DISTURBI DEPRESSIVE E DISSOCIATIVI CORRELATE AL CONSUME DI SOSTANZE: NUOVE DIMENSIONI CLINICHE E PRINCIPI DI TRATTAMENTO

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Disclosure / Conflict of interest

I have an interest in relation to one or more organizations that could be perceived as a possible conflict of interest in the context of the subject of this presentation. The relationships are summarized below.

Interest	Name of the Organization
Speaker fees	Otsuka, Lundbeck, Novartis, FB Health, Janssen-Cilag, Lundbeck, Otsuka, Pfizer, Servier, Wyeth, Italfarmaco, Angelini, DOC generici
Consultancy fees	Otsuka, Lundbeck, Janssen-Cilag, Angelini, Servier, Pfizer
Independent Investigator	Janssen-Cilag, , Lundbeck, Otsuka,
Advisory Board	Otsuka, Lundbeck, Janssen-Cilag

Agenda

- Depressione e Anedonia: classificazione, definizione, psicopatologia
- Anedonia e sostanze
- NPS e psicosi fredde
- Come trattare la anedonia nei Disturbi da Uso di Sostanze

Anedonia come dimensione psicopatologica

ANEDONIA: differenze

Il termine anedonia (ἀν-, ”senza” e ἡδονή, "piacere”). Fu introdotto in psichiatria da Ribot nel 1896

Apatia: assenza o perdita della risposta emozionale di fronte a stimoli positivi e negativi

Appiattimento affettivo: assenza o perdita di risposta affettiva e emozionale nel campo delle relazioni

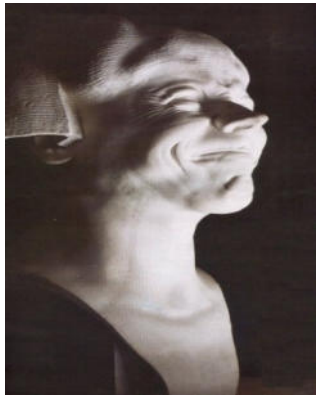
Abulia: patologia della azione volontaria diretta a fini concreti

Umore, emozioni, regolazione emozionale

Anedonia

Incapacità di sperimentare piacere (esperienze di piacere sia anticipatorie sia consumatorie)

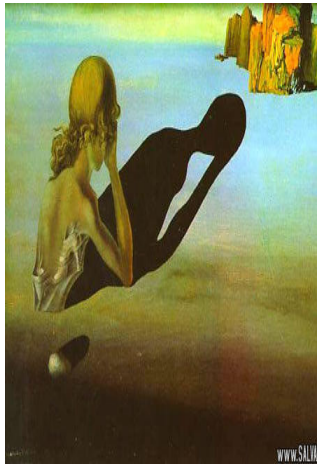
(Gard et al., 2008)



Blunted affect

Mancanza di reattività emozionale da parte dell'individuo. Si manifesta come un fallimento nell'esprimere sentimenti.

(Kholer et al., 2008)



ANEDONIA: differenze

Per tipologia:

-Anedonia sociale
-Anedonia física

Un livello significativo di anedonia è stato descritto nel 50% dei soggetti con patologia psichiatrica

Silverstone P. *Is anhedonia a good measure of depression?* Acta Psychiatr Scand 1991;83:249-50.

Secondo il disturbo psichiatrico:

- **Anedonia psicotica**
- **Anedonia depressiva**
- **Anedonia nei disturbi dell'alimentazione**
- **Anedonia nei disturbi da uso di sostanza e alcol**
- **Anedonia nel Parkinson**

IL PIACERE

Si caratterizza per la presenza di 4 principali elementi psicologici:

1) un' intensa anticipazione delle esperienze che lo evocano;
2) il ricordo appagante di quelle stesse esperienze;
3) la volontà di impegnarsi a fondo per portarle a termine
4) la tendenza a ripetere tutti quei comportamenti che lo producono.

Ettenberg A. *Anhedonia. In: Costello C, eds. Symptoms of schizophrenia. New York: Wiley 1993, pp.* 121-44.

2 LIVELLI:
- Livello **appetitivo (Wanting)**: attira l' individuo verso il suo compimento [piacere della conquista], e mediato dalla dopamina.
- Livello **consumatorio (Liking)**: accompagna continuativamente l' intera durata di ogni attività gratificante [piacere della consumazione], è mediato dal circuito degli oppioidi.

Anedonia e disturbo da uso di sostanze

Piacere e Sostanze

Sostanza: piacere senza sforzo (low cost pleasure experience)

L'uso cronico di sostanze provoca un aumento del "costo" del piacere, fino alla ipo-edonia e alla anedonia (fisica e sociale)

Tutte le sostanze provocano un aumento dei livelli di dopamina nel Nucleus Accumbens, alterando il meccanismo del **wanting**.

Alcune sostanze alterano il meccanismo del Wanting (cocaina, stimolanti)

Alcune sostanze alterano il meccanismo del Liking (oppiacei)

Altre quello del Dis-Liking (Depressori)

Addiction, Anhedonia, and Comorbid Mood Disorder. A Narrative Review

*Marianne Destoop [1,2], Manuel Morrens [1,3], Violette Coppens [1,3] and Geert Dom [1,2]**

[1] Collaborative Antwerp Psychiatric Research Institute (CAPRI), Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium, [2] Psychiatric Hospital Multiversum, Campus Alexianen, Boechout, Belgium, [3] University Department of Psychiatry, Campus Duffel, Duffel, Belgium

1) anhedonia is associated with substance use problems/disorders and their severity;

2) anhedonia is especially prominent in DUS with comorbid depression and early life stress experiences;

3) anhedonia may be both a trait and a state dimension in its relation to DUS;

4) anhedonia tends to negatively impact DUS treatment outcome.

5) Most evidence points to motivational anhedonia as the most involved subdimension of anhedonia within its relationship with DUS.

Original Paper

Neuropsychobiology

Neuropsychobiology 018
DOI: 10.1159/0000XXXXX

Published online: ■■■

Anhedonia and Substance-Related Symptoms in Detoxified Substance-Dependent Subjects: A Correlation Study

L. Janiri[a] G. Martinotti[a] T. Dario[a] D. Reina[a] F. Paparello[a] G. Pozzi[a]
G. Addolorato[b] M. Di Giannantonio[a] S. De Risio[a]

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L'anedonia è largamente rappresentata nei soggetti che abusano sostanze, soprattutto nella fase successiva alla disintossicazione

