

Abnormal Anhedonia as a Potential Endophenotype in Obsessive–Compulsive Disorder

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Background: Obsessive–compulsive disorder (OCD) is often accompanied by cognitive, particularly executive function, impairments. Recently, anhedonia has emerged as an apparently important symptom of OCD reflecting altered emotion regulation. These two aspects are often comorbid in OCD. However, little is known about whether anhedonia may be a trait marker for OCD.

Methods: To verify the role of executive function and evaluate the role of anhedonia in OCD and its relationship with OCD symptoms, we recruited 60 OCD patients, 30 unaffected first-degree relatives (FDRs), and 60 healthy controls (HCs). Participants completed psychometric testing to assess depression, anxiety, and anhedonia symptoms, as well as two cognitive tests to assess executive function, namely the Wisconsin Card Sorting Test (WCST) and the Stroop Color-Word Test (SCWT).

Results: Compared to HCs, OCD patients and FDRs had significantly lower anticipatory and consummatory pleasure scores. The severity of anticipatory anhedonia correlated positively with obsessive–compulsive symptoms ($r = 0.253, p = 0.009$), even after controlling for depression and anxiety symptoms. Compared to HCs, OCD patients and FDRs made more errors and achieved fewer categories in the WCST. For all three SCWT components, OCD patients and FDRs took more time to name colors than HCs, but the three groups had similar numbers of errors.

Conclusion: This family-based study showed dampened pleasure together with cognitive dysfunction in OCD patients. The similar consummatory pleasure findings between OCD and FDR groups suggest anhedonia may be considered as a candidate OCD endophenotype.

Keywords: anhedonia, obsessive–compulsive disorder, executive function, endophenotype

Background

Anhedonia is defined as an inability to experience pleasure or a reduced ability to feel happiness.^{1,2} Numerous investigations have characterized anhedonia and depressed mood as the most important diagnostic criteria for major depression.^{3–5} Anhedonia is also the most common negative symptom of schizophrenia^{6,7} and may also be seen in patients with Parkinson's disease, drug dependence, post-traumatic stress disorder, and bipolar disorder.^{8–11} Recently reported findings have suggested that obsessive–compulsive disorder (OCD) may also be associated with anhedonia symptoms.^{12,13} Abramovitch et al¹⁴ reported a significantly higher prevalence of anhedonia among individuals with OCD, compared with the general population, and also found that OCD symptoms correlated directly with anhedonia severity. Observations of anhedonia in obsessive–compulsive personality disorder¹⁵ are suggestive of a transdiagnostic dimension.¹⁶ However, there has been little research into anhedonia

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in the context of OCD, and whether the symptom of anhedonia is a trait or phenotype characteristic.

Cognitive flexibility, an ability to flexibly and quickly adapting to a changing environment.¹⁷ The flexibility and emotion regulation ability as two aspects of cognition, or named “hot” and “cold” cognition,¹⁸ are the two subdomains of executive functions.¹⁹ The anhedonia and deficits of cognitive flexibility are often comorbid in depression disorder. Recently, some researchers find OCD is characterized by repetitive thoughts and behaviors, not only reflecting deficits in the subdomain of cognitive flexibility in executive function but also the emotion regulation subdomain.^{19–21} On one hand, OCD patients exhibit impaired emotion regulation.^{22,23} When OCD patients repeat behaviors over and over, they may be experiencing anxiety and depression symptoms, which might lead to infrequent experiences of pleasure or anhedonia at the moment.²⁴ On the other hand, OCD has been associated with deficits in cognitive flexibility,^{25,26} which is important for adjusting one’s thoughts and behaviors to a changeable environment or rewards. Some researchers have observed the characteristic of inflexible mind in OCD patients²⁷ and this inflexibility of mind appears to be driven by perfectionistic tendencies.²⁸ It may be difficult for these patients to terminate an ongoing behavior even when the goal of the behavior has been devalued.²⁹ They do not attain consummatory pleasure readily from repeated behaviors.³⁰ Thus, OCD patients may have deficits in both cognitive flexibility and the ability to experience pleasure. Anhedonia may be closely related to cognitive dysfunction. In particular, these two are influenced by the abnormal metabolism of the ventrolateral prefrontal cortex in major depressive disorder.¹⁹ However, there have been no studies focusing on anhedonia and cognitive flexibility in the context of OCD.

