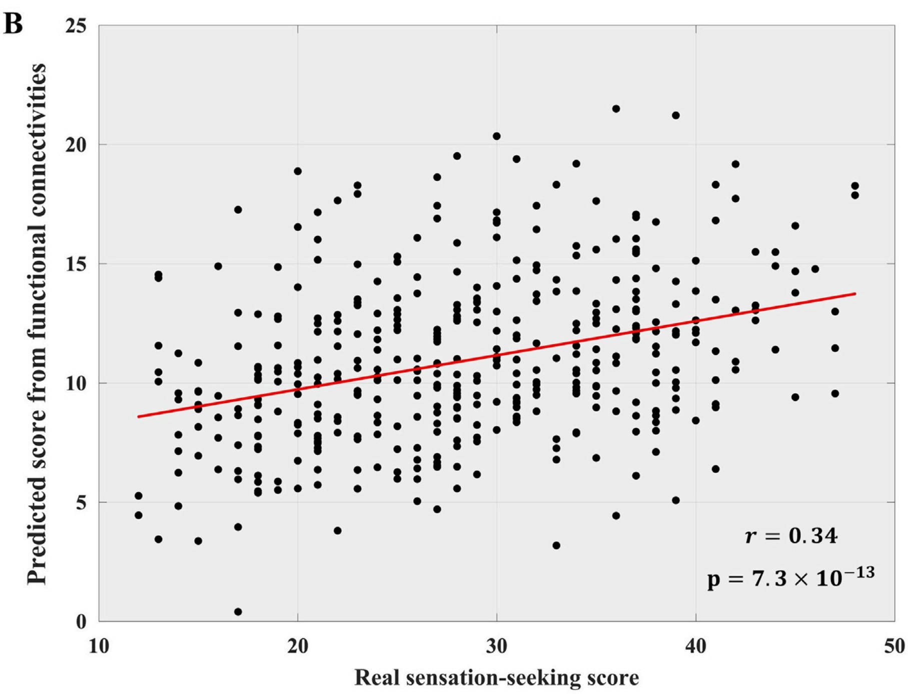

Fig. 1. a. Schematic overview of the prediction method.
1b. The correlation was 0.34 between the predicted sensation-seeking score from the functional connectivities and the actual score of each of the 414 individuals obtained with the optimal p-threshold value for selecting which functional connectivity links to use, which was 0.001. Each data point is from a different individual.

regression model was used to make the predictions because it is a powerful approach when there is some correlation between the features. The functional connectivity matrix includes functional connectivity links that have some correlations with each other. We made a comparison and found that the elastic net regression had a considerably better prediction performance than a support vector regression (SVR) in the current study (see Fig. 1B).

Elastic-net regression combines L1-norm and L2-norm regularizations in the standard linear regression loss function to make predictions (Zou and Hastie, 2005). The regression model used is as follows:

$$\widehat{Y} = \sum_{j=1}^{p} \beta_j X_j + \beta_0$$

where $\widehat{Y}$ is the best estimate of the predicted value of the sensation-seeking scores, X_j is the value of the j^{th} feature used in the prediction model, β_j is the regression coefficient of the j^{th} feature and p is the number of features. The aim of the regression model is to find a function $F(X) = \sum_{j=1}^{p} \beta_j X_j + \beta_0$ that can best predict the actual behavioural score by examining the regression coefficients. The objective function takes the form:

$$\min_{\beta} \sum_{i=1}^{N} \left(f(x_i) - y_i \right)^2 + \lambda \sum_{j=1}^{p} \left(\alpha |\beta_j| + \frac{1}{2}(1-\alpha) \|\beta_j\|^2 \right)$$

where $f(x_i)$ is the value of the predicted behavioural score for the i^{th}subject, y_i is the observed behavioural score, and N is the number of subjects. A mixing parameter α, is used to control the relative weighting of the L1-norm and L2-norm contributions. In addition, a regularization parameter λ is used to control the trade-off of penalties between bias and variance.

The *LASSO* function in MATLAB was used to implement elastic net regression. The optimal λ value and α-value were obtained by cross-validation within the training dataset of each leave-one-out loop.

2.5. Individual prediction framework

A schematic overview of the prediction method is shown in Fig. 1A. In this prediction model, a leave-one-out cross-validation was implemented because it provides efficient use of the data in the cross-validation, and is stable. However, the same prediction procedure was also implemented with 10-fold cross-validation to provide an additional check, as shown in the Supplementary Material. In each leave-one-out iteration, the most significantly correlated functional connectivity (FC) links were selected by performing a partial correlation between the functional connectivity and the sensation-seeking score across all samples in the training set except for the single test sample. The effects of age, sex, ethnicity, race and head motion were regressed out. The individual prediction was performed with groups of functional connectivities more significant than a certain p threshold (i.e. the p value of the partial correlation between the functional connectivity and the sensation-seeking score had to be under the p threshold) (Liu et al., 2018a). Many different p values were implemented in order to find the links optimal for making the prediction. The p threshold was obtained within the training dataset of each leave-one-out loop. The elastic net regression model was trained with the training set with the group of the most significant functional connectivities defined in this way and tested by predicting the test sample with leave-one-out cross-validation. The Pearson correlation coefficients between the actual scores and the predicted scores were computed to quantify the accuracy of the prediction (Erus et al., 2015; Siegel et al., 2016). To be specific, the predicted score of each participant in each iteration was saved in one vector, and the correlation between the predicted scores and actual scores was calculated across all 414 participants.