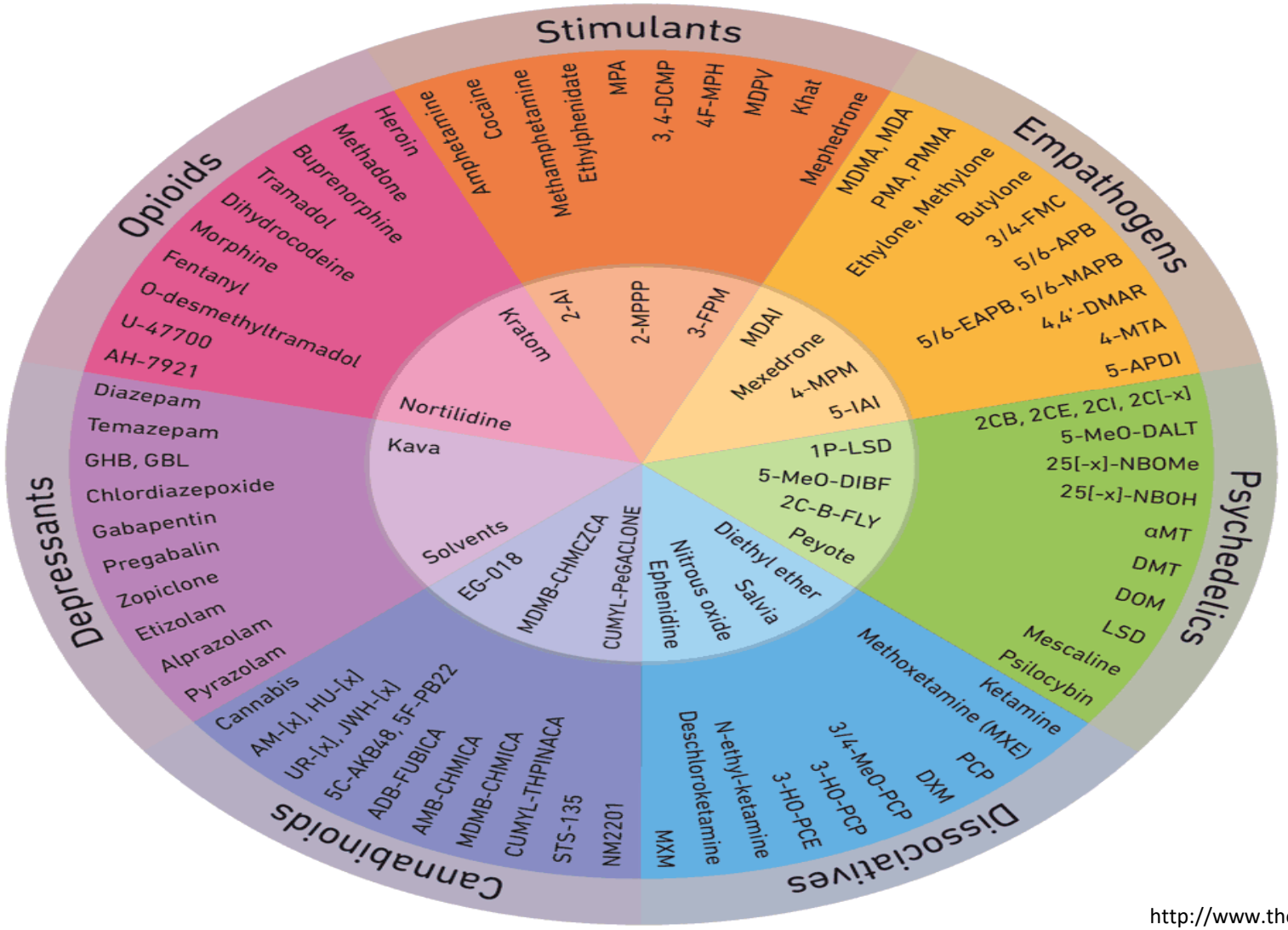
La presenza di anedonia si associa ad un forte craving per le sostanze

Alti livelli di anedonia sono predittivi di una ricaduta in tempi brevi

Nuove sostanze psicoattive, sostanze tradizionali potenziate e riduzione della dimensione edonica

The Drugs Wheel

A new model for substance awareness



http://www.thedrugswheel.com/

> CNS Spectr. 2020 Jun 25;1-20. doi: 10.1017/S1092852920001479. Online ahead of print.

Substance Related Exogenous Psychosis: a post-modern syndrome

Giovanni Martinotti, Luisa De Risio, Chiara Vannini, Fabrizio Schifano, Mauro Pettorruso, Massimo Di Giannantonio

TABLE 1 Overview of Diagnostic Criteria for Substance-Induced Psychosis in ICD-10 and DSM

	ICD-10	DSM-IV/V
Core	Cluster of psychotic phenomena that occur during/immediately after psychoactive substance use	
Characteristics	Hallucinations, delusions, psychomotor disturbances, abnormal affect	*Prominent* hallucinations or delusions
Insight/level of consciousness	Usually clear, some level of clouding of consciousness may occur, though not severe confusion	No insight into symptoms being substance induced
When/duration	Includes psychosis occurring during/immediately after drug use (<48 h) as long as not due to withdrawal or delirium Resolves at least partially within 1 month, fully within 6 months	Either (1) or (2): 1. Symptoms developed during/within 1 month of substance intoxication or withdrawal 2. Medication is etiologically related to the disturbance Does not occur exclusively during delirium
Notes		Not better accounted for by disorder that is not substance induced Should only be made *instead of intoxication or withdrawal if symptoms in excess of what is expected* and when *symptoms severe enough to warrant clinical attention*

Substance Related Exogenous Psychosis (SREP)

Caratteristiche

- **Alterazioni qualitative e quantitative della coscienza (stato crepuscolare, oniroide), dissociazione**
- Disturbi della coscienza dell'Io (Somato/Allo-psichica)
- Disturbi della senso-percezione (Somatici > Visivi >Uditivi)
- Primarietà dell'esperienza percettiva abnorme sulla quale si organizza il delirio, spesso di tipo ON-OFF
- Egodistonia, critica oscillante
- Psicosi "concrete", calate nel presente
- Psicosi "calde" nella fase iniziale, mania/ipomani/disforia
- **Psicosi "fredde" nalla fase successiva (Anedonia/Vuoto)**
- Discontrollo degli impulsi, Aggressività etero/auto diretta

Martinotti, Schifano, Murray, et al., J Psychopathology. 2015

Anedonia

Abulia

Appiattimento

Affective Blunting

Asocialità

Apatia

Sindrome Amotivazionale

Come trattare l’anedonia:

Antidepressivi ?
Antipsicotici ?
Brain Stimulation ?

frontiers in
PSYCHIATRY

REVIEW ARTICLE
published: 17 March 2011
doi: 10.3389/fpsyt.2011.00010

Anhedonia and substance dependence: clinical correlates and treatment options

Daniele Stavros Hatzigiakoumis, Giovanni Martinotti, Massimo Di Giannantonio and Luigi Janiri*

Istituto di Psichiatria e Psicologia, Università Cattolica del S. Cuore, Roma, Italy

1) Antidepressivi appartenenti ad altre classi di antidepressivi (Trazodone, Bupropione, Agomelatina, Vortioxetina)

2) Antipsicotici atipici a bassi dosaggi (Aripiprazolo, Brexpiprazolo, Cariprazina, Amisulpride, Quetiapina)

3) Stabilizzanti dell'umore con proprietà antidepressive (Lamotrigina, Litio?)

4) Altre molecole (Amantadina, L-Acetyl-Carnetina, S-Adenosil-Metionina, N-Acetyl-Cisteina)

Anedonia e antidepressivi

Anedonia e risposta farmacologica

L'anedonia è un sintomo estremamente difficile da trattare: evidenze dicono che gli attuali farmaci di prima-linea nella depressione (e.g.,SSRIs) non trattano adeguatamente i deficit motivazionali e di reward-processing (APA, 2000; Dunlop and Nemeroff, 2007; McCabe et al.,2009; Nutt et al., 2007; Price et al., 2009; Shelton and Tomarken, 2001)

Attualmente la presenza di sintomi anedonici è considerata predittiva di scarsa risposta ai trattamenti. (Spijker et al., 2001)

ADDICTION

SSA SOCIETY FOR THE STUDY OF ADDICTION

Review

Efficacy and tolerability of antidepressants in the treatment of adolescents and young adults with depression and substance use disorders: a systematic review and meta-analysis

Xinyu Zhou, Bin Qin, Cinzia Del Giovane, Junxi Pan, Salvatore Gentile, Yiyun Liu, Xinghui Lan, Jia Yu, Peng Xie ✉

"Antidepressant medication has a small overall effect in reducing depression in young patients with combined depressive and substance-use disorders, but does not appear to improve substance use outcomes"

International Journal of Neuropsychopharmacology (2002), **5**, 147–151. Copyright © 2002 CINP
DOI: 10.1017/S1461145702002870

Emotional blunting associated with SSRI-induced sexual dysfunction. Do SSRIs inhibit emotional responses?