The results of case-control OCD studies may be influenced by patient characteristics as well as medication effects.³¹ It is difficult to identify whether some symptoms or deficits may be trait markers in patients. Furthermore, although OCD is a highly hereditary neuropsychiatric disorder,^{32,33} a specific OCD-causative gene has not been found. These issues have led researchers to pursue family-based research.

Gottesman and Shields et al^{34,35} proposed the concept of the “endophenotype” as an intrinsic manifestation that can be found only through biochemical testing or microscopic examination.³⁴ It represents an intermediary between disease phenotype and genotype but is more closely related to genetics than environment. The criteria

for a presentation to be deemed an endophenotype are coexisting with a disease or disorder, heritability, state independence, and co-segregation with illness within a family, with a higher rate among family members than in the general population. Because endophenotypes are useful in complex mechanism studies of psychiatric disorders, family-based studies are increasingly being used to elucidate psychiatric disorders. To our knowledge, although recent studies have recognized anhedonia as an appropriate endophenotype of depression,^{36,37} there is no pedigree research on anhedonia symptoms in OCD. Therefore, assessing and discussing anhedonia in unaffected first-degree relatives (FDRs) is meaningful for early detection and diagnosis of OCD.

Previous studies have described anhedonia as a clinical manifestation and typical symptom of OCD.¹² We are interested in anhedonia symptoms experienced by OCD patients and their unaffected FDRs, as well as whether these patients and FDRs with anhedonia also have deficits in cognitive flexibility. We designed a family-based study to investigate these issues. We hypothesized that: (1) compared to healthy controls (HCs), OCD and FDR groups would have lower Temporal Experience of Pleasure Scale (TEPS) subscale scores; (2) anhedonia severity would correlate with Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) total scores in the OCD group; and (3) compared to HCs, OCD and FDR groups would perform worse on the Wisconsin Card Sorting Test (WCST) and Stroop Color-Word Test (SCWT), cognitive tests of executive function.

Methods

Participants

OCD patients and their relatives were recruited in and out of our psychiatric institution in Guangzhou, China. HCs were recruited via advertisements targeted at college students and workers. The study enrolled 150 subjects, including 60 OCD patients, 30 unaffected FDRs, and 60 HCs, within the age range of 18–50 years old. All OCD patients were diagnosed using the Mini-International Neuropsychiatric Interview, version 7.0 for the DSM-V and were diagnosed with OCD by two psychiatrists at the psychiatric institution in Guangzhou. The patients had no history of any neurological disorder, Tourette’s syndrome, head injury, serious medical conditions, or a history of drug or alcohol addiction. Treatment details of the OCD patients can be found in [Table S1](#). The FDR group, which consisted of parents and siblings of the OCD patients, was screened to exclude any

Table 1 Demographic Characteristics of Individuals with OCD and HC in Preliminary Analysis

	OCD (N=60)	HC (N=60)	p
Age (M ± SD)	25.87 ± 7.39	27.89 ± 8.81	0.176
Education (M ± SD)	13.63 ± 2.71	14.31 ± 3.52	0.241
IQ (M ± SD)	109.88 ± 10.56	110.72 ± 13.86	0.707
Gender (male/female)	40/20	38/22	0.702
Marital status (married/single)	14/46	19/41	0.926

Abbreviations: OCD, obsessive-compulsive disorder; HC, healthy comparison subjects.

history of neurological disorders. The HC subjects did not use psychotropic medications and were without a known family history of OCD.