2.6. Statistical test: Permutation analysis

To determine whether the predicted scores obtained from the prediction model were significantly better than random, a nonparametric permutation procedure was adopted. In each permutation, the symptom scores across all participants were randomly shifted, and then the elastic net prediction analysis was conducted. The null distribution for the highest correlation between the actual scores and predicted scores was formed by running the permutation procedure 10000 times, resulting in a significance level of $p < 0.0001$ (Fig. S1).

2.7. Association of sensation-seeking with risking-taking, and substance use

The correlation between the sensation-seeking score and the risk-taking score was also measured to examine whether the sensation-seeking score is associated with risk-taking behaviours. The risk-taking score was provided by the Domain-Specific Risk-Taking Scale (DOSPERT) (Blais and Weber, 2006), which assesses risk-taking in five content domains: financial decisions (separately for investing versus gambling), health/safety, recreational, ethical, and social decisions. The associations between the sensation-seeking and the overall risk-taking score and its five subscales were examined.

In addition, the correlation between the sensation-seeking score and the substance use scores available in the NKI dataset was also measured to examine whether the sensation-seeking score is associated with substance use behaviours. The measure of substance use was obtained with the adult self-report questionnaire (ASR) (Achenbach and Rescorla, 2003) made available in the NKI dataset. The associations between the sensation-seeking and alcohol, tobacco, and drug use were examined.

3. Results

3.1. Functional connectivities that predict and are correlated with sensation-seeking

Five functional connectivities were significantly correlated with the sensation-seeking scores across all participants at $p < 0.05$ FDR corrected, corresponding to a p threshold of 3.83×10^{-5} in the partial correlations (shown in Table 1, indicated by *). All of these five functional connectivities were between the medial orbitofrontal cortex and the anterior cingulate cortex. The AAL2 areas (Rolls et al., 2015) included here as medial orbitofrontal cortex were OFCmed, OFCpost, OFCant, Rectus, and olfactory tubercle (Rolls et al., 2018) (see Table S1).

For the prediction approach as outlined in Fig. 1, functional connectivities were used to predict the sensation-seeking score with an elastic net regression model. The overall accuracy of this prediction model given by the correlation r value between the predicted score and the actual score across

Table 1
The eleven functional connectivities that were common across subjects for predicting sensation-seeking using an elastic net regression model. The r values show the correlation between the functional connectivity and the sensation-seeking score, and the p values show the significance level. Five functional connectivities that were significantly correlated with the sensation-seeking score at $p < 0.05$. FDR corrected are indicated by *.

Region 1	Region 2	r value	p value
Amygdala_L	Rolandic_Oper_L	0.175	3.81E-04
OFCmed_L	Cingulate_Ant_R	0.220	7.28E-06 *
OFCmed_L	Cingulate_Ant_L	0.206	2.75E-05 *
OFCmed_R	Cingulate_Ant_R	0.192	9.00E-05
OFCpost_L	Cingulate_Ant_L	0.191	1.03E-04
Olfactory_L	Cingulate_Ant_R	0.207	2.43E-05 *
Olfactory_L	Cingulate_Ant_L	0.203	3.61E-05 *
Olfactory_L	Frontal_Inf_Orb_2_L	0.188	1.35E-04
Rectus_R	Cingulate_Ant_R	0.236	1.34E-06 *
Rectus_R	Cingulate_Ant_L	0.202	3.83E-05
Rectus_R	Frontal_Sup_2_R	0.189	1.23E-04

all 414 participants was 0.34 ($p = 7.3 \times 10^{-13}$) (shown in Fig. 1B). (The result was shown to remain highly significant with 10-fold cross-validation showing $r = 0.2$, $p = 5.6 \times 10^{-5}$, as described in the Supplementary Material.) Random permutation analysis was used to test the significance level of the prediction. The sensation-seeking scores were shuffled with respect to the values predicted from the functional connectivities across all participants randomly in each iteration. In ten thousand iterations of the random permutation test, the results were significant at the maximum level obtainable of $p < 0.0001$ (Fig. S1).

Eleven functional connectivities were found to be common across participants in making the optimal prediction of sensation-seeking (Table 1 and Figs. 2 and 3). 10 of these 11 links involved medial orbitofrontal cortex areas, and eight of the medial orbitofrontal cortex links were with the anterior cingulate cortex. One link involved the lateral orbitofrontal cortex, and one the amygdala. Five of the links, all involving the medial orbitofrontal cortex and anterior cingulate cortex were individually significantly correlated ($p < 0.05$ after FDR correction) with sensation-seeking with all the participants involved.