Adam Opbroek[1], Pedro L. Delgado[2], Cindi Laukes[3], Cindy McGahuey[1], Joanna Katsanis[1], Francisco A. Moreno[1] and Rachel Manber[4]

Compared to controls, patients reported significantly ($p<0.05$) less ability to cry, irritation, care about others' feelings, sadness, erotic dreaming, creativity, surprise, anger, expression of their feelings, worry over things or situations, sexual pleasure, and interest in sex.

Emotional blunting may be an under-appreciated side-effect of SSRIs that may contribute to treatment non-compliance and/or reduced quality of life.

Trazodone

Il trazodone è ben tollerato e la co-assunzione con l'alcol non desta particolari preoccupazioni (se non a dosaggimolto elevati)

Favorisce l'induzione del sonno in una popoazione in cui il sonno è alterato

Può avere una discreta capacità antidolorifica

Ha un basso potenziale di abuso

Trazodone

J Addict Dis. 2003 ; 22(2): 91–103.

Treatment of Sleep Disturbance in Alcohol Recovery: A National Survey of Addiction Medicine Physicians

Peter D. Friedmann, MD, MPH, **Debra S. Herman, PhD**, **Shelby Freedman, BA**, **Stephenie C. Lemon, MS**, **Susan Ramsey, PhD**, and **Michael D. Stein, MD**
Division of General Internal Medicine, Departments of Medicine and Community Health, Brown University School of Medicine and Rhode Island Hospital, Providence, RI

THE AMERICAN JOURNAL ON ADDICTIONS

AAP American Academy of Addiction Psychiatry

Trazodone and Alcohol Relapse: A Retrospective Study Following Residential Treatment

Bhanu Prakash Kolla MRCPsych, Terry D. Schneekloth MD, Joanna M. Biernacka PhD, Mark A. Frye MD, Meghna P. Mansukhani MBBS, Daniel K. Hall-Flavin MD, Victor M. Karpyak MD, PhD ... **See all authors**

Bupropione

Nella pratica clinica è l'antidepressivo più usato per il trattamento dell'anedonia

Inibitore del reuptake di NA - DA, e antagonista del recettore dell'acetylcolina

In un campione di soggetti con disturbo dell'umore ha mostrato una efficacia consistente sulla dimensione anedonia

Data la scarsa propensione a sviluppare switch maniacali è l'antidepressivo consigliato nei casi di anedonia in pazienti bipolari

Cryan et al., 2004; Bruijnzeel and Markou, 2003; Sachs et al., 2007

Acetyl-L-carnitine

Acetyl-L-carnitine (ALC) è un composto endogeno

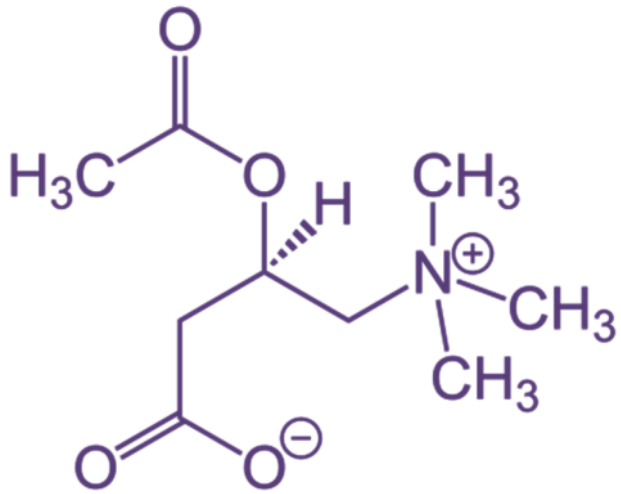
Contribuisce alla omeostasi del Coenzima A, esportando dal mitocondrio gruppi acetyl-CoA.

Aumenta i livelli di dopamina nella corteccai, nell'ippocampo, nello striato e nell'accumbens

Facilita la trasmissione colinergica

Modula il recettore NMDA

Aumenta le β-endorfine plasmatiche



Acetyl-L-carnitine

ALC si dimostrò efficace nel ridurre l'anedonia e il craving in soggetti alcolisti disintossicati, in modo marcato e rapido

L'efficacia risultò tale solo con la somministrazione in via EV

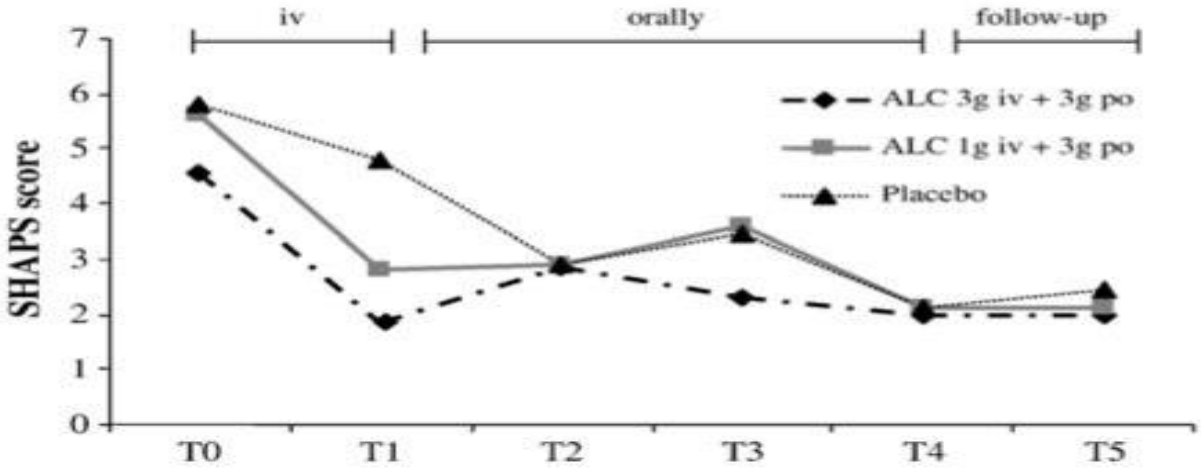


Fig. 2. Snaith–Hamilton Pleasure Scale (SHAPS) scores between times in ALC groups and placebo. Intravenous therapy was given for 10 days, oral therapy for 80 days. Follow-up assessment was made after 45 days.

Martinotti et al., 2010; Martinotti et al., 2011

> CNS Spectr. 2020 Aug 10;1-32. doi: 10.1017/S109285292000173X. Online ahead of print.

Effect of Vortioxetine in Subjects with Major Depressive and Alcohol Use Disorders: A Six-Months Retrospective Analysis

Marco Di Nicola, Maria Pepe, Isabella Panaccione, Lorenzo Moccia, Luigi Dattoli, Marzia Molinaro, Gabriele Sani, Luigi Janiri, Roger S McIntyre

- 57 MDD+AUD and 56 MDD outpatients, matched for baseline characteristics.
- Patients were assessed after 1, 3, and 6 months-treatment with vortioxetine (10-20 mg/daily, flexibly dosed) in combination with continuous psychosocial support.
- The primary outcome was improvement in depressive symptoms measured by the Montgomery-Åsberg Depression Rating Scale.
- Changes in anxiety, anhedonia, cognition, functioning, quality of life, were also evaluated

Table 1. Demographic and clinical baseline characteristics.

