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# Anhedonia in Schizophrenia and Major Depressive Disorder Clinical and Functional MRI Study

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

**Background:** Anhedonia, is defined as reduced capacity to gain pleasure from pleasurable experiences, is a key symptom of major depression. Several studies had investigated anhedonia in schizophrenia and major depressive disorder, using different psychometric and radiological assessment tools with controversy results in either severity of anhedonia or radiological findings. The aim of this study was to differentiate the nature of the issue of anhedonia in schizophrenia versus major depressive disorder; from clinical and brain function part of view, and to study different variables in this regard.
**Methods:** This study was carried on 60 participants who were divided into three groups: Group 1: 20 schizophrenic patients, diagnosed according to DSM-5. The symptoms of schizophrenic patients must include anhedonia as a main symptom, Group 2: 20 patients with major depressive disorder according to DSM-5 criteria, and anhedonia was one of their prominent symptoms, Group 3: 20 control subjects.
**Results:** Our results revealed statically significant differences between participants as regards age of onset, occupational career. Statically significant differences were found between 3 groups. Most

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of patients in group 1 lacks the interest for social activities and intimate relationships. Statically significant Difference was found between patients in both groups compared to controls. Striatal activity (mainly caudate) was significantly diminished in group 2 (P value <0.001) and group 1 (P value 0.002) relative to controls. Prefrontal activity (ventromedial area "vmPFC" and dorsolateral area "DLPFC") was increased significantly in group 2 more than control group (P value 0.034). Group 1 shows significantly decreased activation than controls (P value 0.019). Significant differences were found between group 1 and 2 (P value <0.001). Orbito-frontal activity was increased significantly in depressed patients more than group 1 (P <0.001) and controls (P =0.019).

**Conclusions:** Anhedonia is a highly disabling symptom in patients with schizophrenia or MDD, associated with poor outcome. Depressed anhedonic patients have higher incidence of suicidal ideas, thoughts, and behavior. Depressed patients showed significant striatal hypoactivation associated with hyper activation of prefrontal and orbitofrontal areas. Schizophrenic patients showed diminished activation at striatal areas and frontal cortex. We fail to find significant correlation between severity of anhedonia in both patient groups and degree of fMRI activation in different brain areas involved in reward processing.

*Keywords: Anhedonia; schizophrenia; major depressive disorder; functional MRI.*

## 1. INTRODUCTION

The term “anhedonie” was introduced in clinical psychiatry over a century ago when Ribot, 1896 first defined anhedonia as the “insensibility relating to pleasure alone” and highlighted the role of anhedonia in the diagnosis of melancholia [1].

Anhedonia, is defined as reduced capacity to gain pleasure from pleasurable experiences, is a key symptom of major depression and schizophrenia [2].

The DSM-IV-TR defined anhedonia as diminished interest or pleasure in response to stimuli that were previously perceived as rewarding during a pre-morbid state [3].

The importance of anhedonia in psychopathology (and hedonic capacity more generally) is further supported by its inclusion as a key domain in the Research Domain Criteria (RDoC), a new conceptual framework for psychopathology research recently promoted by the United States’ National Institute of Mental Health that focuses on trans-diagnostic domains, rather than disorders [4].

Scientific and clinical literatures use the term "anhedonia" in a different ways, within a different contexts to describe broad range of emotional experiences [4].

The concept of anhedonia is multifactorial; Anhedonia can arise from deficits in various aspects of reward process, e.g. desire for reward, anticipation or prediction of reward, effort to gain reward, consummatory pleasure and cognitive aspects of learning stimulus - reward associations [5].

However, recent neuroimaging findings suggest a more complex model of reward which includes the nucleus accumbens (NAc), ventral tegmental area (VTA), amygdala, prefrontal cortex, caudate, putamen, and orbitofrontal cortex [6].

Currently there is no available treatment approved by the Food and Drug Administration (FDA) selective for improving anhedonia in major depression or schizophrenia [7].

Moving forward, a more comprehensive understanding of the neurotransmitter profile in patients with MDD having anhedonic symptoms will be necessary to delineate the interplay between dopamine, norepinephrine, and serotonin [8].

By studying the core symptoms of an illness, a candidate symptom approach is a promising step towards improved characterization of subgroups of disorders and eventually to the identification of specific vulnerability markers. A good example of such an approach is the study of anhedonia [9].

Several studies had investigated anhedonia in schizophrenia and major depressive disorder, using different psychometric and radiological assessment tools with controversy results in either severity of anhedonia or radiological findings [8].

The aim of this study was to differential nature of the issue of anhedonia in schizophrenia versus major depressive disorder; from clinical and brain function part of view, and to study different variables in this regard.

## 2. PATIENTS AND METHODS

Patients divided into three groups: Group 1: included 20 schizophrenic patients, diagnosed according to DSM-5. The symptoms of schizophrenic patients must include anhedonia as a main symptom, Group 2: included 20 patients with Major depressive disorder according to DSM-5 criteria, and anhedonia was one of their prominent symptoms, Group 3: included 20 control subjects (were selected from employees of Tanta university hospitals).

Included patients were age above 18 years old and less than 55 years old, Drug naïve patients or non-compliant patients who stopped their medication for at least 3 months prior to the time conducting the study (not receiving antidepressant or antipsychotic medications; depot or oral forms), Anhedonia must be one of the prominent symptoms of selected patients (group 1 and 2), Subjects in control group (group 3) had no history of any psychiatric illness or substance abuse.

Exclusion criteria were Age less than 18 or more than 55 years old, Presence of comorbid other psychiatric disorders, Presence of substance use, Suicidal, excited and catatonic patients, Patients with concomitant major medical illness.

All subjects in the study were subjected to the following: Clinical assessment: Semi-structured interview for diagnosis of both schizophrenia and major depressive episode was applied according to DSM-5 criteria.

Semi-structured interview*:* A specially designed semi-structural interview "psychiatric observation sheet" in psychiatry department, Tanta University (was used to obtain demographic data, personal data, present history, past history and family history).

Present State Examination 10th revision of the Schedules of Clinical Assessment in Neuropsychiatry (SCAN) (PSE-10): Short English-Arabic version translated by Hamdi et al., (2007) [10], back translated and tested for reliability [11]. The PSE includes 11 sections with 85 questions. We used this test to diagnose and verify the depressive and psychotic symptoms and exclude anxiety or obsessive symptoms.