In more detail, these 11 links were those that were common to all runs of the leave-one-out cross-validation, which typically used 18 links with a threshold for the correlation matrix that gave the optimal prediction. We checked that these 11 links were able, if used alone in an elastic net prediction model, to obtain a good prediction, and that was found to be the case, in that the predicted sensation-seeking scores were correlated with $r = 0.335$ ($p = 2.4 \times 10^{-12}$) with just the 11 links shown in Table 1. We can, therefore, have confidence that good predictions can be made from just the 11 functional connectivity links shown in Table 1. In addition, 8 of the 11 links that were common for all participants were between the medial orbitofrontal cortex and the anterior cingulate cortex. With these 8 links between the medial orbitofrontal cortex and the anterior cingulate cortex used alone, the prediction of sensation-seeking scores yielded an accuracy $r = 0.30$ ($p = 4.8 \times 10^{-10}$) which still remains highly significant.

3.2. Other UPPS-P subscales

In the present study, only the sensation-seeking subscale of the UPPS-P had significant correlations with functional connectivities after FDR correction, and in addition, the scores could be predicted from the functional connectivities for the sensation-seeking scores. The other four subscales were investigated, but none had a significant correlation with any functional connectivity after FDR correction, and the prediction from the functional connectivities for these four subscales were low.

As these five subscales stand for different dimensions of impulsivity, there could be similarities and differences between these subscales. Hence, correlation analyses between the five subscales to check their similarity was performed. The sensation-seeking subscale showed a relatively low correlation with the other four subscales, providing an explanation for the different results for sensation-seeking compared to the other four subscales of impulsive behaviour in the UPPS (Table 2).

3.3. Relation between sensation-seeking and risk-taking behaviours

The sensation-seeking score was significantly correlated with the overall risk-taking score with $r = 0.49$ ($p = 3.92 \times 10^{-26}$) across 412 participants (the intersection of the number of participants having fMRI data, and UPPS-P and DOSPERT scores available). The correlations between the sensation-seeking and risk-taking subscales are shown in Table 3. The highest correlation of sensation-seeking was with the 'recreational' risk-taking subscale.

In addition, of the 5 functional connectivities which were significantly correlated with sensation-seeking after FDR correction, three all involving the medial orbitofrontal cortex and the anterior cingulate cortex were significantly correlated ($p < 0.05$) with the overall risk-taking score as shown in Table 4.

3.4. Relation between sensation-seeking and substance use (drinking, smoking and other drugs)

The sensation-seeking score was correlated with the drug usage (including cannabis and cocaine) per day $r = 0.29$ ($p = 3.13 \times 10^{-7}$), correlated with alcohol usage per day $r = 0.21$ ($p = 1.89 \times 10^{-4}$), and correlated with tobacco usage per day $r = -0.024$ ($p = 0.67$) across 298 participants (intersection number of participants having fMRI data, UPPS-P score and DOSPERT score available).

The 5 functional connectivities that were significantly correlated with sensation-seeking after FDR correction did not, in general, have significant correlations with these measures of drug abuse, as shown in Table 4.

4. Discussion

In this investigation, it was found that it was possible to predict the sensation-seeking score of 414 individuals from resting-state functional connectivities, which mainly involved the medial orbitofrontal cortex and anterior cingulate gyrus. The method used in this investigation involved selection of an optimal threshold for the functional connectivity

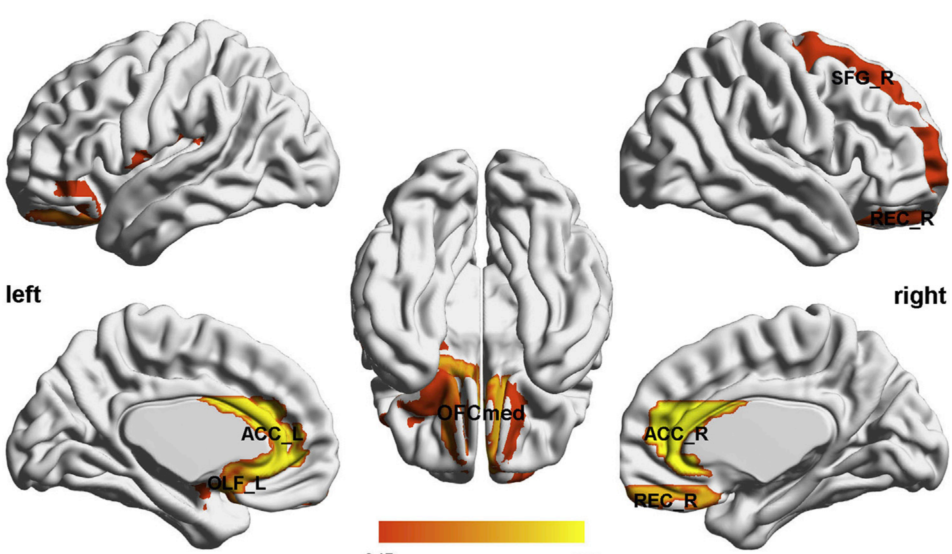

Fig. 2. The brain regions related to the 11 functional connectivities that were optimal in predicting sensation-seeking. The brain regions were from the AAL2 atlas (Rolls et al., 2015). The AAL2 regions shown are medial and posterior orbitofrontal cortex (OFCmed), gyrus rectus (REC), anterior cingulate cortex (ACC), OLF, inferior frontal gyrus orbital part, amygdala, FrontalSup2 (SFG), and Rolandic operculum as shown in Table 1, and the color bar indicates the sum of the r values shown in Table 1 for each AAL2 region included in Table 1.