	MDD+AUD (n=57)	MDD (n=56)	χ^2/t	*df*	*p*
Psychometric Assessment					
CGI-S	4.25 ± 0.43	4.20 ± 0.40	-.62	1	.53
MADRS	27.61 ± 1.61	27.73 ± 1.72	.38	1	.71
HARS	22.63 ± 1.87	22.91 ± 2.64	.65	1	.52
SHAPS	3.54 ± 1.41	3.44 ± 1.42	-.40	1	.69

- Vortioxetine significantly improved mood in MDD+AUD patients (p<.001), with no differences when compared to MDD (p=.36).
- A substantial rate (45.6%) of comorbid subjects obtained clinical remission at endpoint (p=.36 vs. MDD).
- Baseline to endpoint improvements of all secondary outcomes (p<.001), with no significant difference between groups, were observed.
- Overall, vortioxetine was safe and well-tolerated.

Di Nicola et al., 2020

Neuropsychiatric Disease and Treatment

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Open Access Full Text Article

ORIGINAL RESEARCH

A Feasibility Study of Patients with Major Depression and Substance Use Disorders: Vortioxetine as Maintenance Treatment

Ignacio Basurte-Villamor[1], Pablo Vega[2], Carlos Roncero[3–5], José Martínez-Raga[6], Lara Grau-López[7–10], Lourdes Aguilar[3–5], Marta Torrens[11], Nestor Szerman[12]

Background: Limited studies have evaluated the effectiveness of vortioxetine in real-world settings, and none of them has involved patients with dual depression (major depressive disorder [MDD] and substance use disorder [SUD]). The objective of the study was to describe the effectiveness of vortioxetine in clinical practice and determine its effect on affective symptoms, cognitive function, quality of life, and substance use in patients with MDD and SUD.

Methods: Post-authorization, retrospective, multicenter, descriptive, and observational study in 80 patients with MDD and SUD receiving a maintenance treatment with vortioxetine for six months between January 2017 and April 2021.

Results: Compared with baseline, scores significantly decreased after 3 and 6 months of treatment in the Montgomery-Åsberg Depression Rating Scale total (from 28.9 to 17.7 and 12.0), and global functional impairment of the Sheehan Disability Inventory (from 26.3 to 19.1 and 16.7). The number of correct answers in the symbol digit modalities test significantly improved during vortioxetine treatment (from 40.4 to 43.8 and 48.4). Regarding the clinical global impression scale, the score for disease severity significantly decreased from 3.8 to 3.0 and 2.4. Compared with baseline, there was a significant reduction in consumption of practically all substances, especially of alcohol, cannabis, and cocaine.

Conclusion: Vortioxetine was effective in clinical practice for alleviating depressive symptoms and functional impairment, and in improving cognitive and executive functions and disease severity in patients with MDD and SUD. Moreover, the treatment with vortioxetine favored a reduction in substance use and the severity of the SUDs.

Keywords: vortioxetine, major depressive disorder, substance use disorder, dual disorder, major dual depressive disorder, real-world evidence

Anedonia e antipsicotici

Current Pharmaceutical Design, 2022, *28*, 2241-2259

SYSTEMATIC REVIEW

Atypical Antipsychotic Drugs in Dual Disorders: Current Evidence for Clinical Practice

Giovanni Martinotti[1,2,#], Stefania Chiappini[1,2,#], Alessio Mosca[1], Andrea Miuli[1], Maria Chiara Santovito[1], Mauro Pettorruso[1,*], Valentin Skryabin[3], Stefano L. Sensi[1] and Massimo Di Giannantonio[1]

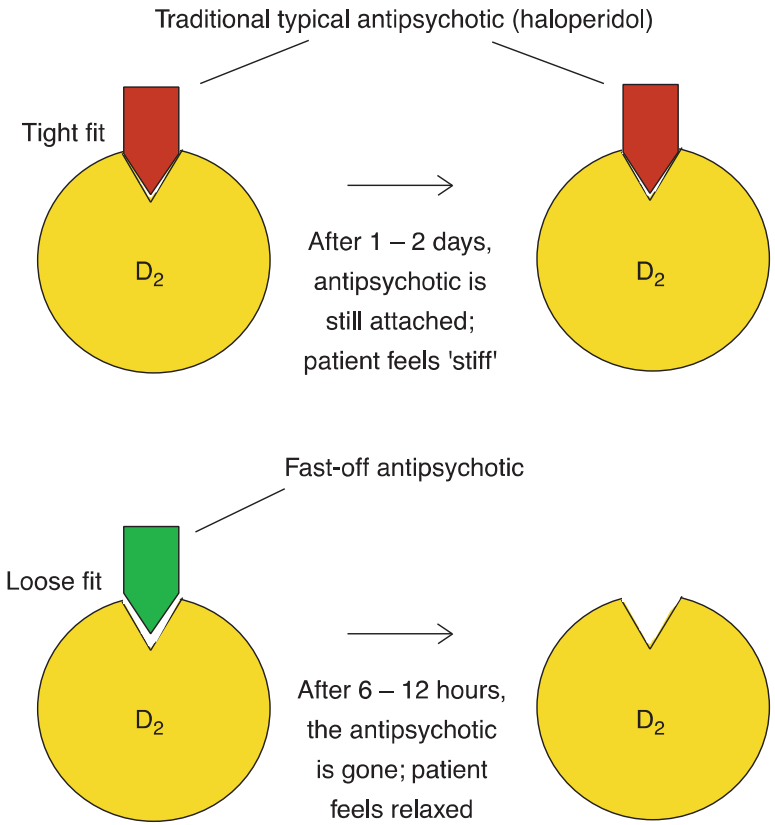

Figure 4. Antipsychotics that are tightly bound to D_2 markedly reduce dopamine neurotransmission and elicit Parkinsonism and prolactinaemia. Antipsychotics that are loosely bound to D_2 desorb quickly from D_2 and elicit little or no Parkinsonism or prolactinaemia.

Table 3. Fast-off-D_2 antipsychotics generally elicit no or low Parkinsonism.

	Time for 50% offset from D_2 [57]	K_i or K_d (nM)	Parkinsonism
Remoxipride (5 nM)	13 s	67	Absent
Clozapine (200 nM)	15 s	75	Absent
Quetiapine (200 nM)	16 s	140	Absent or low
Perlapine (140 nM)	24 s	138	Absent or low
S-(-)-Amisulpride (4 nM)	42 s	1.7*	Absent or low
Aripiprazole (10 nM)	52 s	1.8‡	Low
9-Hydroxy-risperidone (2 nM)§	60 s	1.6	Low
Amoxapine (40 nM)	66 s	21	Low
Loxapine (20 nM)	16 min	9.2	Dose-dependent
Olanzapine (5 nM)	17 min	7.4	Dose-dependent
Dopamine at D_2^{High} state		1.7	
Raclopride (4 nM)	23 min	1.6	Dose-dependent
Risperidone (2 nM)	27 min	1.09	Dose-dependent
Chlorpromazine (1.5 nM)	30 min	1.2	Common
Haloperidol (2 nM)	38 min	0.4 – 0.74	Common, dose-dependent

The times for 50% offset from the cloned D_2^{Long} receptor are shown in column 2. The K_i or K_d values are from **Table 1**. The K_i values are the dissociation constants or inhibition concentrations which inhibited the binding of the [^{3}H]ligand by 50%, corrected for the concentration of the [^{3}H]ligand; the K_d values are the dissociation constants obtained by means of saturation data, using the titrated form of the drug, as indicated. The antipsychotics with *K* values lower than that for dopamine (at D_2^{High}) desorb slowly from D_2 and are consistently associated with Parkinsonism. Antipsychotics with *K* values > 20 nM dissociate quickly and elicit little or no Parkinsonism. Antipsychotics with intermediate values (loxapine and olanzapine) elicit dose-dependent Parkinsonism. Data from [30,57]. *Amisulpride has low and slow permeation into brain. ‡Aripiprazole is a partial agonist. §Paliperidone.

