

**VI Seminario Nazionale per Dottorandi in Farmacologia e Scienze Affini
Siena, Certosa di Pontignano, 23 - 26 Settembre 2002**

REBOXETINE ANTAGONIZES THE AVOIDANCE DEFICIT PRODUCED BY ACUTE OR CHRONIC EXPOSURE TO UNAVOIDABLE STRESS IN RATS

Leggio B., 2° anno di corso del Dottorato in Medicina Molecolare, XVI ciclo. Durata del Dottorato in anni: 3. Sede di servizio: Dipartimento di Neuroscienze, Sezione di Farmacologia, Università di Siena, Via A. Moro,4 – Siena.

Reboxetine (Rbx), a noradrenaline selective reuptake inhibitor, is a clinically efficacious antidepressant. We investigated whether Rbx would counteract the effects of unavoidable stress exposure in the following behavioral paradigms previously validated with classical antidepressants: acute Escape Deficit (ED) is a stress-induced transient hyporeactivity; chronic ED is a paradigm of chronic hyporeactivity; stress-disrupted Vanilla sugar sustained Appetitive Behavior (VAB) is a model of anhedonia. Acute Rbx had a protective activity on the development of acute ED; this activity was retained and enhanced when the treatment was continued for 21 days. Rbx effect was selectively antagonized by the acute administration of the beta-adrenergic antagonist propranolol. A 21 days Rbx treatment did not modify pain threshold nor did it increase locomotor activity. In rats exposed to chronic stress, a 21 days Rbx treatment restored the avoidance response. Dopamine (DA) output was determined in the nucleus accumbens shell (NAcS) of Rbx and saline treated rats, exposed or not to a chronic stress protocol. Chronically stressed rats showed a reduced DA output in the NAcS; long-term Rbx administration reinstated DA output to control values. Control rats easily learn VAB, while stressed rats do not. Antidepressant treatment during chronic stress exposure counteracts the disruptive effect of stress on VAB acquisition. Rats treated with Rbx during stress exposure did not acquire VAB, and at the end of the training phase they showed a DA output in the NAcS similar to that of stressed rats. Rats are very fond of vanilla sugar and they consume it even when fed ad libitum. Rats administered Rbx, either acutely or repeatedly, when presented with vanilla sugar pellets refused to eat them. All efforts were made to minimize the number of rats and their suffering, in accordance to the directive of the European Communities Council (86/609/EEC).

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