To make full use of the subjects' data, the entire group of 60 OCD patients and 60 HCs were included in the preliminary analysis (Table 1). However, some of these OCD patients did not have FDRs in this study. To conduct a 1:1:1 matched family-based study, we selected 30 subjects from the OCD and HC groups randomly for the latter analyses. One-way analysis of variance (ANOVA) or chi-square (χ^2) testing showed that years of education, IQ, and gender were similar among all three groups, and that FDRs were older on average than members of the other two groups and also included more married individuals (Table 2).

All subjects gave written informed consent after receiving a detailed introduction to the study. The study was approved by the Institutional Research and Ethics Committee of Guangzhou Huiai Hospital. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Assessment of Clinical Symptoms

The Y-BOCS³⁸ is used to measure OCD symptom severity and consensually acknowledged as the gold standard for rating obsessive-compulsive symptomatology.³⁹ In our

study, we used the 10-item Chinese version of the Y-BOCS. Scores for each item ranged from 0 (no symptoms) to 4 (extreme symptoms). The instrument has been shown to be appropriate for clinical and non-clinical samples, with good reliability and validity.^{40–42}

The TEPS⁴³ was designed to capture the anticipatory and consummatory facets of pleasure. Consummatory pleasure is defined as a sense of joy at the moment or the pleasure of having one's desires met, such as the pleasure of eating. Anticipatory pleasure is considered to be the pursuit of joy, related to motivation and goal-directed behavior, such as a hungry man watching a sumptuous lunch being prepared for him. The Chinese version of the TEPS used in this study is comprised of 20 items, including 2 items not in the original scale.⁴⁴ Each item is answered on a 6-point Likert scale ranging from "1" (very false for me) to "6" (very true for me), with lower total scores reflecting more severe anhedonia.

The Beck Depression Inventory⁴⁵ is a 21-item self-report instrument designed to assess depression severity. The Chinese version of the Beck Depression Inventory used in this study has good internal consistency and sensitivity.^{46,47} Each item is rated from "0" (not present) to "3" (severe), with a total score ranging from 0 to 63.

The State-Trait Anxiety Inventory⁴⁸ consists of two subscales that measure state anxiety and trait anxiety, respectively. The state anxiety subscale (S-AI) is designed to assess in-the-moment feelings of fear, tension, nervousness, and worry. The trait anxiety subscale (T-AI) is used to measure how one feels generally. The Chinese version of the State-Trait Anxiety Inventory used in this study has been shown to have acceptable psychometric properties and high internal consistency.⁴⁹

Assessments of Cognitive Function

The WCST⁵⁰ is a neuropsychological test of set-shifting (ie, the ability to display flexibility in the face of changing environmental contingencies). Four cards (one red

Table 2 Demographic Characteristics for OCD, FDR and HC Groups in Latter Analysis

	OCD (N=30)	FDR (N=30)	HC (N=30)	p
Age (M ± SD)	25.10 ± 5.99	30.73 ± 8.92	25.17 ± 4.80	0.001**
Education (M ± SD)	13.73 ± 3.15	13.37 ± 2.75	14.10 ± 3.39	0.584
IQ (M ± SD)	107.63 ± 16.22	106.13 ± 12.29	111.23 ± 15.60	0.445
Gender (male/female)	18/12	16/14	18/12	0.929
Marital status (married/single)	6/24	15/15	8/22	0.011*

Notes: * $p < 0.05$. ** $p < 0.01$.

Abbreviations: OCD, obsessive-compulsive disorder; FDR, unaffected first-degree relatives; HC, healthy comparison subjects.

triangle, two green stars, three yellow crosses, and four blue circles) are presented on the top of the screen as stimuli. A response card that varies in the shape (triangle, star, cross, or circle), color (red, green, yellow, or blue), and number of shapes (one to four) shown appears on the bottom of the screen during each trial. The participant pairs the response card with stimulus cards, according to criteria of similitude. After every pairing, the computer provides feedback about whether the choice was correct. The number of stages completed and total errors were recorded.

