# Bupropion and dual pathology

Carlos Roncero[1, 2]
Cristina López-Ortiz[3]
Facund Fora[4]
Verónica Gálvez-Ortiz[5]
Narcís Cardoner-Álvarez[5]
Jose M. Crespo-Blanco[5]
Victor Navarro-Odriozola[6]
Gemma García-Parés[7]
Josefina Pérez-Blanco[8]
Manel Sánchez-Pérez[9]
Grupo EUCB

[1]Servicio de Psiquiatría-CAS Vall d'Hebron
Hospital Universitario Vall d'Hebron
Agencia de Salud Pública de Barcelona (ASPB)
[2]Departamento de Psiquiatría
Universidad Autónoma de Barcelona
[3]Servicio de Psiquiatría del Parc Sanitari Sant Joan de Déu
Sant Boi Llobregat (Barcelona)
[4]Psiquiatra
Centro Médico Teknon
[5]Servicio de Psiquiatría
Hospital Universitari de Bellvitge-IDIBELL
CIBERSAM
[6]Programa Clínico Depresión
Servicio de Psiquiatría
Instituto Clínico de Neurociencias
Hospital Clínic de Barcelona
[7]Programa Clínico Depresión
Servicio de Psiquiatría
[8]Instituto Clínico de Neurociencias
Hospital Clínic de Barcelona
[9]Unitat de Psiquiatria Geriàtrica
Sagrat Cor, Serveis de Salut Mental
Martorell. Barcelona

## INTRODUCTION

Dual pathology is defined as the coexistence of an addiction in persons suffering another mental disorder.[1] The course, prognosis and treatment of patients are different from those who do not have dual pathology.[2] It is known that smoking determines worse prognosis and greater clinical severity of bipolar disorder (BD), schizophrenia and schizoaffective disorder (SAD).[3]

It has been described that patients with mental disorders smoke more and spend more on this habit than the general population and have a greater frequency of associated medical conditions.[4] In patients with schizophrenia and SAD, nicotine dependence has been related with a higher rate of suicide attempts and with alcohol and cannabis consumption.[3] Treatments effective in the general population are also effective in patients with psychiatric disorders and little attention has been given to this population.[4] Bupropion is a norepinephrine-dopamine reuptake inhibitor and is one of the treatments used most for smoking cessation and as an antidepressant drug.[5] However, few specific works exist on the use of bupropion in patients with dual pathology, even though it has been used as a drug for smoking cessation, in patients with dual diagnosis of affective and psychotic disorders. Furthermore, there are signs about the use of bupropion in the treatment of addiction in patients with cocaine dependence who are receiving maintenance treatment with methadone[6] or even in patients affected by an attention deficit hyperactivity disorder (ADHD) or dual ADHD.[5]

## TREATMENT WITH BUPROPION OF DEPRESSED PATIENTS WITH DUAL PATHOLOGY

Bupropion can be used in the treatment of depressive patients with dual pathology, aiming to obtain the antidepressant effect or to facilitate smoking cessation, since its efficacy as smoking cessation treatment is independent of its antidepressant action.[8]

It is known that drug abuse in depressed patients is associated to greater suicidal risk and attempts, earlier onset of depression, more anxiety disorders and functioning alterations.[9] However, treatment of patients with dual pathology has been studied little and the results of its efficacy have not always been consistent.[10] In relationship to smoking cessation treatment, in spite of the strong association between smoking and depression, the studies on smoking cessation usually exclude depressed patient[11] or this population has been studied little.[4] Of these specific works, it is known that patients with backgrounds of major depressive disorders benefit the same as the general population from psychotherapy and pharmacological treatments for smoking cessation.[4] However, drug usage can modulate the efficacy of these treatments. The risk of failure or relapse in alcohol-dependent patients who quit smoking has been related with the severity and type of alcohol consumption. Specifically, patients with elevated or very frequent alcohol consumption have more relapses.[12] Thus, the existence of dual pathology should be taken into account when initiating the treatment.