The authors applied the following sections: Section 3: anxiety & phobias, Section 4: obsessions, Section 5: thinking/concentration/energy/interest, Section 6: depressive symptoms, Section 7: bodily functions: appetite/ sleep/ libido, Section 9: perceptual disorders, Section 10: thought disorder & replaced well and Section 11: delusions.

### 2.1 Psychometric Study

Anhedonia – Asociality subscale of Scale for assessment of negative symptoms "SANS".) Andreasen, 1984). SANS measures negative symptoms on 25 items, 6-point scale; i.e., each item is rated from 0 (absent/ no deficit) to 5 (severely/ extremely decreased).

Items are listed under five domains; affective blunting, alogia, avolition/apathy, anhedonia/asociality, and attention [12]. Each item is rated from 0 (absent/ no deficit), 1 (minimally decreased), 2 (mild decrease), 3 (moderately decreased), 4 (markedly decreased) and 5 (severely/ extremely decreased).

Snaith Hamilton Pleasure Scale (SHAPS): [13], Arabic version [14]. SHAPS is a well-validated, 14-item instrument used to assess anhedonia. Participants were asked to rate whether they agree, strongly agree, disagree, or strongly disagree that they would enjoy various experiences that are generally considered pleasurable (e.g., “I would find pleasure in my hobbies and past-times”) with either of the Disagree responses receiving a score of 1 and either of the Agree responses receiving a score of 0 [15].

Thus, the SHAPS was scored as the sum of the 14 items, total scores ranged from 0 to 14. A higher total SHAPS score indicated higher levels of present state of anhedonia [16].

Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979): "MADRS" a ten-item diagnostic questionnaire used to measure the severity of depressive episodes in patients with mood disorders [17]. Arabic version was validated [18].

MADRS includes questions on the following symptoms; apparent sadness, reported

sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts. Each item has a score of 0 to 6, with overall score ranges from 0 to 60. Higher MADRS score indicates more severe depression. From 0 to 6: normal /symptom absent, from 7 to 19: mild depression, from 20 to 34: moderate depression and > 34 severe depression.

## 2.2 Imaging Study

All participants will be scanned while viewing a group of selected pictures using block design (alternating action and rest tasks) showing real-life emotional situations (divided into three conditions, based on emotional content: positive, neutral and negative pictures). Stimuli will be generated by a laptop computer and projected via a LCD projector and mirror system.

Imaging was done on a MRI scanner operating at 1.5 T (GE HealthCare, Sigma HDX., WI) using a standard head coil. For anatomic reference, High-resolution 3D T1-weighted spoiled gradient echo pulse sequence was acquired; (TR/TE/TI, 9.7/4.6/400 ms, flip angle (θ) = 35°, 124 slices 0.8 mm thick, 208 × 170 matrix, field of view (FOV) 23 cm 260 contiguous sections, acquisition time 5.25 min).

For functional imaging, a T2*-weighted gradient-echo echo-planar imaging (EPI) sequence was used (TR/TE, 2540/45 ms; matrix, 64x64; FOV,224 mm; section thickness, 5 mm; 50 contiguous sections) to obtain blood oxygen level dependent (BOLD). Total fMRI scan time was approximately 5 min 12 seconds.

The procedure was performed using a block design of alternating task and rest periods, each lasting 30 seconds; the active task consisted of 6 consecutive images, each image to be viewed for 5 seconds. Images were reflected on a mirror in front of the patient's eyes from a screen showing pictures (positive, neutral and negative). We used fMRI to test the activation pattern produced related to emotional experience.

## 2.3 Statistics

Statistical presentation and analysis were conducted, using the mean, standard deviation, student t- test, Chi-square and Analysis of variance [ANOVA] tests by SPSS V20. Qualitative data were expressed as frequency and percentage and were statistically analyzed by Chi-square test. Unpaired Student T-test was used to compare between two groups in quantitative data. ANOVA test was used for comparison among different times in the same group in quantitative data. Significance of the obtained results was judged at ≤ 0.05.

## 3. RESULTS

The comparison shows insignificant differences between groups as regard the age, years of formal education, sex, marital status and residence. There were significant differences between groups in Distribution of occupation. **Error! Reference source not found.**.

The differences regarding the duration of the illness and mean age of onset of illness in both groups were statically significant. The differences regarding the course of the illness and family history in both groups were statically non-significant. Table 2.

No evident symptoms of anxiety or phobias or obsessions were present in all participants in the study. Loss of interest was markedly affected in group 1 (schizophrenia) and group 2 (MDD). Loss of energy (drive) was markedly affected in group 1 (schizophrenia) and moderately in group 2 (MDD) between groups were statically significant. Table 3.

Suicidal thoughts / acts were markedly evident in group 2 (MDD) than group 1 (schizophrenia), differences were statically significant (p value 0.001*). Social withdrawal was markedly evident in group 1 (schizophrenia) than group 2 (MDD), differences were statically significant (p value 0.001*). Table 4.

80% of patients in group 2 (MDD) have poor appetite (p value 0.001*), 65% have delayed sleep (p value 0.036*), 80% have poor quality sleep (p value 0.001*). Results showed that 55% of patients in group 1 (schizophrenia) have Auditory hallucination (P value 0.001*), 35% have delusional mood (P value 0.006*), 20% have thought possession (P value 0.014*), 35% have delusions of persecution (P value 0.002*), 45% have delusions of reference (P value 0.002*) and 20% have delusions of grandeur (P value 0.014*).