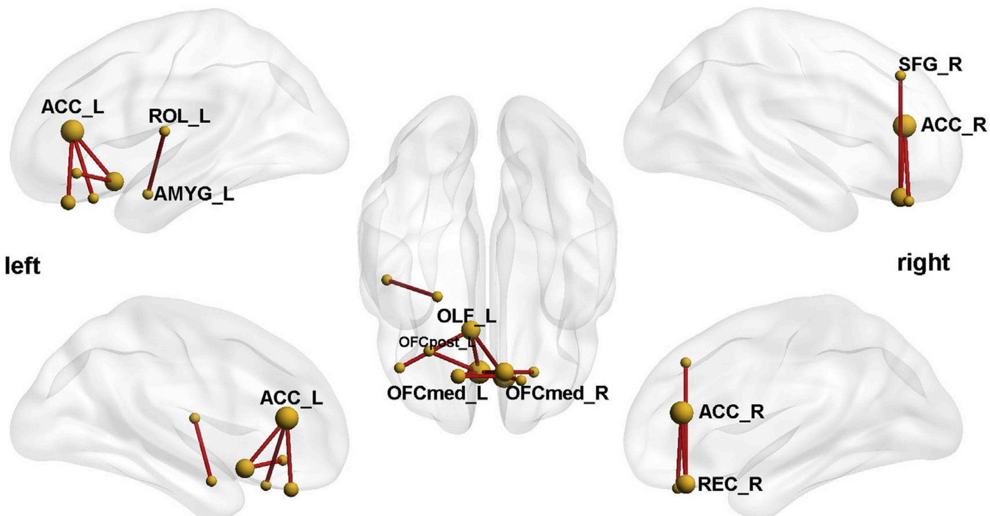

Fig. 3. The 11 functional connectivities that were used in the optimal prediction of sensation-seeking. Lateral, medial and dorsal views are shown. The AAL2 regions shown are OFCmed, OFCpost, OLF, rectus, anterior cingulate, inferior frontal gyrus orbital part, amygdala, FrontalSup2, and Rolandic operculum.

Table 2
The correlation matrix between the five subscales and the total score of the UPPS-P. The number of participants was 414.

	Negative Urgency	Lack of Premeditation	Lack of Perseverance	Sensation Seeking	Positive Urgency	*Total UPPS-P*
Negative Urgency	1.000	0.353	0.402	0.240	0.691	0.795
Lack of Premeditation	0.353	1.000	0.473	0.154	0.312	0.589
Lack of Perseverance	0.402	0.473	1.000	0.045	0.293	0.553
Sensation Seeking	0.240	0.154	0.045	1.000	0.317	0.616
Positive Urgency	0.691	0.312	0.293	0.317	1.000	0.802
Total UPPS-P	0.795	0.589	0.553	0.616	0.802	1.000

Table 3
Correlations between the different risk-taking subscales of the DOSPERT and sensation-seeking across 412 participants.

Risk-Taking	r value	p value
Ethical	0.26	7.16e-08
Financial	0.25	4.56e-07
Health	0.35	1.21e-13
Recreational	0.58	4.11e-39
Social decision	0.19	8.36e-05

correlation matrix to make the prediction of the sensation-seeking score, which was $r = 0.34$, $p = 7.3 \times 10^{-13}$. The prediction method used an elastic net regression model, which was found to be more effective than support vector regression. 10 of the 11 common links used in each leave-one-out iteration to predict sensation-seeking involved the medial orbitofrontal cortex areas and eight of the medial orbitofrontal cortex links were with the anterior cingulate cortex. This was supported by the finding that 5 of these links were individually significantly correlated with the sensation-seeking score after FDR correction.

The behavioural assessment used was UPPS, which measures impulsive behaviour. The sub-score of the UPPS that produced the most significant correlations with the functional connectivities was the sensation-seeking score, and for that reason is the focus of this paper. Sensation-seeking may be one factor that can lead to impulsive behaviour. Impulsive behaviour has many components or subtypes (Dalley and Robbins, 2017), and one component may be related to decreased sensitivity to non-reward in which the lateral orbitofrontal cortex is implicated (Rolls, 2019b, c). Another component may involve not being sensitive to a signal to change behaviour, which activates the lateral orbitofrontal cortex and the adjacent part of the inferior frontal gyrus (Deng et al., 2019), and damage to which impairs performance in the stop-signal task (Aron et al., 2014). However, there may be another type of impulsivity, in that Cheng et al. (2019) found that increased functional connectivity involving medial orbitofrontal areas in drinkers of alcohol was also associated with increased impulsivity, so they argued that increased sensitivity to reward might also lead to high impulsivity. That could be another component or type of impulsivity. The association of sensation-seeking with impulsivity was supported in the present investigation by the finding that risk-taking (an aspect of impulsivity) was somewhat correlated with the sensation-seeking score with $r = 0.49$, and that 3 of the 5 medial orbitofrontal cortex links with the anterior cingulate cortex that were implicated in sensation-seeking had significant correlations with risk-taking as measured by the DOSPERT (Blais