The SCWT⁵¹ evaluates cognitive flexibility. It includes color, color-word, irrelevant color-word tasks. For the color task, there are 24 dots (6 rows $\times$ 4 columns) printed on a card and colored in green, blue, yellow, or red. In the color-word task, four Chinese color characters (green, blue, yellow, red) are printed in inconsistent colors (eg, the word “red” printed in green font). Every color character is printed in the other colors and presented in a table (6 rows $\times$ 4 columns) shown twice to participants. In the irrelevant color-word task, 24 Chinese characters irrelevant to color (eg, “ask”, “go”, “live”) are displayed in each of the four colors (eg, the word “go” printed in red) in a table (6 rows $\times$ 4 columns), with each color presented 6 times. Participants were required to identify stimulus color from left to right and top to bottom as fast and accurately as possible. The number of errors and time required to name the colors in the entire card were recorded by the experimenter.

Statistical Analysis

In the preliminary analysis, independent t-tests were conducted to compare clinical task performance and neuropsychological scores between the OCD and HC groups. Then, Pearson correlation analyses were performed to assess whether the severity of anhedonia relates to the total Y-BOCS score. In the latter analysis, ANOVAs were performed to identify differences among the OCD, FDR, and HC groups in the TEPS and neuropsychological tasks. Statistically significant results were further analyzed by post-hoc inter-group least significant difference (LSD) testing.

Results

The 60 OCD patients and 60 HC subjects in the preliminary analysis were matched for age, years of education, IQ, gender, and marital status (see Table 1). OCD patients scored higher than HCs on the Y-BOCS, BDI, and S-AI/

T-AI (t-tests, $p < 0.01$). The OCD group had significantly lower TEPS-consummatory pleasure (CON) scores than HCs, reflecting greater consummatory anhedonia severity in OCD, but only a near-significant trend toward a difference in TEPS-anticipatory pleasure (ANT) scores. In terms of neuropsychological cognitive testing, OCD patients performed significantly worse than HCs on the WCST and SCWT. The OCD group had higher total error scores and lower stage numbers than the HC group on the WCST. Similarly, the OCD group took more time than the HC group to name colors during the color, color-word, and irrelevant color-word components of the SCWT. There was no significant difference between the groups in the number of errors made in any of these three components of the SCWT (Table 3).

Pearson correlation analysis examining the potential association of Y-BOCS total scores with TEPS subscale scores in the OCD sample indicated that only anticipatory anhedonia scores correlated with Y-BOCS total scores ($r =$

Table 3 Clinical Characteristics of OCD Patients and Healthy Comparison Subjects in Preliminary Analysis

Outcome Measure	OCD (N=60)	HC (N=60)	p
Y-BOCS			
Obsessions	12.97 $\pm$ 5.30	1.07 $\pm$ 1.38	<0.001**
Compulsions	10.35 $\pm$ 5.96	0.61 $\pm$ 1.05	<0.001**
Total score	23.32 $\pm$ 8.21	1.67 $\pm$ 1.98	<0.001**
BDI	17.05 $\pm$ 10.80	7.52 $\pm$ 7.5	<0.001**
STAI			
State anxiety	51.23 $\pm$ 14.48	39.47 $\pm$ 9.30	<0.001**
Trait anxiety	52.75 $\pm$ 13.15	40.85 $\pm$ 9.53	<0.001**
TEPS			
Anticipatory pleasure	37.06 $\pm$ 7.58	39.53 $\pm$ 6.53	0.058
Consummatory pleasure	56.94 $\pm$ 13.84	65.25 $\pm$ 12.81	0.001**
WCST			
WCST-E	9.39 $\pm$ 5.78	7.38 $\pm$ 4.52	0.036*
WCST-Cate	5.25 $\pm$ 1.11	5.75 $\pm$ 0.54	0.003**
SCWT			
Dot-RT	17.16 $\pm$ 4.80	15.25 $\pm$ 3.87	0.018*
Color-Word-RT	19.23 $\pm$ 5.78	17.00 $\pm$ 4.50	0.020*
Color-RT	31.44 $\pm$ 12.12	26.81 $\pm$ 8.86	0.018*

Notes: * $p < 0.05$. ** $p < 0.01$.