**Table 1. Patient's characteristics in groups**

| | | Group 1 (schizophrenia) (n=20) | Group 2 (MDD) (n=20) | Group 3 (control) (n=20) | t-test | P value |
|---|---|---|---|---|---|---|
| **Sex** | **Male** | 11 (55%) | 7 (35%) | 12 (60%) | 2.800 | 0.247 |
| | **Female** | 9 (45%) | 13 (65%) | 8 (40%) | | |
| **Age (years)** | | 32.05 ± 7.022 | 28.95 ± 5.306 | 31.2 ± 6.187 | 1.330 | 0.273 |
| **years of formal education** | | 12.65 ± 2.254 | 13.9 ± 1.89 | 13.65 ± 1.66 | 2.299 | 0.110 |
| **Distribution of** | **Unemployed** | 8 (40%) | 3 (15%) | 0 (0%) | 23.869 | 0.002 |
| **occupation** | **Unskilled** | 3 (15%) | 1 (5%) | 4 (20%) | | |
| | **Semi-skilled** | 3 (15%) | 4 (20%) | 7 (35%) | | |
| | **Highly skilled** | 2 (10%) | 5 (25%) | 9 (45%) | | |
| | **House wife** | 4 (20%) | 7 (35%) | 0 (0%) | | |
| **marital status** | **Single** | 11 (55%) | 4 (20%) | 6 (30%) | 7.949 | 0.242 |
| | **Married** | 5 (25%) | 11 (55%) | 10 (50%) | | |
| | **Divorced** | 3 (15%) | 2 (10%) | 3 (15%) | | |
| | **widow** | 1 (5%) | 3 (15%) | 1 (5%) | | |
| **Distribution of** | **Rural** | 11 (55%) | 7 (35%) | 12 (60%) | 2.800 | 0.247 |
| **residence** | **Urban** | 9 (45%) | 13 (65%) | 8 (40%) | | |

*Data are presented as mean ± SD or frequency (percent)*

**Table 2: Clinical assessment in groups.**

| | | Group 1 (schizophrenia) (n=20) | Group 2 (MDD) (n=20) | Group 3 (control) (n=20) | t-test | P value |
|---|---|---|---|---|---|---|
| **Age of onset** | | 22.80 ± 2.687 | 25.80 ± 4.408 | | -2.599 | 0.013 |
| **Duration of illness (in months)** | | 104.15 ± 66.4 | 33.3 ± 30.72 | | 4.330 | < 0.001 |
| **Course of illness** | **1st episode** | 4 (20%) | 6 (30%) | | 1.271 | 0.530 |
| | **Recurrent episodes** | 9 (45%) | 10 (50%) | | | |
| | **Chronic illness** | 7 (35%) | 4 (20%) | | | |
| **Family history of psychiatric disorders** | **None** | 11 (55%) | 4 (20%) | 6 (30%) | 5.816 | 0.242 |
| | **History of mood disorder** | 5 (25%) | 11 (55%) | 10 (50%) | | |
| | **History of psychosis** | 3 (15%) | 2 (10%) | 3 (15%) | | |
| | **widow** | 1 (5%) | 3 (15%) | 1 (5%) | | |

*Data are presented as mean ± SD or frequency (percent)*

**Table 3. Symptoms of section 5: (thinking & concentration)**

| | Group 1 (schizophrenia) (n=20) | Group 2 (MDD) (n=20) | Group 3 (control) (n=20) | P value |
|---|---|---|---|---|
| Inefficient thinking | 14 (70%) | 8 (40%) | 3 (15%) | 0.002* |
| Concentration difficulties | 16 (80%) | 13 (65%) | 4 (20%) | <0.001* |
| Loss of interest | 18 (90%) | 17 (85%) | 3 (15%) | <0.001* |
| Loss of energy (drive) | 19 (95%) | 13 (65%) | 4 (20%) | <0.001* |
| Feeling of being overwhelmed by everyday tasks | 7 (35%) | 15 (75%) | 5 (25%) | 0.004* |
| No symptoms | 0 (0%) | 0 (0%) | 13(65%) | <0.001* |

**Table 4. Symptoms of section 6: (Depression)**

| | Group 1 (schizophrenia) (n=20) | Group 2 (MDD) (n=20) | Group 3 (control) (n=20) | P value |
|---|---|---|---|---|
| Depressed mood | 10 (50%) | 17 (85%) | 5 (25%) | 0.001* |
| Crying | 3 (15%) | 5 (25%) | 1 (5%) | 0.208 |
| Hopelessness | 5 (25%) | 11 (55%) | 3 (15%) | 0.018* |
| Suicidal plans or acts | 7 (35%) | 14 (70%) | 1 (5%) | <0.001* |
| Social withdrawal | 15 (75%) | 8 (40%) | 3 (15%) | 0.001* |
| Loss of self esteem | 8 (40%) | 13 (65%) | 3 (15%) | 0.006* |
| Loss of confidence | 7 (35%) | 9 (55%) | 2 (10%) | 0.045* |
| Guilt | 5 (25%) | 14 (70%) | 3 (15%) | 0.001* |
| No symptoms | 2 (10%) | 0 (0%) | 13 (65%) | <0.001* |

Marked impairment was found in group 1 (schizophrenia ophrenia) compared with moderate impairment in group 2 (MDD). Differences between 3 groups were statically significant (P value < 0.001) as regard Scale for assessment of negative symptoms. Marked impairment was found in group 1 (schizophrenia) and group 2 (MDD). No significant difference between group 1 and 2 (P value 0.879). Significant difference between group 1 and 3 (P value 0.001*) and between group 2 and 3 (P value 0 0.001*) as regard Snaith – Hamilton Pleasure Scale (SHAPS) total scores. Results showed non-significant difference between patients in groups 1 and 2 (P value 0.078) while significant difference between patients in groups 1 and 2 compared to controls (P value <0.001*) as regard total Montgomery-Åsberg Depression Rating Scale (MADRS) score for all groups. Table 5.

Results showed that striatal activity (mainly caudate) was significantly diminished in group 2 (MDD) (P value <0.001*) and group 1 (schizophrenia) (P value 0.002*) relative to controls. No significant differences were found between group 1 (schizophrenia) and 2 (MDD). No significant differences between right and left side activation in all groups. Table 6.

Prefrontal activity (ventromedial area "vmPFC" and dorsolateral area "DLPFC") was increased significantly in depressed patients (group 2) more than control group (P value 0.034*). Schizophrenic patients (group 1) shows significantly decreased activation than controls (P value 0.019*). Significant differences were found between group 1 (schizophrenia) and 2 (MDD) (P value <0.001*). No significant differences were found between right and left side activation in all groups. Table 7.

