

# Depersonalisation-derealisation syndrome induced by reboxetine

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## Summary

A high variety of factors have been implicated in the emergence of depersonalisation and derealisation episodes, including different drugs. A case abruptly induced by two applications of reboxetine, a selective and specific norepinephrine reuptake inhibitor, is reported occurring in a 50-year-old woman treated for a major depressive episode. The episode rapidly remitted after discontinuation

of reboxetine. Previous data having indicated a role of the serotonin system in the pathophysiology of the phenomenon, a noradrenaline induced serotonin liberation of Raphe neurons is suggested as possible underlying mechanism.

*Key words: reboxetine; derealisation; depersonalisation; antidepressant drug; noradrenaline; serotonin*

## Introduction

Depersonalisation is a state characterised by experiences of feeling detached from one's mental processes or body while reality testing remains intact [1]. Sensory anaesthesia or the sensation of not being in complete control of one's actions may occur, the phenomenon being egodystonic and non-delusional, and frequently lacking accompanying emotions. The phenomenon is frequently accompanied by derealisation, which is evidenced by an altered perception of reality of the external world. A wide variety of factors have been implicated in the emergence of depersonalisation

episodes, such as: lack of sleep, sensory deprivation, stress, meditative techniques, acute ingestion of hallucinogens, as well as different psychiatric and organic disorders [2]. Drugs that have been reported to potentially cause depersonalisation syndromes include meta-chlorophenylpiperazine [2], quetiapine [3], and fluoxetine [4]. We report what is, to our knowledge, the first case of depersonalisation-derealisation syndrome induced by reboxetine, a selective and specific norepinephrine reuptake inhibitor.

## Case report

Ms A, a 50 year-old woman treated for a first major depressive episode had not responded to a 3-month citalopram 60 mg/d treatment. In order to combine serotonergic and noradrenergic mechanisms, reboxetine 4 mg/d was added to the citalopram treatment. After about 24 hours, ie, after the second application of reboxetine, the patient experienced an abrupt but persisting feeling of unreality, complaining of an increased feeling of detachment from surroundings, as though she were taking part in a movie or a dream. She also described feeling as if she were observing herself from the outside. She said: "I seem to be living in a world, which I recognise but don't feel. I feel as though I'm not alive, everything feels unreal". Her level of depression was unchanged and she had not developed

suicidal ideas or psychotic or obsessive thoughts. Whereas she recognised these sensations as unreal, she found them extremely distressing, reporting severe related anxiety. Previous similar experiences and medical conditions such as febrile illness or viral infection that could have explained her symptoms were excluded. Furthermore, she had never previously experienced any type of dissociative disorder, and there were no other possible predisposing factors for dissociation such as traumatic experiences. Reboxetine was stopped after 2 days and the syndrome significantly improved within 24 hours, remitting gradually within 5 days. A switch to venlafaxine up to 300 mg made 3 months later did not lead to new depersonalisation-derealisation symptoms.

## Discussion

Little is known about the neurobiology of depersonalisation symptoms or depersonalisation disorder. Whereas some previous data indicate a role of the serotonin system [5], alteration of the noradrenaline system has received little attention.

Different mechanisms may account for the observed reboxetine-associated depersonalisation-derealisation syndrome. The serotonin liberation of Raphe neurons is modulated by noradrenaline [6]. A reboxetine-associated autonomic response, such as decreased vagal tone [7], may furthermore have contributed to the syndrome as well as the modulation of brain neural activity previously associated with these phenomena [1].

The role of citalopram as a contributing factor has to be questioned. There are, to our knowledge, no reports of depersonalisation induced by any SSRI. This drug class has by contrast repeatedly been proposed as an efficacious treatment for this

phenomenon [2]. A pharmacokinetic interaction that could have contributed to the reaction also seems very unlikely. Whereas several cytochrome enzymes (CYP2D6, CYP2C19, CYP3A4) are implicated in the metabolism of citalopram, this antidepressant is not associated with clinically significant inhibition of these enzymes [8]. On the other hand, reboxetine is characterised by the absence of inhibitory properties towards the major CYP isoforms [9].

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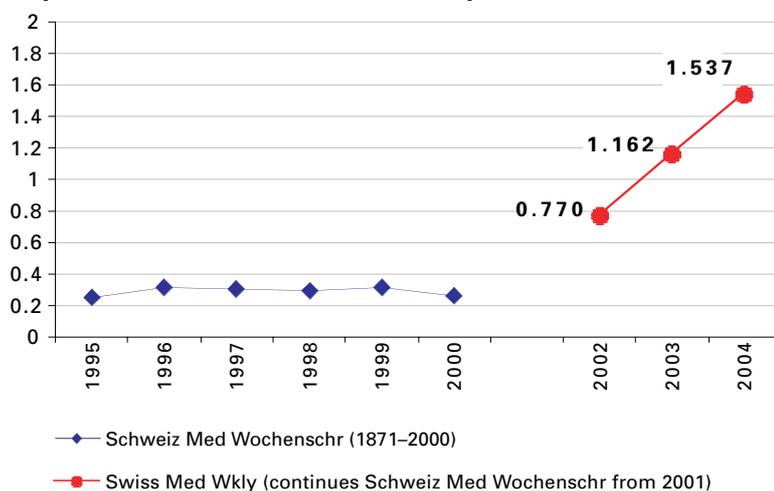
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