Quetiapine

Published in final edited form as:
J Clin Psychopharmacol. 2007 August ; 27(4): 344–351. doi:10.1097/JCP.0b013e3180ca86e5.

A Double-Blind, Placebo-Controlled Pilot Trial of Quetiapine for the Treatment of Type A and Type B Alcoholism

Kyle M. Kampman, MD[*], Helen M. Pettinati, PhD[*], Kevin G. Lynch, PhD[*], Tom Whittingham, BS[*], Wayne Macfadden, MD[†], Charles Dackis, MD[*], Carlos Tirado, MD[*], David W. Oslin, MD[*], Thorne Sparkman, MD[‡], and Charles P. O'Brien, MD, PhD[*]

[*]Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, PA

- Efficacia in soggetti ad insorgenza precoce
- Alcolisti Tipo B, con alti livelli di impulsività e aggressività

HUMAN PSYCHOPHARMACOLOGY
Hum. Psychopharmacol Clin Exp 2008; **23**: 417–424.
Published online 21 April 2008 in Wiley InterScience
(www.interscience.wiley.com) **DOI**: 10.1002/hup.944

Quetiapine decreases alcohol consumption, craving, and psychiatric symptoms in dually diagnosed alcoholics

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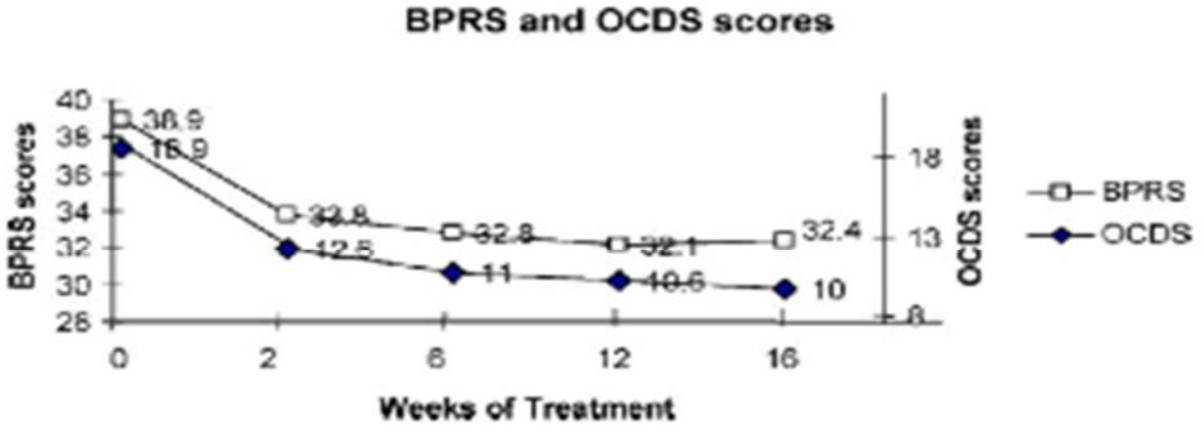

Figure 1. Correlation between the Brief Psychiatric Rating Scale (BPRS) and Obsessive-Compulsive Drinking Scale (OCDS) scores at baseline and after 2 (T1), 6 (T2), 12 (T3), and 16 (T4) weeks of treatment

Aripiprazolo

Aripiprazolo agisce come agonista parziale D_2 e 5-HT_{1A}

Nel confronto con altri antipsicotici ha mostrato una specificità rispetto alla gestione della dimensione anedonica

Scale	Baseline	16-weeks	*P*
MADRS, mean (S.D.)	27.6 (5.7)	18 (3.7)	<0.0001
SHAPS, mean (S.D.)	6.8 (4.55)	2.83 (2.9)	<0.001
YMRS, mean (S.D.)	4.8 (2.2)	4.6 (1.9)	<0.87

Mazza et al., 2009; Liemburg et al., 2011

Psychopharm

Journal of Psychopharmacology
xxx(xx) (2008) 1–7

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Aripiprazole in the treatment of patients with alcohol dependence: a double-blind, comparison trial vs. Naltrexone

G Martinotti *PHD Department of Psychiatry, Catholic University Medical School, Rome.*
M Di Nicola *MD Department of Psychiatry, Catholic University Medical School, Rome.*
M Di Giannantonio *Head of the Department of Psychology, Department of Psychology, G. D'Annunzio University, Chieti.*
L Janiri *Associate Professor, Department of Psychiatry, Catholic University Medical School, Rome.*

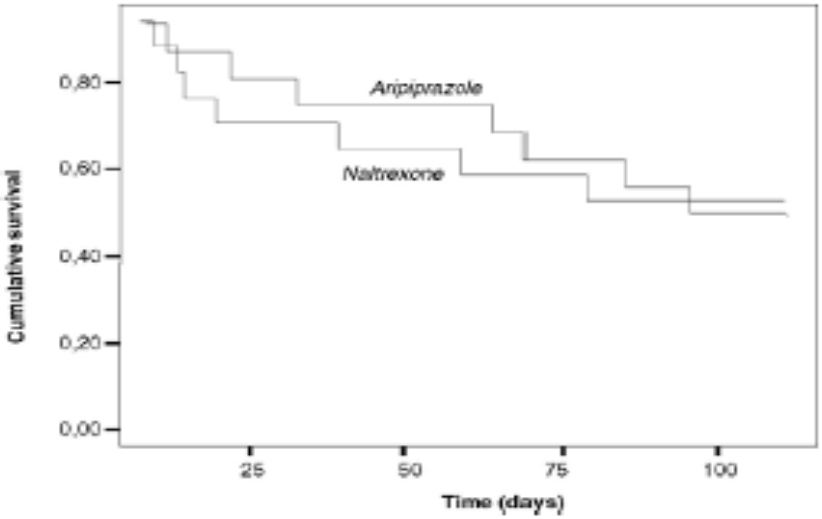


Figure 2 Survival remaining abstinent.

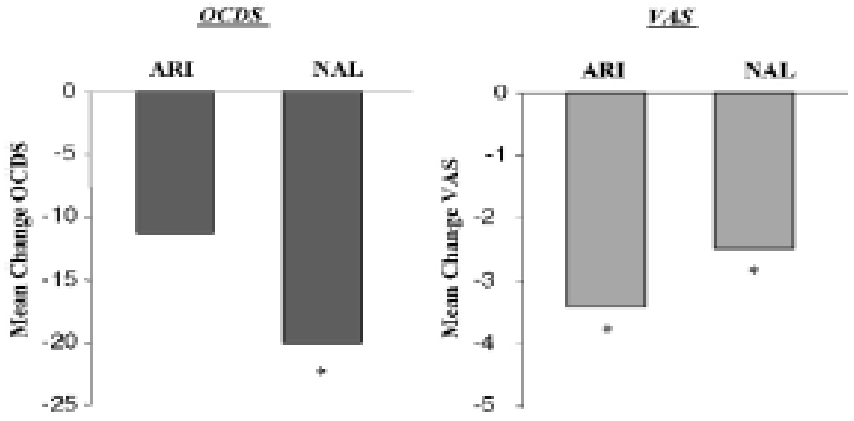


Figure 3 Obsessive Compulsive Drinking Scale (OCDS), and Visual Analogue Scale for craving (VAS) mean change from baseline at the last assessment (T2) * = p<.01.