Results showed that orbito-frontal activity was increased significantly in depressed patients (group 2) more than schizophrenic patients (group 1) (P value <0.001*) and controls (P value 0.019*). While schizophrenic patients (group 1) show non-significant diminished activity than controls (P value 0.055). No significant differences were found between right and left side activation in all groups.
Table 8.

In agreement with our results Milev et al. [19] study show that the anhedonia is a significant determinant predicting functional disability and poor long-term outcome in schizophrenia with a particularly strong and direct effect on interpersonal skills and social function [19].

**Table 5. Anhedonia - Asociality subscale of Scale for assessment of negative symptoms "SANS" total score, Snaith – Hamilton Pleasure Scale (SHAPS) total scores and total Montgomery-Åsberg Depression Rating Scale (MADRS) score for all groups**

| | Group 1 (schizophrenia) (n=20) | Group 2 (MDD) (n=20) | Group 3 (control) (n=20) |
|---|---|---|---|
| **Scale for assessment of negative symptoms "SANS" total score** | | | |
| **Total score (mean) ± SD** | 12.8 ± 2.53 | 8.05 ± 1.85 | 5.25 ± 1.45 |
| **ANOVA (F)** | | 73.515 | |
| **P value** | | < 0.001* | |
| **TUKEY'S Test** | Groups 1&2 < 0.001 | Groups 1&3 <0.001 | Groups 2&3 <0.001 |
| **Snaith – Hamilton Pleasure Scale (SHAPS) total scores** | | | |
| **Total (mean) ± SD** | 8.7 ± 1.3 | | 8.95 ± 2.2 |
| **ANOVA (F)** | | 73.718 | |
| **P value** | | < 0.001* | |
| **TUKEY'S Test** | Groups 1&2 0.879 | Group 1&3 < 0.001* | Group 2&3 < 0.001* |
| **Total Montgomery-Åsberg Depression Rating Scale (MADRS)** | | | |
| **Total (mean) ± SD** | 26.8 ± 6.61 | | 31.45 ± 6.56 |
| **ANOVA (F)** | | 42.813 | |
| **P value** | | < 0.001* | |
| **TUKEY'S Test** | Groups 1&2 0.078 | Group 1&3 < 0.001* | Group 2&3 < 0.001* |

**Table 6. Mean values of BOLD signal magnitude activation at striatum**

| Striatum | | Groups | | | ANOVA | | TUKEY'S Test | | |
|---|---|---|---|---|---|---|---|---|---|
| | | schizophrenia | MDD | Control | F | P-value | I&II | I&III | II&III |
| Right | Mean | 3.665 | 3.388 | 4.517 | 12.398 | <0.001* | 0.491 | 0.002* | <0.001* |
| | SD | 0.582 | 0.585 | 0.861 | | | | | |
| Left | Mean | 3.706 | 3.419 | 4.544 | 12.181 | <0.001* | 0.469 | 0.002* | <0.001* |
| | SD | 0.598 | 0.594 | 0.849 | | | | | |
| Differences | Mean | -0.041 | -0.031 | -0.028 | | | | | |
| | SD | 0.094 | 0.070 | 0.067 | | | | | |
| Paired Test | P value | 0.090 | 0.096 | 0.096 | | | | | |