Table 4
Correlations and associated p values for the relation between the 5 links related to sensation-seeking after FDR correction and other behaviours including risk-taking.

Region1	Region2	Risk-Taking		Drug Use		Drinking		Smoking	
		r value	p value	r value	p value	r value	p value	r value	p value
Rectus_R	Cingulate_Ant_R	0.108	0.030	−0.012	0.832	−0.009	0.873	−0.147	0.012
OFCmed_L	Cingulate_Ant_R	0.082	0.101	0.031	0.596	0.021	0.718	−0.064	0.273
Olfactory_L	Cingulate_Ant_R	0.107	0.031	0.041	0.489	0.026	0.655	−0.084	0.153
OFCmed_L	Cingulate_Ant_L	0.088	0.078	0.028	0.628	0.022	0.714	−0.026	0.653
Olfactory_L	Cingulate_Ant_L	0.144	0.004	0.055	0.351	0.038	0.513	−0.036	0.542

and Weber, 2006). A concept then related to the present investigation is that some types of impulsive behaviour can be related in part to increased functional connectivity of the medial orbitofrontal cortex reward system with the anterior cingulate cortex action-outcome system; and that this functionality makes a contribution to sensation-seeking. Consistent with this concept, we found that the sensation-seeking score was correlated with positive affect ($r = 0.14$, $p < 0.003$), which relates the sensation-seeking score to some types of positive behaviour.

The method of making optimal predictions of behaviour from functional connectivity by searching for the best threshold for the functional connectivity correlation matrix has been used in only a few studies before (Liu et al., 2018a, 2018b) to the best of our knowledge. Its use in combination with an elastic net regression for making the prediction was found to be more powerful than using support vector regression.

A previous task-related fMRI study showed that high sensation seekers have a high activation to arousing images from the IAPS set in the posterior medial orbitofrontal cortex (Abler et al., 2006; Joseph et al., 2009). In addition, activations in the nucleus accumbens (which receives from the orbitofrontal cortex) are high in sensation-seekers in a monetary incentive delay task (Abler et al., 2006). There is also extensive evidence that the human medial OFC areas, including BA13, are activated by rewarding stimuli that are subjectively pleasant (including pleasant odours, pleasant touch, pleasant flavour, and monetary reward) (Grabenhorst and Rolls, 2011; O'Doherty et al., 2001; Rolls, 2014, 2019c). It was very interesting that in our study, without any task, differences in the functional connectivity of the medial orbitofrontal cortex were related to sensation-seeking.

The anterior cingulate cortex is relevant to emotion for it receives input from the orbitofrontal cortex about the value of emotion stimuli and implements instrumental goal-directed actions using action-outcome learning (Rolls, 2019a). In this study, 5 functional connectivities that were individually significantly correlated with sensation-seeking scores after FDR correction were between the anterior cingulate cortex (ACC) areas and the medial OFC areas. This provides evidence to elucidate further the hypothesis that the orbitofrontal cortex sends reward and non-reward information to the ACC where the reward/non-reward signals can be interfaced to cingulate systems that learn actions to obtain reward and avoid non-reward and punishers (Rolls, 2014, 2019a, c; Rushworth et al., 2012; Rushworth et al., 2011). The effects of high functional connectivity described here between the medial orbitofrontal cortex and the anterior cingulate cortex may be related to a strong effect of reward on promoting actions, which is expressed as sensation-seeking.

Although as described in the Introduction there have been a number of activation studies of sensation-seeking, this is the first large-scale study we know of how resting-state functional connectivity is related to sensation-seeking. The advantage of the resting state approach taken here is that as no task was being performed by the participants, any differences in task performance can not contribute to differences in the functional connectivities that are measured. The concept is that the resting-state functional connectivities may provide an indication of the basic connectivity structure of the brain, and differences in this connectivity framework may then show how the strengths of the connections between pairs of brain regions may underlie the differences in the behaviour. In this investigation, the results provide evidence that increased connectivity between the medial orbitofrontal cortex and the anterior cingulate cortex, which connect reward-related regions to a part of the brain involved in the initiation of actions to obtain the goals (Rolls, 2019a, b), is involved in sensation-seeking. This sets sensation-seeking somewhat apart from impulsivity, which is frequently related to reduced processing of punishment and/or non-reward in the lateral orbitofrontal cortex/inferior frontal gyrus (Aron et al., 2014; Rolls, 2019b, c; Whelan et al., 2012).