Abbreviations: Y-BOCS, Yale-Brown Obsessive-Compulsive Scale; BDI, Back Depression Inventory; STAI, State-Trait Anxiety Inventory; TEPS, Temporal Experience of Pleasure Scale; WCST, Wisconsin Card Sorting Test; WCST-E, total error score; WCST-Cate, number of categories achieved; SCWT, Stroop Color-Word Test; DOT-RT, reaction time on color task; Color-Word-RT, reaction time on color-word task; Color-RT, reaction time on irrelevant color-word task.

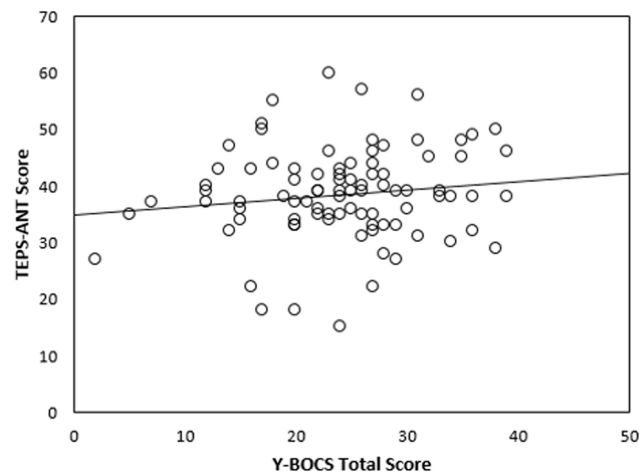


Figure 1 Correlation between severity of anticipatory anhedonia (TEPS-ANT scores) and OCD symptom severity (Y-BOCS scores). A linear regression graph is presented.

0.253, $p = 0.009$; Figure 1). Anticipatory anhedonia scores correlated with Y-BOCS total scores, regardless of depression and anxiety symptom severity ($r = 0.248$, $p = 0.011$). The procedure in our study to control the influence of depression on obsessive-compulsive symptoms is the same as a previous study, which just regressed out the total scores of BDI.³⁰

The demographic characteristics of the OCD, FDR, and HC groups ($N = 30/\text{group}$) in the latter analyses were similar among the three groups in terms of years of education, IQ, and gender, but there were more married persons among FDRs than in the other two groups, owing to FDRs being older than members of the other two

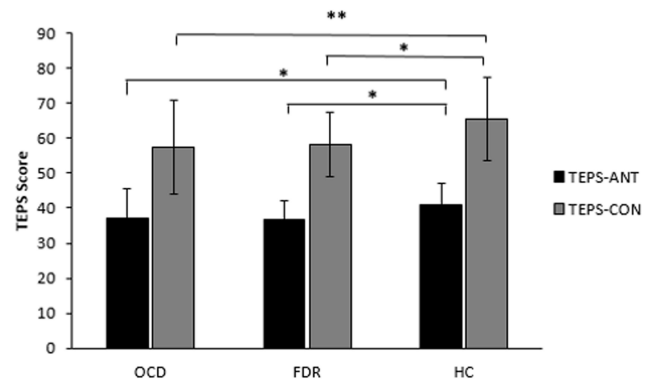


Figure 2 Comparisons of Anticipatory pleasure and consummatory pleasure among OCD, unaffected FDR, and HC groups. Anticipatory pleasure and consummatory pleasure are indexed by each group's mean TEPS-ANT score and TEPS-CON score, respectively. Bars represent standard error of the mean. ANOVA post hoc tests, * $p < 0.05$. ** $p < 0.01$.