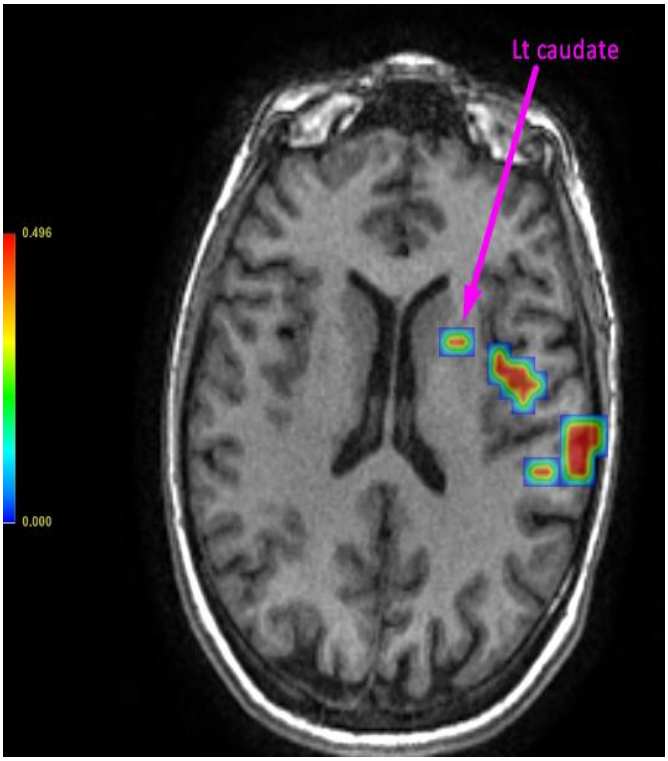


**Fig. 1. Diminished activation at striatum in group 2 (MDD)**

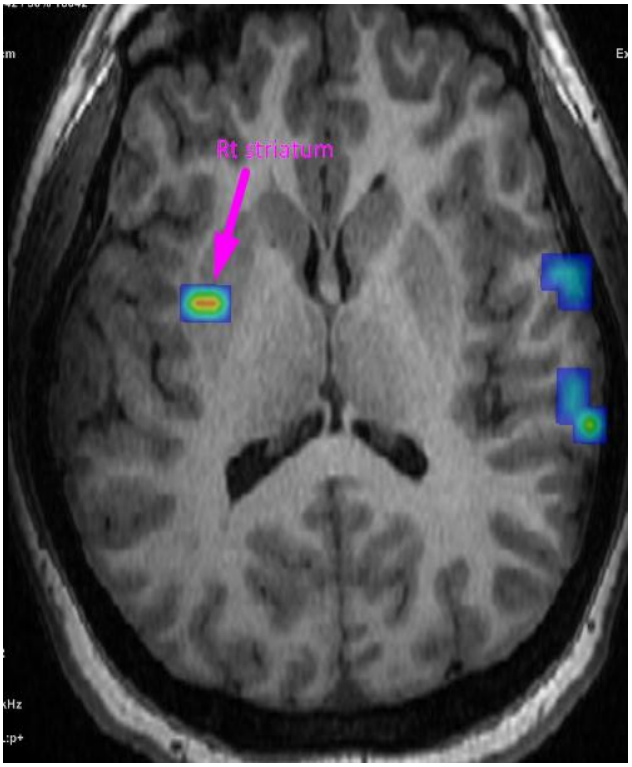


**Fig. 2. Diminished activation at striatum in group 1 (schizophrenia)**

**Table 7. Mean values of BOLD signal magnitude activation at prefrontal cortex "PFC"**

| prefrontal cortex | | Groups | | | ANOVA | | TUKEY'S Test | | |
|---|---|---|---|---|---|---|---|---|---|
| | | schizophrenia | MDD | Control | F | P-value | I&II | I&III | II&III |
| Right | Mean | 3.389 | 4.989 | 4.205 | 13.480 | <0.001* | <0.001* | 0.026* | 0.034* |
| | SD | 0.860 | 1.002 | 0.906 | | | | | |
| Left | Mean | 3.356 | 4.961 | 4.195 | 14.020 | <0.001* | <0.001* | 0.019* | 0.035* |
| | SD | 0.821 | 0.998 | 0.903 | | | | | |
| Differences | Mean | 0.033 | 0.028 | 0.010 | | | | | |
| | SD | 0.077 | 0.067 | 0.032 | | | | | |
| Paired Test | P value | 0.083 | 0.096 | 0.163 | | | | | |

**Table 8. Mean values of BOLD signal magnitude activation at orbito-frontal cortex (OFC)**

| orbito-frontal cortex | | Groups | | | ANOVA | | TUKEY'S Test | | |
|---|---|---|---|---|---|---|---|---|---|
| | | schizophrenia | MDD | Control | F | P-value | I&II | I&III | II&III |
| Right | Mean | 3.206 | 5.019 | 4.022 | 13.082 | <0.001* | <0.001* | 0.055 | 0.019* |
| | SD | 1.061 | 1.044 | 0.990 | | | | | |
| Left | Mean | 3.178 | 5.006 | 3.989 | 13.393 | <0.001* | <0.001* | 0.056 | 0.016* |
| | SD | 1.049 | 1.040 | 0.998 | | | | | |
| Differences | Mean | 0.028 | 0.012 | 0.033 | | | | | |
| | SD | 0.102 | 0.081 | 0.069 | | | | | |
| Paired Test | P value | 0.263 | 0.544 | 0.055 | | | | | |

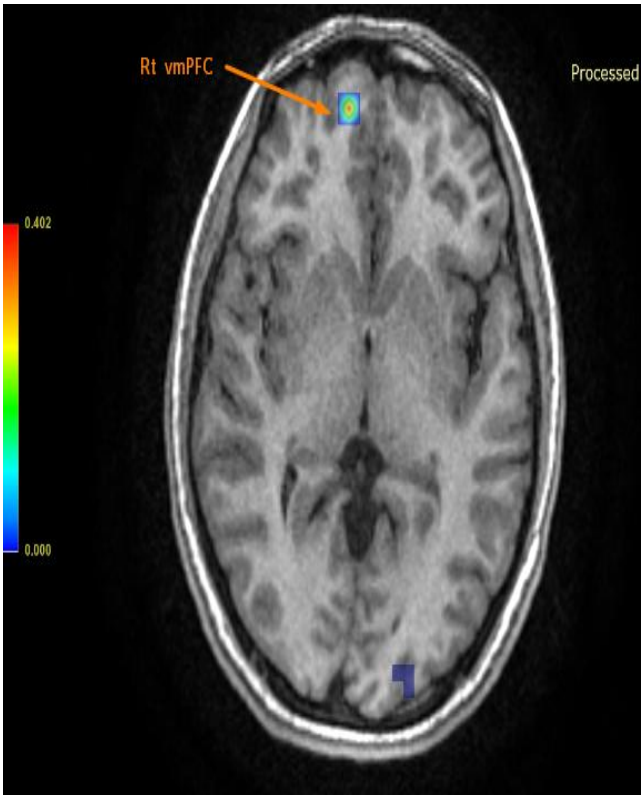


**Fig. 3: Decreased (at ventromedial area "vmPFC") in schizophrenic patients (group 1)**

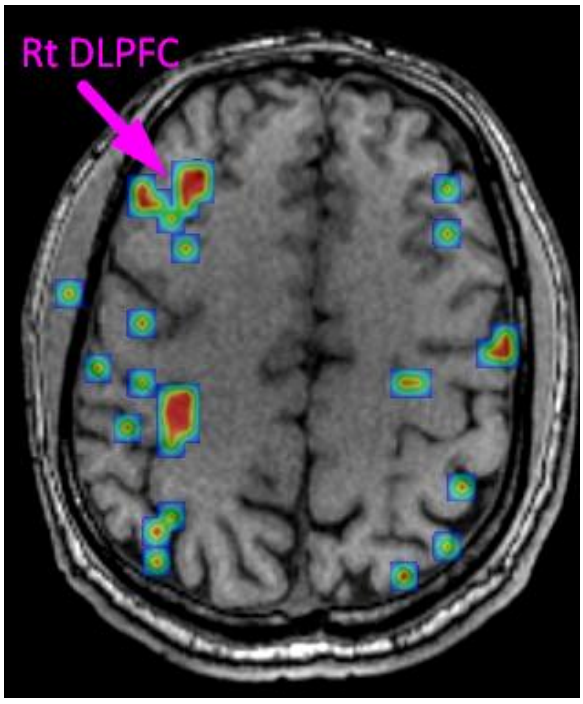


**Fig. 4. Increased activity at dorso-lateral prefrontal area "DLPFC' in depressed patients (group 2)**

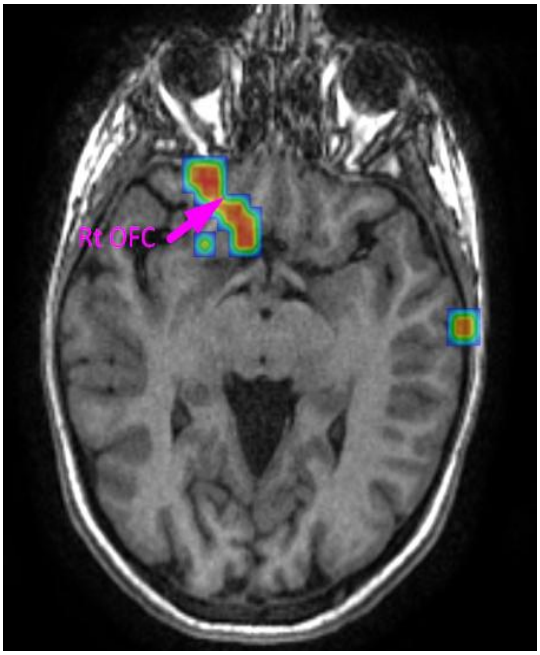


**Fig. 5. Increased orbito-frontal activity in group 2 (MDD) Discussion**

In agreement with our results William and Kring, 2006 study show that the anhedonia-asociality subscale has several strengths in assessment of anhedonia. Patients are asked how frequently they engage in social and recreational activities, and how much they enjoy and experience pleasure in such activities [20].