A possible limitation of the investigation is that sensation-seeking as a measure is available in the NKI dataset, but we have not found the same measure in other large-scale resting state fMRI datasets, so the results described are based on the NKI dataset, without cross-validation in a different dataset. However, within the NKI dataset, we were able to confirm the robustness of the results using both leave-one-out and ten-fold cross-validation approaches.

In conclusion, this research reveals a clear association between functional connectivity involving the medial orbitofrontal cortex and sensation-seeking, with connectivity involving medial orbitofrontal cortex areas and the anterior cingulate cortex especially prominent. What was quite remarkable was that it was possible to predict the sensation-seeking score from only 8 links involving different medial orbitofrontal cortex areas and the anterior cingulate cortex with a correlation of $r = 0.30$ ($p = 4.8 \times 10^{-10}$). (The corresponding value with the best 11 links shown in Table 1 was $r = 0.335$ ($p = 2.4 \times 10^{-12}$).) This provides clear evidence that the relation between these two brain areas, the medial orbitofrontal cortex, and the anterior cingulate cortex, is strongly involved in sensation-seeking. Moreover, the concept was advanced that one type of impulsivity, which is related to sensation-seeking, is related to increased functional connectivity of a reward-related cortical region, the medial orbitofrontal cortex.

Data and code availability statement

The NKI dataset is available at (http://fcon_1000.projects.nitrc.org/indi/enhanced/). Standard code functions available in Matlab abd SPM were used.

Ethics statement

No new data were collected in this investigation. The data were from the anonymised NKI dataset, and ethical permission for that investigation was obtained by the Nathan Kline Institute and Montclair State University, with details at http://fcon_1000.projects.nitrc.org/indi/enhanced/

CRediT authorship contribution statement

Zhuo Wan: Conceptualization, Investigation, Data curation, Formal analysis, Methodology, Software, Writing - original draft, Writing - review & editing. **Edmund T. Rolls:** Conceptualization, Investigation, Methodology, Supervision, Validation, Writing - original draft, Writing - review & editing. **Wei Cheng:** Conceptualization, Data curation, Methodology, Software, Writing - review & editing. **Jianfeng Feng:** Conceptualization, Funding acquisition.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroimage.2020.116845.

References

Abler, B., Walter, H., Erk, S., Kammerer, H., Spitzer, M., 2006. Prediction error as a linear function of reward probability is coded in human nucleus accumbens. Neuroimage 31, 790–795.

Achenbach, T.M., Rescorla, L., 2003. Manual for the ASEBA Adult Forms & Profiles. Research Center for Children, Youth and Families. University of Vermont, Burlington.

Aron, A.R., Robbins, T.W., Poldrack, R.A., 2014. Inhibition and the right inferior frontal cortex: one decade on. Trends Cognit. Sci. 18, 177–185.

Bardo, M.T., Donohew, R.L., Harrington, N.G., 1996. Psychobiology of novelty seeking and drug seeking behavior. Behav. Brain Res. 77, 23–43.

Benjamini, Y., Hochberg, Y., 1995. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J. Roy. Stat. Soc. B 57, 289–300.

Biswal, B., Yetkin, F.Z., Haughton, V.M., Hyde, J.S., 1995. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. Magn. Reson. Med. 34, 537–541.

Blais, A.-R., Weber, E.U., 2006. A domain-specific risk-taking (DOSPERT) scale for adult populations. Judgement Decis. Making 1, 33–47.

Chase, H.W., Fournier, J.C., Bertocci, M.A., Greenberg, T., Aslam, H., Stiffler, R., Lockovich, J., Graur, S., Bebko, G., Forbes, E.E., Phillips, M.L., 2017. A pathway linking reward circuitry, impulsive sensation-seeking and risky decision-making in young adults: identifying neural markers for new interventions. Transl. Psychiatry 7, e1096.

Cheng, W., Rolls, E.T., Qiu, J., Liu, W., Tang, Y., Huang, C.C., Wang, X., Zhang, J., Lin, W., Zheng, L., Pu, J., Tsai, S.J., Yang, A.C., Lin, C.P., Wang, F., Xie, P., Feng, J., 2016. Medial reward and lateral non-reward orbitofrontal cortex circuits change in opposite directions in depression. Brain 139, 3296–3309.

Cheng, W., Rolls, E.T., Robbins, T.W., Gong, W., Liu, Z., Lv, W., Du, J., Wen, H., Ma, L., Quinlan, E.B., Garavan, H., Artiges, E., Papadopoulos Orfanos, D., Smolka, M.N., Schumann, G., Kendrick, K., Feng, J., 2019. Decreased brain connectivity in smoking contrasts with increased connectivity in drinking. Elife 8, e40765.

Cox, R.W., 1996. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput. Biomed. Res. 29, 162–173.

Crane, N.A., Gorka, S.M., Phan, K.L., Childs, E., 2018. Amygdala-orbitofrontal functional connectivity mediates the relationship between sensation seeking and alcohol use among binge-drinking adults. Drug Alcohol Depend. 192, 208–214.