groups (Table 2). ANOVAs indicated that TEPS subscale scores differed significantly among the groups (TEPS-ANT, $F_{2, 87} = 3.706$, $p = 0.029$; TEPS-CON, $F_{2, 87} = 4.487$, $p = 0.014$). Post-hoc analyses showed that, compared to HCs, OCD patients and unaffected FDRs had significantly lower levels of pleasure (Table 4 and Figure 2). Post-hoc analyses also revealed that OCD patients and FDRs had greater numbers of WCST errors and completed fewer categories than HCs. In the SCWT, OCD patients took more time to identify colors than FDRs and HCs (post hoc $p < 0.05$), but the three groups had similar numbers of errors on the color, color-word, and irrelevant color-word tasks. FDRs did not differ significantly from

Table 4 Clinical Characteristics of OCD Patients, Unaffected First-Degree Relatives and Healthy Comparison Subjects in Latter Analysis

Outcome Measure	Test Score ($M \pm SD$)			ANOVA		p value		
	OCD (N=30)	FDR (N=30)	HC (N=30)	$F(df = 2)$	p	OCD vs FDR	OCD vs HC	FDR vs HC
Y-BOCS	23.37 $\pm$ 8.61	2.04 $\pm$ 2.92	1.38 $\pm$ 1.87	163.419	<0.001**	<0.001**	<0.001**	0.634
OBS	13.50 $\pm$ 5.52	1.00 $\pm$ 1.62	0.88 $\pm$ 1.21	137.019	<0.001**	<0.001**	<0.001**	0.887
COMP	9.87 $\pm$ 6.75	1.04 $\pm$ 1.63	0.50 $\pm$ 0.95	50.689	<0.001**	<0.001**	<0.001**	0.609
TEPS-ANT	37.20 $\pm$ 8.17	36.79 $\pm$ 5.39	41.00 $\pm$ 5.94	3.706	0.029*	0.809	0.029*	0.015*
TEPS-CON	57.40 $\pm$ 13.36	58.18 $\pm$ 9.31	65.57 $\pm$ 11.93	4.487	0.014*	0.796	0.008**	0.016*
WCST-E	10.43 $\pm$ 6.11	9.30 $\pm$ 5.63	5.73 $\pm$ 3.63	6.592	0.002**	0.402	0.001**	0.010*
WCST-Cate	5.20 $\pm$ 1.03	5.26 $\pm$ 1.28	5.87 $\pm$ 0.35	4.363	0.016*	0.813	0.009**	0.017*
Dot-RT	18.36 $\pm$ 5.38	18.81 $\pm$ 4.85	13.94 $\pm$ 3.31	10.312	<0.001**	0.705	<0.001**	<0.001**
Color-Word-RT	20.12 $\pm$ 6.87	18.87 $\pm$ 4.23	15.16 $\pm$ 3.37	7.848	0.001**	0.341	<0.001**	0.005**
Color-RT	30.74 $\pm$ 9.46	29.34 $\pm$ 9.65	23.64 $\pm$ 6.45	5.665	0.005**	0.534	0.002**	0.012*

Notes: * $p < 0.05$. ** $p < 0.01$.

Abbreviations: OBS, Y-BOCS Obsessions; COMP, Y-BOCS Compulsions; TEPS-ANT, TEPS anticipatory pleasure subscale; TEPS-CON, TEPS consummatory pleasure subscale; WCST-E, total error score on the WCST; WCST-Cate, number of categories achieved on the WCST; DOT-RT, reaction time on color task in the SCWT; Color-Word-RT, reaction time on color-word task in the SCWT; Color-RT, reaction time on irrelevant color-word task in the SCWT.

OCD patients in terms of TEPS, WCST, or SCWT scores (Table 4).