In agreement with our results Arndt and Andreasen, [21] study show that the limited engagement and/or diminished interest in recreational, sexual, or social activities may be a consequence of anhedonia. They may also result from a variety of social, motivational, and emotional factors other than a diminished ability to experience pleasure [21].

In agreement with our results William and Kring, 2006 study show that the limited engagement with friends, romantic partners, and family could reflect such factors as limited financial resources, social anxiety, paranoia, or intentional avoidance of stressful or uncomfortable social situations, rather than an inability to experience pleasure from interpersonal sources [20].

In agreement with our results Rizvi et al., [5] study show that the SHAPS remains the gold standard tool for measuring anhedonia in depression. SHAPS focus exclusively on "consummatory" pleasure, i.e. "state anhedonia" [5].

In agreement with our results Rizvi et al., [5] study show that the ability to measure acute changes in anhedonia; i.e. can be used to assess the current pleasure experience in the last few days. So, it can be more beneficial in evaluation of a current depressive episode, and evaluation of treatment response Rizvi, [5] #1587.

In agreement with our results Strauss and Gold, 2013 study in Maryland Psychiatric Research Center (MPRC), show that the approximately 82% of schizophrenia patients meet criteria for at least mild severity of anhedonia and 58% for moderate or higher using the Scale for the Assessment of Negative Symptoms (SANS, 26) (n = 385) Thus, patients report less pleasure when reporting on feelings from the past {Strauss, 2012 #1603}.

In disagreement with our results Pelizza and Ferrari, [22] study found that anhedonia reaches clinically significant levels in 45% of schizophrenic patients, and correlates to high levels of negative symptoms and disorganization [22,23].
In agreement with our results Strauss and Gold, 2013 study found that confusion regarding the nature of anhedonia in schizophrenia comes from a consistent set of contradictory findings in

the empirical literature, which have come to be termed "Emotion paradox" [24].

In agreement with our results Kring & Caponigro, [25] stated that patients with schizophrenia in response to emotionally pleasant stimuli (consummatory pleasure) e.g. pictures, films or pleasurable day-to-day life activities; they report feeling as much pleasure as healthy people.

In agreement with our results Tremeau et al. 2009 [26] presented evocative stimuli and had subjects rate their immediate emotional experience, as well as their pre-test anticipated and post-test remembered pleasure. Their results indicated that anticipated pleasure was not impaired in schizophrenia.

In agreement with our results Gard et al. 2007, reported Contradictory findings; they examined daily report of pleasure using the experience sampling method, and found that patients differed from healthy controls in the amount of enjoyment they anticipated they would get out of goal-directed activities, but reported similar levels of consummatory pleasure as controls [27].

In agreement with our results Horan WP, et al. [28] found that schizophrenic patients when asked to evaluate their feelings as part of a questionnaire or a clinical interview – presumably activating “anticipatory” hedonic neurocircuity, they report diminished hedonic experience.

Another meta-analysis by Cohen and Minor [29] supported the conclusions of previous studies, indicating that schizophrenic patients report experiencing state pleasure (consummatory pleasure) similar to controls in response to pleasant stimuli. However, patients did report experiencing increases in negative affectivity in relation to unpleasant, neutral, and pleasant stimuli.

In disagreement with our results Cohen and Minor found that anhedonia should no longer be considered a diminished capacity for pleasure in schizophrenia [29].

In disagreement with our results Strauss and Gold, 2013 revealed a noticed dis-junction between the "state" and "trait" reports; i.e. "current" / "non-current" feelings of the emotional experience in schizophrenia "emotion paradox" [24].

In agreement with our results Sherdell et al, [30] proposed that MDD patients experienced similar levels of consummatory pleasure as healthy controls, lower levels of reward anticipation were associated with reduced motivation for effort expenditure.

In disagreement with our results Pizzagalli, [31] showed alternative explanation is that the ability to translate the prospect of reward into motivation is impaired. This fits evidence that MDD patients display a reduced ability to detect reward and incorporate experience of reward into reward-learning associations [31].

In agreement with our results Rizvi et al., [5] study showed that still unclear whether anhedonia is a stable construct over time in depressed patients (trait) or a symptom that fluctuates depending on severity or even antidepressant mechanism (state) [5].

Our findings are in agreement with Harvey, Armon and Malla, [32]; Park et al., [33] studies on schizophrenic patients; that revealed blunted or diminished striatal activity and/or diminished frontal activation ; [32,33].

In disagreement with our results Harvey [32] study investigated physical anhedonia in 30 patients with schizophrenia and 26 healthy individuals. The orbitofrontal cortex and putamen/ventral striatum activity was negatively correlated with anhedonia severity in schizophrenic patients [32].

They proposed that a link between anhedonia and the activity of the ventral striatum and orbitofrontal cortex "OFC" found in schizophrenia could reflect the specific impairment of indirect factors, such as reward anticipation deficits, that influence the measurement of anhedonia severity through self-report questionnaires [32].

Park, [33] also supported previous findings; they revealed hypo activation of dorsomedial prefrontal cortex "dmPFC" correlated with physical anhedonia in schizophrenic patients. These findings provide further evidence for the relation of functional hypofrontality to the deficit syndrome in schizophrenic [33].

In contrast with our finding Dowd and Barch, [34] study have reported intact patterns of increased ventral striatum responses to reward receipt itself as healthy individuals [34].