EXPERT REVIEWS

The preclinical profile of brexpiprazole: what is its clinical relevance for the treatment of psychiatric disorders?

Leslie Citrome*[1], Tine Bryan Stensbøl[2] and Kenji Maeda[3]

Expert Rev. Neurother. 15(10), 1219–1229 (2015)

Key issues

- Brexpiprazole is a serotonin–dopamine activity modulator.
- Brexpiprazole has high binding affinities for 5-HT_{1A} and D_2 receptors, where it acts as a partial agonist. Compared with aripiprazole, it is more potent at 5-HT_{1A} receptors and displays less intrinsic activity at D_2 receptors. Brexpiprazole also has antagonistic activity at several 5-HT receptors including 5-HT_{2A}, as well as at $\alpha_{1B/2C}$-adrenergic receptors.

BREXPIPRAZOLO: INDICAZIONI CLINICHE IN RELAZIONE AGLI ALTRI AGONISTI PARZIALI

Table 1. US Food and Drug Administration approved indications for aripiprazole, brexpiprazole, and cariprazine [Actavis, 2015; Alkermes, 2015; Otsuka, 2014, 2015a, 2015b].

	Aripiprazole	Brexpiprazole	Cariprazine
Schizophrenia (adults)	✓	✓	✓
Schizophrenia (adolescents)	✓		
Schizophrenia or bipolar mania associated agitation (adults) *via* intramuscular route	✓		
Schizophrenia depot injection	✓		
Bipolar disorder (adults and pediatric patients), acute monotherapy for mania	✓		
Bipolar disorder (adults and pediatric patients), acute adjunctive treatment to lithium or valproate for mania	✓		
Bipolar disorder (adults only), acute treatment of manic or mixed episodes	✓		✓
Bipolar disorder (adults only), maintenance treatment	✓		
Adjunctive treatment of major depressive disorder (adults)	✓	✓	
Tourette's disorder (pediatric patients)	✓		
Irritability associated with autistic spectrum disorder (pediatric patients)	✓		

Maeda et al., 2014

Anedonia e Brain Stimulation

MIT Technology Review

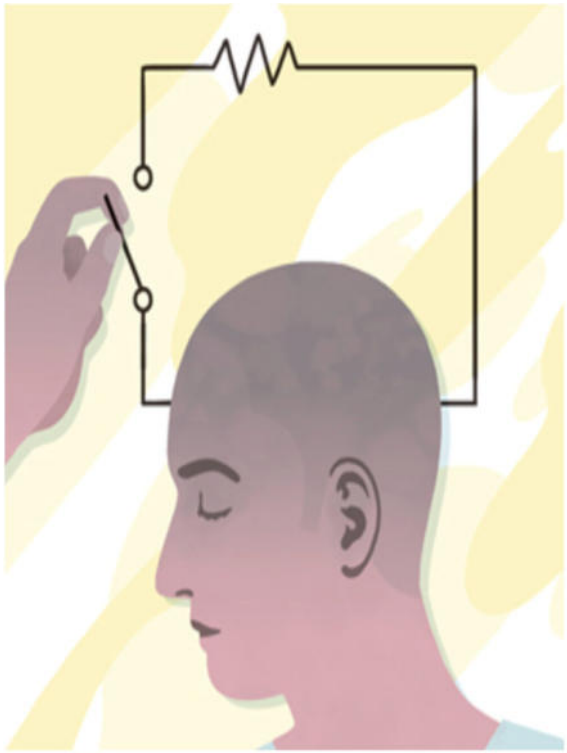
The Best Biomedicines stories of 2015

Rewriting Life

For Cocaine Addicts, Treatment with Magnets May Stop Craving

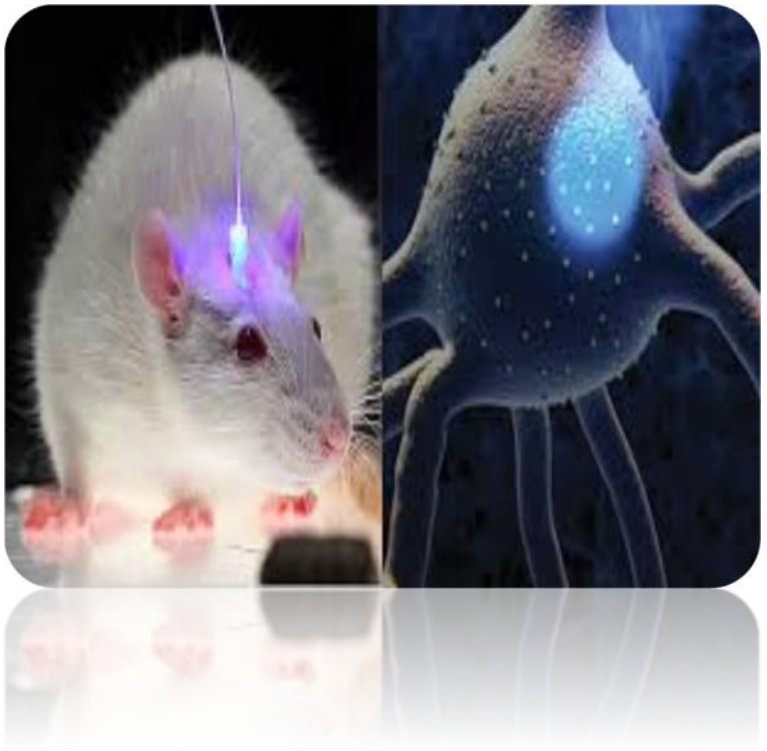
Can magnetic stimulation of the brain shake drug users out of their habits?