Cservenka, A., Herting, M.M., Seghete, K.L., Hudson, K.A., Nagel, B.J., 2013. High and low sensation seeking adolescents show distinct patterns of brain activity during reward processing. Neuroimage 66, 184–193.

Cui, Z., Gong, G., 2018. The effect of machine learning regression algorithms and sample size on individualized behavioral prediction with functional connectivity features. Neuroimage 178, 622–637.

Dalley, J.W., Robbins, T.W., 2017. Fractionating impulsivity: neuropsychiatric implications. Nat. Rev. Neurosci. 18, 158–171.

Deng, W., Rolls, E.T., Ji, X., Robbins, T.W., Banaschewski, T., Bokde, A.L.W., Bromberg, U., Buechel, C., Desrivieres, S., Conrod, P., Flor, H., Frouin, V., Gallinat, J., Garavan, H., Gowland, P., Heinz, A., Ittermann, B., Martinot, J.L., Lemaitre, H., Nees, F., Papadopoulos Orfanos, D., Poustka, L., Smolka, M.N., Walter, H., Whelan, R., Schumann, G., Feng, J., 2019. Separate neural systems for behavioral change and for emotional responses to failure during behavioral inhibition. Hum. Brain Mapp. 38, 3527–3537.

Erus, G., Battapady, H., Satterthwaite, T.D., Hakonarson, H., Gur, R.E., Davatzikos, C., Gur, R.C., 2015. Imaging patterns of brain development and their relationship to cognition. Cerebr. Cortex 25, 1676–1684.

Friston, K.J., Williams, S., Howard, R., Frackowiak, R.S., Turner, R., 1996. Movement-related effects in fMRI time-series. Magn. Reson. Med. 35, 346–355.

Grabenhorst, F., Rolls, E.T., 2011. Value, pleasure, and choice in the ventral prefrontal cortex. Trends Cognit. Sci. 15, 56–67.

Greve, D.N., Fischl, B., 2009. Accurate and robust brain image alignment using boundary-based registration. Neuroimage 48, 63–72.

Harris, N., Newby, J., Klein, R.G., 2015. Competitiveness facets and sensation seeking as predictors of problem gambling among a sample of university student gamblers. J. Gambl. Stud. 31, 385–396.

Hawes, S.W., Chahal, R., Hallquist, M.N., Paulsen, D.J., Geier, C.F., Luna, B., 2017. Modulation of reward-related neural activation on sensation seeking across development. Neuroimage 147, 763–771.

Hoyle, R.H., Fejfar, M.C., Miller, J.D., 2000. Personality and sexual risk taking: a quantitative review. J. Pers. 68, 1203–1231.

Jenkinson, M., Beckmann, C.F., Behrens, T.E., Woolrich, M.W., Smith, S.M., 2012. Fsl. Neuroimage 62, 782–790.

Jonah, B.A., 1997. Sensation seeking and risky driving: a review and synthesis of the literature. Accid. Anal. Prev. 29, 651–665.

Joseph, J.E., Liu, X., Jiang, Y., Lynam, D., Kelly, T.H., 2009. Neural correlates of emotional reactivity in sensation seeking. Psychol. Sci. 20, 215–223.

Kruschwitz, J.D., Simmons, A.N., Flagan, T., Paulus, M.P., 2012. Nothing to lose: processing blindness to potential losses drives thrill and adventure seekers. Neuroimage 59, 2850–2859.

Liu, Z., Zhang, J., Xie, X., Rolls, E.T., Sun, J., Zhang, K., Jiao, Z., Chen, Q., Zhang, J., Qiu, J., Feng, J., 2018a. Neural and genetic determinants of creativity. Neuroimage 174, 164–176.

Liu, Z., Zhang, J., Zhang, K., Zhang, J., Li, X., Cheng, W., Li, M., Zhao, L., Deng, W., Guo, W., Ma, X., Wang, Q., Matthews, P.M., Feng, J., Li, T., 2018b. Distinguishable brain networks relate disease susceptibility to symptom expression in schizophrenia. Hum. Brain Mapp. 39, 3503–3515.

Lynam, D.R., Smith, G.T., Whiteside, S.P., Cyders, M.A., 2006. The UPPS-P: Assessing Five Personality Pathways to Impulsive Behavior. Purdue University, West Lafayette.

Nooner, K.B., Colcombe, S.J., Tobe, R.H., Mennes, M., Benedict, M.M., Moreno, A.L., Panek, L.J., Brown, S., Zavitz, S.T., Li, Q., Sikka, S., Gutman, D., Bangaru, S., Schlachter, R.T., Kamiel, S.M., Anwar, A.R., Hinz, C.M., Kaplan, M.S., Rachlin, A.B., Adelsberg, S., Cheung, B., Khanuja, R., Yan, C., Craddock, C.C., Calhoun, V., Courtney, W., King, M., Wood, D., Cox, C.L., Kelly, A.M., Di Martino, A., Petkova, E., Reiss, P.T., Duan, N., Thomsen, D., Biswal, B., Coffey, B., Hoptman, M.J., Javitt, D.C., Pomara, N., Sidtis, J.J., Koplewicz, H.S., Castellanos, F.X., Leventhal, B.L., Milham, M.P., 2012. The NKI-rockland sample: a model for accelerating the pace of discovery science in psychiatry. Front. Neurosci. 6, 152.