Our findings are in agreement with several researches that proposed diminished striatal activity in depressed patients, with either hypo or hyper activation in frontal areas [5,9,35,36].

In agreement with our results Pizzagalli [36] investigated anticipatory and consummatory phases of reward processing in depression. Depressed patients showed reduced putamen activation during reward anticipation as well as reduced caudate, nucleus accumbens (NAcc), and dorsal anterior cingulate (ACC) activation to partially unpredictable rewards [36].

In agreement with our results Zhang [37] performed a meta-analysis of fMRI studies on MDD, Results showed decreased activation in bilateral caudate, cerebellum, left thalamus, anterior cingulate, right putamen and insula. While increased activation was found in bilateral cuneus, middle frontal gyrus, left superior frontal gyrus, fusiform gyrus, right frontal lobe and lingual gyrus [37].

In agreement with our results Tommy Ng, [35] performed a meta-analysis on 41 studies (794 patients with MDD and 803 healthy controls). Their findings argue against the common idea that MDD is primarily linked to deficits within the reward system. Instead, they demonstrate that major depressive disorder is associated with opposing abnormalities in the reward circuit: hypo-responses in the ventral striatum and hyper-responses in the orbitofrontal cortex [35].

Several studies revealed blunted or diminished striatal activation to reward in MDD relative to Healthy Controls [38,39].

In agreement with our results Arrondo and colleges performed fMRI with a modified Monetary Incentive Delay (MID) paradigm on 22 schizophrenic, 24 depressed patients (all patients having anhedonia on medications) and 21 controls. Results showed diminished activation in bilateral ventral striatum in reward anticipation in schizophrenic and depressed patients compared to controls. No differences were found between the two patient groups.

A negative correlation between severity of depression and anhedonia symptoms and ventral striatum activity was found in the schizophrenia group [40].

In contrast, other studies reported reduced activation in frontal areas (orbitofrontal cortex "OFC" and prefrontal cortex "PFC") in both depression and schizophrenia; In disagreement with our results Segarra, [41] studied brain responses to unexpected rewards during a simulated slot-machine game in 24 patients with depression, 21 patients with schizophrenia, and 21 healthy controls using fMRI [41].

There was reduced activation in the orbitofrontal cortex "OFC", medial prefrontal cortex "PFC", ventral striatum, inferior temporal gyrus, and occipital cortex in both depression and schizophrenia in comparison with healthy participants during receipt of unexpected reward [41].

Thus, the association between prefrontal regions and MDD remains equivocal, both in activation (i.e., hyper- or hypo-responses) and location (e.g., orbitofrontal cortex "OFC", dorsolateral prefrontal cortex "DLPFC", ventromedial prefrontal cortex "vmPFC" and/or anterior cingulate cortex "ACC") [35].

## 4. CONCLUSIONS

Anhedonia is a highly disabling symptom in patients with schizophrenia or MDD, associated with poor outcome. Depressed anhedonic patients have higher incidence of suicidal ideas, thoughts and behavior. Depressed patients showed significant striatal hypoactivation associated with hyper activation of prefrontal and orbitofrontal areas. Schizophrenic patients showed diminished activation at striatal areas and frontal cortex. We fail to find significant correlation between severity of anhedonia in both patient groups and degree of fMRI activation in different brain areas involved in reward processing.

## CONSENT AND ETHICAL APPROVAL

This study was conducted on non-randomized sample of 60 participants on the period from April 2017 to April 2020 at Tanta University (Egypt), at Neuropsychiatry and Radiology departments after approval from Ethical Committee and obtaining informed written consent.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Dichter GS, Kozink RV, McClernon FJ, Smoski MJ. Remitted major depression is characterized by reward network hyperactivation during reward anticipation

and hypoactivation during reward outcomes. J Affect Disord. 2012;136:1126-34.
2. Harvey P, Pruessner J, Czechowska Y, Lepage M. Individual differences in trait anhedonia: A structural and functional magnetic resonance imaging study in non-clinical subjects. Molecular Psychiatry. 2007;12:767-75.
3. Ho N, Sommers M. Anhedonia: A concept analysis. Arch Psychiatr Nurs. 2013;27:121-9.
4. Winer ES, Jordan DG, Collins AC. Conceptualizing anhedonias and implications for depression treatments. Psychol Res Behav Manag. 2019;12:325-35.
5. Rizvi SJ, Pizzagalli DA, Sproule BA, Kennedy SH. Assessing anhedonia in depression: Potentials and pitfalls. Neuroscience and Biobehavioral Reviews. 2016;65:21-35.
6. Borsini A, Wallis ASJ, Zunszain P, Pariante CM, Kempton MJ. Characterizing anhedonia: A systematic review of neuroimaging across the subtypes of reward processing deficits in depression. Cogn Affect Behav Neurosci. 2020;20:816-41.
7. American psychiatric association A and association AP. Diagnostic and statistical manual of mental disorders: DSM-5. Washington, DC: American Psychiatric Association; 2013.
8. Lambert C, Da Silva S, Ceniti AK, Rizvi SJ, Foussias G, Kennedy SH. Anhedonia in depression and schizophrenia: A transdiagnostic challenge. CNS neuroscience and therapeutics. 2018;24:615-23.
9. Borsini A, Wallis ASJ, Zunszain P, Pariante CM, Kempton MJ. Characterizing anhedonia: A systematic review of neuroimaging across the subtypes of reward processing deficits in depression. Cognitive, Affective, and Behavioral Neuroscience. 2020;20:816-41.
10. Elwasify M, El-Boraie O, Mohammed H, El-Gilany AH, Sadek M, Amer D, et al. The prevalence and correlates of common mental disorders in Dakahlia Governorate (Egypt). Egypt J Neurol Psychiat Neurosurg. 2011;48:375-81.
11. Sabry N. Inter-rater reliability of the short Arabic form of the Present State Examination (PSE-10). Egypt J Psychiatry. 2009;29:45-54.
12. Kumari S, Malik M, Florival C, Manalai P, Sonje S. An assessment of five (PANSS, SAPS, SANS, NSA-16, CGI-SCH) commonly used symptoms rating scales in Schizophrenia and comparison to newer scales (CAINS, BNSS). J Addict Res Ther. 2017;8:123-5.
13. Nakonezny PA, Carmody TJ, Morris DW, Kurian BT, Trivedi MH. Psychometric evaluation of the snaith-hamilton pleasure scale in adult outpatients with major depressive disorder. Int Clin Psychopharmacol. 2010;25:328-33.
14. Thomas J, Al Ali M, Al Hashmi A, Rodriguez A. Convergent validity and internal consistency of an Arabic snaith hamilton pleasure scale. International Perspectives in Psychology. 2012;1:46-51.
15. Ameli R, Luckenbaugh DA, Gould NF, Holmes MK, Lally N, Ballard ED, et al. SHAPS-C: The snaith-hamilton pleasure scale modified for clinician administration. Peer J. 2014;2:429.
16. Franken IH, Rassin E, Muris P. The assessment of anhedonia in clinical and non-clinical populations: Further validation of the Snaith–Hamilton Pleasure Scale (SHAPS). Journal of Affective Disorders. 2007;99:83-9.
17. Williams JB, Kobak KA. Development and reliability of a structured interview guide for the Montgomery-Åsberg depression rating scale (SIGMA). The British Journal of Psychiatry. 2008;192:52-8.
18. Hallit S, Obeid S, El Hage W, Kazour F. Validation of the Arabic version of the MADRS scale among lebanese patients with depression. L'encephale. 2019;45:195-9.
19. Milev P, Ho B-C, Arndt S, Andreasen NC. Predictive values of neurocognition and negative symptoms on functional outcome in schizophrenia: A longitudinal first-episode study with 7-year follow-up. American Journal of Psychiatry. 2005;162:495-506.
20. Horan WP, Kring AM, Blanchard JJ. Anhedonia in schizophrenia: A review of assessment strategies. Schizophrenia Bulletin. 2006;32:259-73.
21. Arndt S, Andreasen NC, Flaum M, Miller D, Nopoulos P. A longitudinal study of symptom dimensions in schizophrenia: Prediction and patterns of change. Archives of General Psychiatry. 1995;52:352-60.