by Adam Piore December 3, 2015

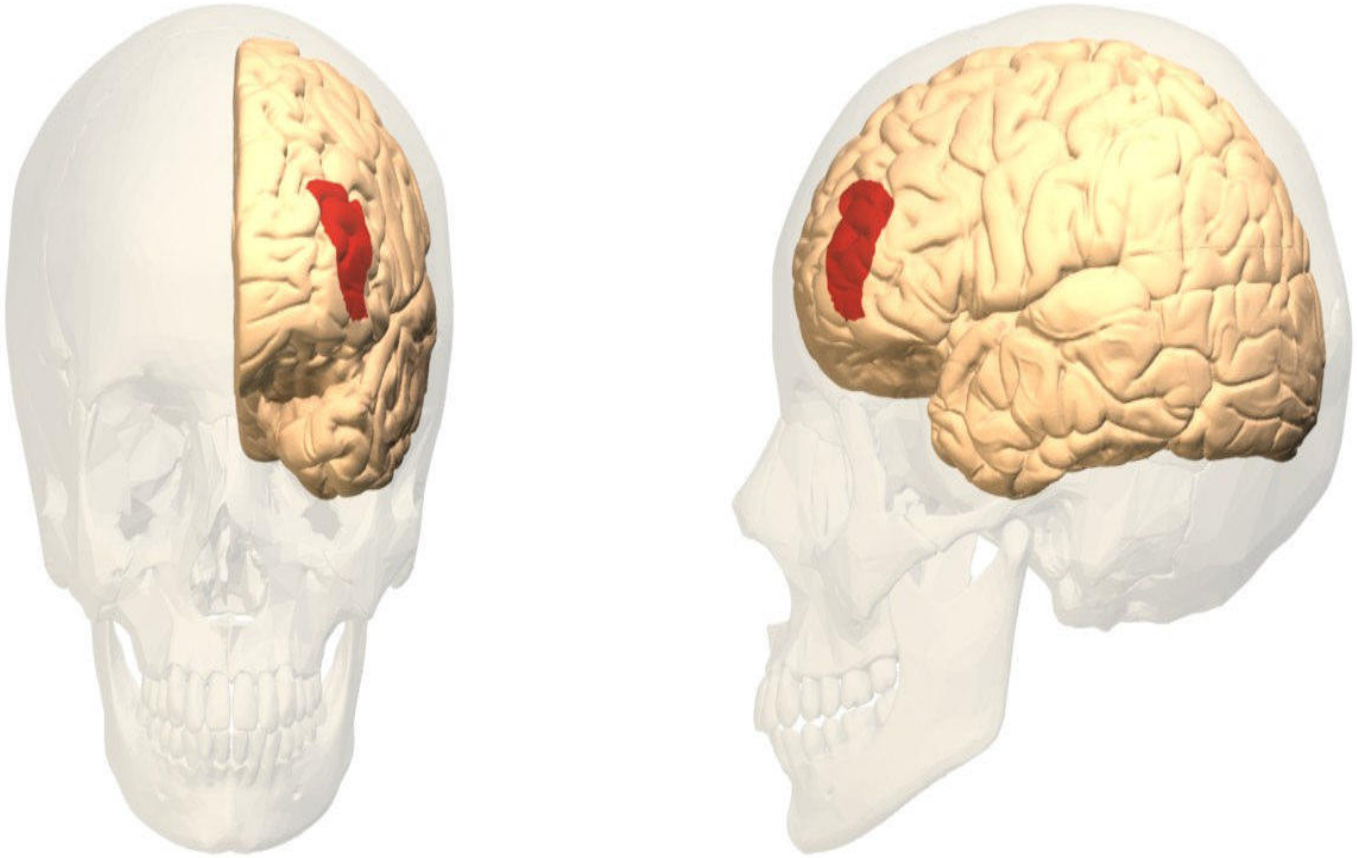


Antonello Bonci, 2009/2013

TRATTAMENTO DEL RATTO DIPENDENTE DA COCAINA CON OPTOGENETICA



DLPFC – Corteccia Prefrontale Dorso-Laterale



Brain Stimulation 11 (2018) 1195–1197

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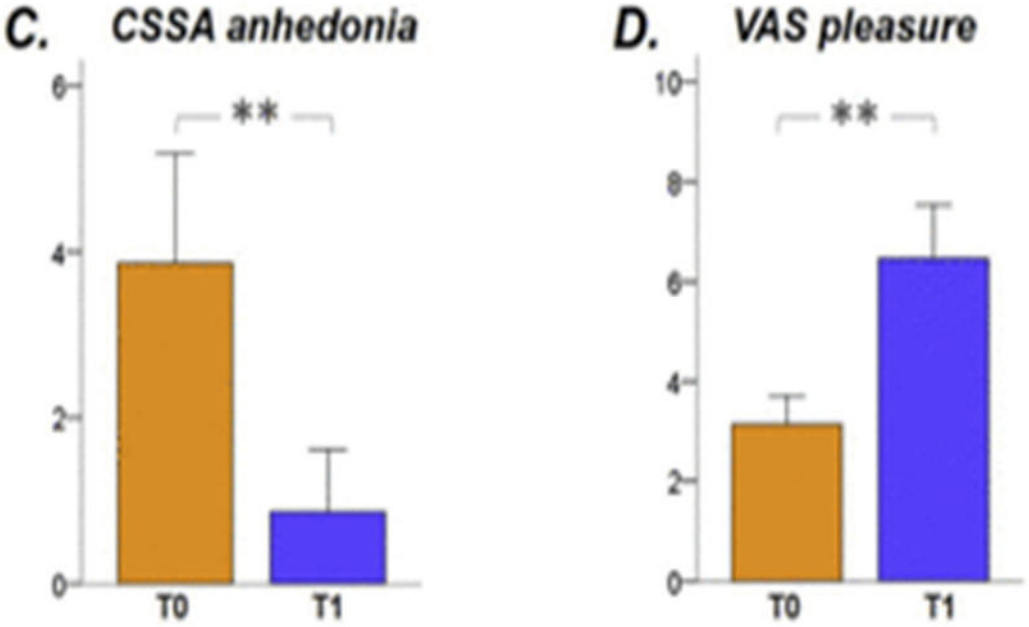
Repetitive transcranial magnetic stimulation of the left dorsolateral prefrontal cortex may improve symptoms of anhedonia in individuals with cocaine use disorder: A pilot study

Pettorruso M[1], Spagnolo PA[2], Leggio L[3], Janiri L[4], Di Giannantonio M[5], Gallimberti L[6], Bonci A[7], Martinotti G[8].

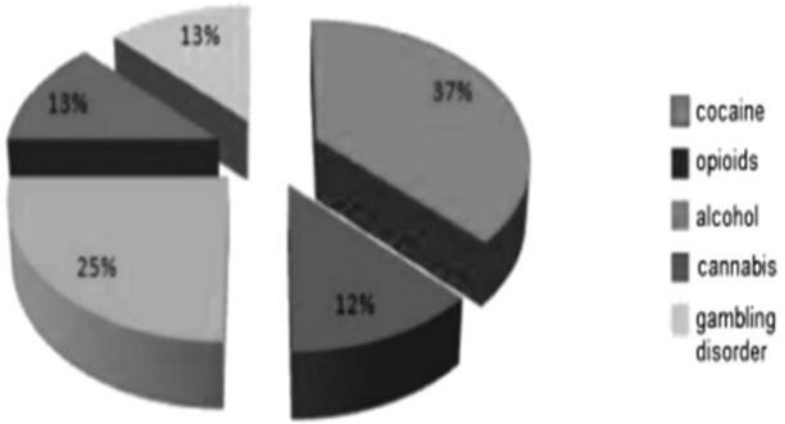


tDCS IN SUBSTANCES USE DISODERS

Transcranial Direct Current Stimulation Reduces Craving in Substance Use Disorders

A Double-blind, Placebo-Controlled Study

Giovanni Martinotti, MD, PhD,†‡ Matteo Lupi, MD,* Chiara Montemitro, MD,* Andrea Miuli, MD,* Chiara Di Natale, MD,* Maria Chiara Spano, MD,* Valerio Mancini, MD,* Marco Lorusso, MD,* Gianfranco Stigliano, MD,* Antonio Tambelli, MD,* Francesco Di Carlo, MD,* Lucia Di Caprio, MD,* Silvia Fraticelli, PsyD,* Eleonora Chillemi, PsyD,‡ Mauro Pettorruso, MD,* Gianna Sepede, MD, PhD,* and Massimo di Giannantonio, MD, PhD**