[*] *Francisca Almansa, Carmen Barral, Milagrosa Blanca, Nagore Benito, Joan Cadevall, Horacio Casté, Nuria Custal, Anna Falcés, Eva Fontova, Juan Manuel Goicolea, Georgina González, Paul Ernesto González, Ana Herrero, Rafael Martín, Leticia Medeiros, Javier Merino, Laura Mora, Josep Mª Otín, Adolfo Pellejero, Rosa Pi, Cristina Pinet, Dolors Robles, Alejandro Rodriguez, Ferran Romaguera, Carme Romero, Carme Sarri, Joan Seguí, Sara Solé, Carmen Sotelo, Josep Tort, Marc Valentí.*

Correspondence:
Narcís Cardoner Alvarez
Servicio de Psiquiatria
Hospital Universitari de Bellvitge-IDIBELL, CIBERSAM
Feixa Llarga s/n
08907
Correo electrónico: ncardoner@bellvitgehospital.cat

Scientific evidence indicates that treatment with bupropion in addicts who also smoke is effective, regardless of whether there is associated depression.[10] When the use of bupropion combined with nicotine patches in patients who receive cognitive behavioral therapy has been studied, it has been demonstrated that abstinence and the depressive symptoms improve in patients who smoke and who have current or have had past unipolar major depression.[11] The type of association of treatments in patients who smoke and are depressed is not clear since, although bupropion has advantages in regards to smoking cessation, a ceiling effect due to the interventions received has been detected in those who remained in the study.[11]

In the patient with behavior disorder, this drug has been used successfully used in the treatment of the depressive phases of the disease and is considered to be first-line treatment, as the selective serotonin reuptake inhibitors (SSRI).[13] Up to date, there are no specific studies with bupropion in patients with dual bipolar disorder, although the increased risk of mania induced by antidepressants is known in bipolar patients with a past history of drug abuse.[14]

## TREATMENT OF DUAL PSYCHOTICS

There are clinical experiences with limited cohorts of schizophrenic patients treated with antipsychotics in which bupropion was used as an antidepressant. In these studies, improvement of the depressive symptoms with good tolerability was described.[15] On the other hand, there is little experience with the treatment of depressive symptoms in dual schizophrenics. Fundamentally, bupropion has been used in the treatment of nicotine dependence in psychotic patients in addition to nicotine patches or gum. In these patients, treatment with bupropion has provided positive efficacy results, good tolerability and even a significant reduction in the negative symptoms characteristic of the evolution of the disease,[3, 16] so that its use has been recommended.[17, 16] Most of the studies conducted in patients with schizophrenia and SAD have not detected psychotic decompensation in relationship with this drug,[18] except for some isolated case.[19] Bupropion reduces tobacco consumption and improves the negative symptoms, without destabilizing the psychotic and depressive symptoms although its long-term benefit is modest.[20] In subsequent works, positive results have been described in psychotic patients when bupropion was administered in combined treatment. In a clinical trial was 58 schizophrenic patients under treatment with bupropion together with nicotine patches,[21] it was demonstrated that this condition was well tolerated and that the results were better than when only nicotine patches were used. Meta-analysis reviews of 7 clinical trials in which patients with schizophrenia were included reported that the use of bupropion is superior to placebo in smoking cessation, the results being maintained at 6 months.[22-23] With the known data, it can be stated that bupropion can be used as a drug that facilitates cessation in dual schizophrenics. [2]

The use of bupropion in patients suffering from SAD should be evaluated with caution due to the possibility of precipitating a manic episode. In general, all patients affected by psychosis treated with bupropion require periodic psychopathological evaluation and regular medical control due to the risk of seizures because of its effect on the decrease of the seizure threshold.[20]

## OPINION OF THE EXPERTS OF THE WORK GROUP

Knowledge on the indications, use and management of bupropion in patients with dual condition are partial.

There is clinical experience and increasingly greater evidence obtained in clinical trials performed in patients with depression or schizophrenia that point to its utility, both as an antidepressant as well as a smoking cessation drug.

Bupropion is well tolerated when combined with other psychopharmaceuticals.

This drug should be used with precaution in patients with risk of appearance of manic pictures.

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