22. Pelizza L, Ferrari A. Anhedonia in schizophrenia and major depression: state or trait? Annals of General Psychiatry. 2009;8:1-9.
23. Sadock BJ, Sadock VA, Ruiz P. Comprehensive textbook of psychiatry 10th edition. United States of America: Wolters Kluwer. 2017;365-9.
24. Strauss GP, Gold JM. A new perspective on anhedonia in schizophrenia. American Journal of Psychiatry. 2012;169:364-73.
25. Kring AM, Caponigro JM. Emotion in schizophrenia: Where feeling meets thinking. Current Directions in Psychological Science. 2010;19:255-9.
26. Trémeau F, Antonius D, Cacioppo JT, Ziwich R, Jalbrzikowski M, Saccente E, et al. In support of Bleuler: Objective evidence for increased affective ambivalence in schizophrenia based upon evocative testing. Schizophrenia Research. 2009;107:223-31.
27. Gard DE, Gard MG, Kring AM, John OP. Anticipatory and consummatory components of the experience of pleasure: A scale development study. Journal of Research in Personality. 2006;40:1086-102.
28. Horan WP, Blanchard JJ, Clark LA, Green MF. Affective traits in schizophrenia and schizotypy. Schizophrenia Bulletin. 2008;34:856-74.
29. Cohen AS, Minor KS. Emotional experience in patients with schizophrenia revisited: Meta-analysis of laboratory studies. Schizophrenia Bulletin. 2010;36:143-50.
30. Sherdell L, Waugh CE, Gotlib IH. Anticipatory pleasure predicts motivation for reward in major depression. Journal of Abnormal Psychology. 2012;121:51.
31. Berghorst LH, Bogdan R, Frank MJ, Pizzagalli DA. Acute stress selectively reduces reward sensitivity. Frontiers in Human Neuroscience. 2013;7:133.
32. Harvey PO, Armony J, Malla A, Lepage M. Functional neural substrates of self-reported physical anhedonia in non-clinical individuals and in patients with schizophrenia. Journal of Psychiatric Research. 2010;44:707-16.
33. Park IH, Kim JJ, Chun J, Jung YC, Seok JH, Park HJ, et al. Medial prefrontal default-mode hypoactivity affecting trait physical anhedonia in schizophrenia. Psychiatry Research: Neuroimaging. 2009;171:155-65.
34. Kring AM, Barch DM. The motivation and pleasure dimension of negative symptoms: Neural substrates and behavioral outputs. European Neuropsychopharmacology. 2014;24:725-36.
35. Ng TH, Alloy LB, Smith DV. Meta-analysis of reward processing in major depressive disorder reveals distinct abnormalities within the reward circuit. Translational Psychiatry. 2019;9:1-10.
36. Pizzagalli DA, Holmes AJ, Dillon DG, Goetz EL, Birk JL, Bogdan R, et al. Reduced caudate and nucleus accumbens response to rewards in unmedicated individuals with major depressive disorder. Am J Psychiatry. 2009;166:702-10.
37. Zhang WN, Chang SH, Guo LY, Zhang KL, Wang J. The neural correlates of reward-related processing in major depressive disorder: A meta-analysis of functional magnetic resonance imaging studies. J Affect Disord. 2013;151:531-9.
38. Whitton AE, Treadway MT, Pizzagalli DA. Reward processing dysfunction in major depression, bipolar disorder and schizophrenia. Curr Opin Psychiatry. 2015;28:7-12.
39. Heshmati M, Russo SJ. Anhedonia and the brain reward circuitry in depression. Current Behavioral Neuroscience Reports. 2015;2:146-53.
40. Arrondo G, Segarra N, Metastasio A, Ziauddeen H, Spencer J, Reinders NR, et al. Reduction in ventral striatal activity when anticipating a reward in depression and schizophrenia: A replicated cross-diagnostic finding. Front Psychol. 2015;6:1280.
41. Segarra N, Metastasio A, Ziauddeen H, Spencer J, Reinders NR, Dudas RB, et al. Abnormal frontostriatal activity during unexpected reward receipt in depression and schizophrenia: Relationship to anhedonia. neuropsychopharmacology. 2016;41:2001-10.



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