O'Doherty, J., Kringelbach, M.L., Rolls, E.T., Hornak, J., Andrews, C., 2001. Abstract reward and punishment representations in the human orbitofrontal cortex. Nat. Neurosci. 4, 95–102.

Patel, A.X., Kundu, P., Rubinov, M., Jones, P.S., Vertes, P.E., Ersche, K.D., Suckling, J., Bullmore, E.T., 2014. A wavelet method for modeling and despiking motion artifacts from resting-state fMRI time series. Neuroimage 95, 287–304.

Rolls, E.T., 2014. Emotion and Decision-Making Explained. Oxford University Press, Oxford.

Rolls, E.T., 2019a. The cingulate cortex and limbic systems for emotion, action, and memory. Brain Struct. Funct. 224, 3001–3018.

Rolls, E.T., 2019b. The Orbitofrontal Cortex. Oxford University Press, Oxford.

Rolls, E.T., 2019c. The orbitofrontal cortex and emotion in health and disease, including depression. Neuropsychologia 128, 14–43.

Rolls, E.T., Cheng, W., Gilson, M., Qiu, J., Hu, Z., Ruan, H., Li, Y., Huang, C.C., Yang, A.C., Tsai, S.J., Zhang, X., Zhuang, K., Lin, C.P., Deco, G., Xie, P., Feng, J., 2018. Effective connectivity in depression. Biol. Psychiatr. Cognit. Neurosci. Neuroimaging. 3, 187–197.

Rolls, E.T., Joliot, M., Tzourio-Mazoyer, N., 2015. Implementation of a new parcellation of the orbitofrontal cortex in the automated anatomical labeling atlas. Neuroimage 122, 1–5.

Ruedl, G., Abart, M., Ledochowski, L., Burtscher, M., Kopp, M., 2012. Self reported risk taking and risk compensation in skiers and snowboarders are associated with sensation seeking. Accid. Anal. Prev. 48, 292–296.

Rushworth, M.F., Kolling, N., Sallet, J., Mars, R.B., 2012. Valuation and decision-making in frontal cortex: one or many serial or parallel systems? Curr. Opin. Neurobiol. 22, 946–955.

Rushworth, M.F., Noonan, M.P., Boorman, E.D., Walton, M.E., Behrens, T.E., 2011. Frontal cortex and reward-guided learning and decision-making. Neuron 70, 1054–1069.

Sargent, J.D., Tanski, S., Stoolmiller, M., Hanewinkel, R., 2010. Using sensation seeking to target adolescents for substance use interventions. Addiction 105, 506–514.

Schonberg, T., Fox, C.R., Poldrack, R.A., 2011. Mind the gap: bridging economic and naturalistic risk-taking with cognitive neuroscience. Trends Cognit. Sci. 15, 11–19.

Siegel, J.S., Ramsey, L.E., Snyder, A.Z., Metcalf, N.V., Chacko, R.V., Weinberger, K., Baldassarre, A., Hacker, C.D., Shulman, G.L., Corbetta, M., 2016. Disruptions of network connectivity predict impairment in multiple behavioral domains after stroke. Proc. Natl. Acad. Sci. U. S. A. 113, E4367–E4376.

Smith, B.D., Davidson, R.A., Perlstein, W., Gonzalez, F., 1990. Sensation-seeking: electrodermal and behavioral effects of stimulus content and intensity. Int. J. Psychophysiol. 9, 179–188.

Whelan, R., Conrod, P.J., Poline, J.B., Lourdusamy, A., Banaschewski, T., Barker, G.J., Bellgrove, M.A., Buchel, C., Byrne, M., Cummins, T.D., Fauth-Buhler, M., Flor, H., Gallinat, J., Heinz, A., Ittermann, B., Mann, K., Martinot, J.L., Lalor, E.C., Lathrop, M., Loth, E., Nees, F., Paus, T., Rietschel, M., Smolka, M.N., Spanagel, R., Stephens, D.N., Struve, M., Thyreau, B., Vollstaedt-Klein, S., Robbins, T.W., Schumann, G., Garavan, H., Consortium, I., 2012. Adolescent impulsivity phenotypes characterized by distinct brain networks. Nat. Neurosci. 15, 920–925.

Whiteside, S.P., Lynam, D.R., 2001. The five factor model and impulsivity: using a structural model of personality to understand impulsivity. Pers. Indiv. Differ. 30, 669–689.

Zou, H., Hastie, T., 2005. Regularization and variable selection via the elastic net. J. Roy. Stat. Soc. B 67, 301–320.

Zuckerman, M., 1994. Behavioral Expressions and Biosocial Bases of Sensation Seeking. Cambridge University Press.