Discussion

Our preliminary analysis showed that OCD patients had more consummatory anhedonia, as indicated by TEPS-CON scores, than HCs, but a similar level of anticipatory anhedonia, as indicated by TEPS-ANT scores, consistent with the findings of a previous report.³⁰ These findings suggest that people with OCD may have a lower pleasure level when performing activities in real time. Reduced consummatory pleasure could be related to an ego-dystonic state of mind⁵² and perfectionism²⁸ in OCD. A previous study also showed that OCD patients had less enjoyable sex.⁵³ Although consummatory pleasure is not attained from repeated behaviors, OCD patients lack the ability to control these behaviors and they still expect the behaviors to produce pleasure and to results in some relief from anxiety.⁵⁴ A normal anticipatory pleasure capacity with a disruption in consummatory pleasure may enable the reinforcement of rigid behavior patterns. Thus, we speculate that restricted, repetitive patterns of behavior may alleviate anxiety, through negative reinforcement, leading to anticipatory pleasure.

We found that more severe obsessive-compulsive symptoms (Y-BOCS scores) were associated with a lack of anticipatory pleasure (TEPS-ANT scores) in OCD patients (Figure 1). This association may provide further evidence of ongoing reinforcement of repetitive patterns in OCD, such that more repeated behaviors yield more anticipatory pleasure. This association remained after controlling for depression and anxiety. Similarly, Abramovitch et al¹² found that depressive severity was not sufficient to explain the presence of anhedonia in OCD. Depression is characterized by putamen hyperactivity, while OCD is characterized by hypoactivity in the orbitofrontal-striatal loop during reward processing,^{55–57} suggesting that the neuromechanism responsible for anhedonia in OCD may differ from those in depression.

In our latter analysis, the FDR group showed higher anhedonia severity (lower TEPS-ANT and TEPS-CON scores) than HCs, without a striking difference from patients with OCD. Simultaneously, there was no significant difference in Y-BOCS total scores between the FDR and HC groups. Moreover, there was no clear relationship between Y-BOCS scores and TEPS-ANT and TEPS-CON anhedonia scores in the FDR group, and no significant

relationship between Y-BOCS and TEPS-CON scores in the OCD group. Statistically speaking, anhedonia, especially consummatory anhedonia was stated independent, as would be needed for it to be an objective and easily measurable endophenotypic marker for OCD. Previously, anhedonia was confirmed to be an endophenotype of depression, schizophrenia, and other diagnoses.^{58,59} Our TEPS results differed in part from a previous study showing significant differences in TEPS-CON but not TEPS-ANT scores between OCD patients and HCs.³⁰ Although we did not find a significant difference in TEPS-ANT scores between our OCD and HC groups in our preliminary analysis, a difference emerged in our later analysis. It may be that TEPS-ANT scores are unstable in OCD patients, perhaps being sensitive to participant selection in relation to factors such as age, obsessive-compulsive symptoms, or medicine status. To some extent, we may have to infer that consummatory, but not anticipatory, anhedonia may be state independent. Our results suggest that OCD patients may have a typical ability to feel anticipatory pleasure, with a specific consummatory pleasure deficit. The neural bases of anhedonia-related reward systems involve both emotional and motivational pathways.⁴³ The emotional pathway related to consummatory pleasure has been reported to be disrupted in OCD patients.^{60,61} Gillan et al⁶² found that OCD patients showed a deficit in goal-directed control in an outcome devaluation test; they did not stop goal-directed behaviors despite the target goal being devalued. Analogously, OCD patients may be hard to stop the use of objects which have no capacity to produce consummatory pleasure. Recent neuroimaging evidence points to reduced functional connectivity between the caudate nucleus, orbitofrontal cortex, and anterior cingulate cortex in OCD patients. These regions have been found to affect goal-directed behavior in animals.⁶³

We applied the WCST and SCWT to test whether OCD patients and FDRs had deficits in domains of executive function, such as cognitive flexibility and interference control.⁶⁴ OCD patients and their relatives showed poorer performance than HCs on the WCST and SCWT, consistent with previous findings⁶⁵ suggesting that alterations in executive function may be considered as an endophenotype for OCD. Moreover, Chamberlain et al³² found that deficits in cognitive flexibility and motor inhibition may be appropriate markers for OCD. Zhang et al⁶⁶ have similarly found that mental flexibility and response inhibition may represent cognitive endophenotypes of early-onset OCD.