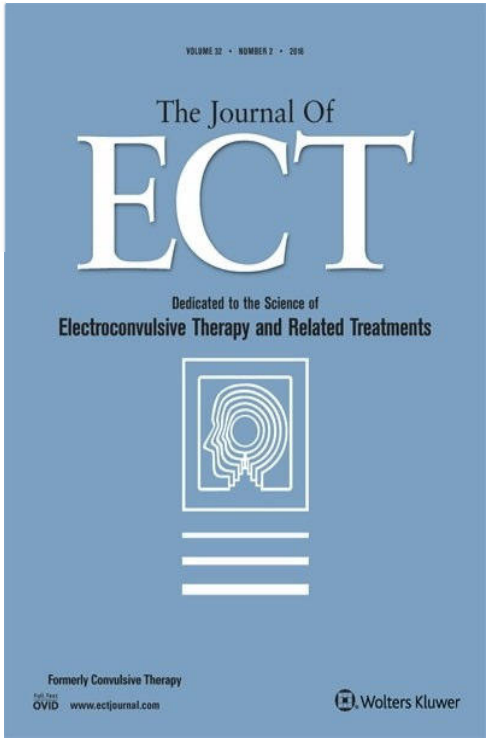


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TABLE 2. Psychometric Measures and Substance Consumption at Baseline (T0) and After Treatment (T1)

	DLPFC		Sham		Analysis of Variance		
Measures	T0	T1	T0	T1	Group	Time	Time × Group
HAM-D, mean (SD)	14.8 (7.8)	7.6 (5.1)	12.4 (8.2)	9.1 (7.4)	$P = 0.862$	T1 < T0, $P < 0.001$	$P = 0.063$
HAM-A, mean (SD)	13.3 (8.6)	7.1 (5.8)	9.9 (7.0)	7.8 (6.2)	$P = 0.565$	T1 < T0, $P < 0.001$	$P = 0.053$
Y-MRS, mean (SD)	3.7 (3.5)	3.1 (3.0)	3.3 (2.9)	2.1 (2.7)	$P = 0.499$	$P = 0.130$	$P = 0.640$
BIS-11, mean (SD)	67.2 (11.8)	63.7 (13.7)	70.8 (10.1)	62.2 (20.0)	$P = 0.805$	T1 < T0, $P = 0.032$	$P = 0.350$
Substance consumption, mean (SD)	4.9 (1.6)	2.2 (2.6)	3.9 (2.1)	1.8 (2.4)	$P = 0.270$	T1 < T0, $P < 0.001$	$P = 0.437$
VAS craving, mean (SD)	6.9 (2.6)	3.2 (2.3)	5.2 (2.4)	4.0 (3.1)	$P = 0.646$	T1 < T0, $P < 0.001$	DLPC: T1 < T0 $P = 0.011$

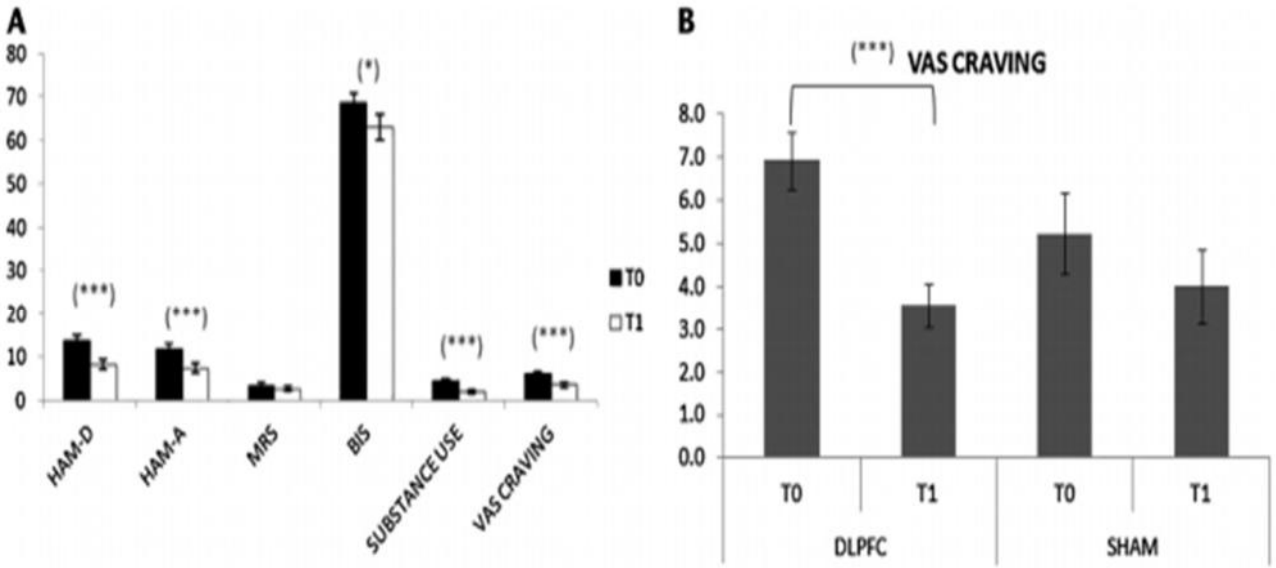
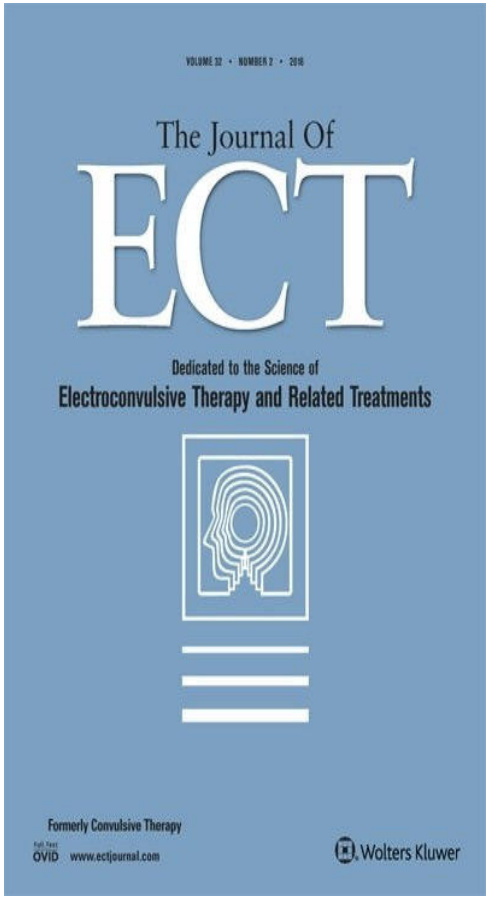


FIGURE 2. A, Time effect for the psychometric variables. Vertical bars denote SEs. Duncan post hoc test results: ***$P < 0.001$; *$P < 0.05$. B, Group × time significant interaction for VAS craving. Vertical bars denote SEs. Duncan post hoc test results: ***$P < 0.001$.



CONCLUSIONI

L’anedonia è un sintomo molto comune nei disturbi da uso di sostanze, non riguarda solamente la capacità di provare piacere ma anche il deficit nella capacità di desiderare: è necessario un rigoroso approccio psicopatologico per valutare l’anedonia nei pazienti psichiatrici

Nei disturbi da uso di sostanza la dimensione anedonica è strettamente legata al craving e alla ricerca del piacere. Senza il trattamento della dimensione anedonica non si tratta il disturbo

Gli SSRI, sebbene efficaci nel trattamento dei sintomi depressivi, non riducono l’anedonia. Altre molecole, come Vortioxetina, Trazodone, Bupropione, L-Acetylcarnetina, Brexpiprazolo, Aripiprazolo, Quetiapina potrebbero svolgere un ruolo importante nella gestione dell’anedonia, come anche le tecniche di Brain Stimulation

Grazie per l’attenzione,

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