On a neuropsychological level, alterations in the frontal lobe and anterior cingulate cortex⁶⁷ have been found in OCD patients during the performance of the WCST⁶⁸ and SCWT.^{51,69} And the deficits in cognitive flexibility may be related to the abnormal ability to achieve pleasure. Franke et al⁷⁰ found that more severe anhedonia was related to worse performance on the WCST and that these deficits were associated with frontal lobe alterations even in healthy siblings of schizophrenics. A previous brain-imaging study⁵⁷ reported blunted reward-associated right medial orbitofrontal cortex responsiveness as well as decreased activities in the dorsolateral and anterior prefrontal cortices in OCD patients performing affective switching in a reversal-learning task. Light et al¹⁹ found a relationship between trait emotionality and executive function in major depressive disorder that was mediated by the ventrolateral prefrontal cortex. These frontal brain region abnormalities may disrupt the ability to get pleasure from rewards in addition to impairing cognitive function.^{19,71–73} If so, OCD patients with anhedonia may also have executive function (eg cognitive flexibility) deficits. This hypothesis could be tested in functional neuroimaging studies.

Limitations

This study had several limitations. First, the generalizability of the study is limited by its small sample size. Further research should enroll larger samples to probe the validity of our conclusions. Secondly, with regard to unaffected FDR, we did not have a specific limit to parents or siblings of OCD patients. Age and genotype factors may also have influenced the results. Thirdly, we did not divide our OCD patients according to OCD symptoms. OCD with checking compulsions may be related to brain regions that are important for motor and attentional functions, whereas OCD with contamination fears may be more associated with dysfunctional emotion processing circuits.⁷⁴ Figeet al⁶⁰ have shown that OCD with contamination fears exhibit reduced nucleus accumbens activity during reward anticipation. Further research is necessary to elucidate anhedonia among different subtypes of OCD patients.

Conclusion

The present family-based study showed an independent role of anhedonia, especially consummatory anhedonia, in OCD beyond depression. Our findings support the qualification of anhedonia as an endophenotype of OCD. Additionally, our exploratory analysis suggested that

OCD patients may have deficits in cognitive flexibility in addition to deficits in experiencing pleasure.

Abbreviations

OCD, obsessive-compulsive disorder; WCST, Wisconsin Card Sorting Test; SCWT, Stroop Color-Word Test; FDR, first-degree relatives; HC, healthy control subjects; PTSD, post-traumatic stress disorder; IGT, Iowa Gambling Task; NAc, nucleus accumbens; OFC, orbitofrontal cortex; fMRI, Functional magnetic resonance imaging; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; IQ, intelligence quotient; ANOVA, analysis of variance; TEPS, Temporal Experience of Pleasure Scale; C-BDI, Chinese version of the Beck Depression Inventory; S-AI, state anxiety questionnaire; T-AI, trait anxiety questionnaire; LSD, least significant difference; TEPS-CON, Temporal Experience of Pleasure Scale–consummatory pleasure scores; TEPS-ANT, Temporal Experience of Pleasure Scale–anticipatory pleasure scale; ACC, anterior cingulate cortex; DLPFC, decreased dorsolateral prefrontal cortex.

Data Sharing Statement

All related data are present in the manuscript.

Ethics Approval and Consent to Participate

This study was approved by the Human Research Ethics Committee for Non-Clinical Faculties of the School of Psychology, South China Normal University (reference number: 114). All participants were provided with an information sheet that provided details about the study, including its purpose, safeguards for their anonymity and use of data. Informed written consent was obtained from all subjects who participated in the current study.

Consent for Publication

Not applicable.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and

interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed on the journal to which the article will be submitted; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest for this work.

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