to be a destabilizing force, which may create segregation of free-flowing constituents, eg. due to differences in particle density.

(c) In the sensitive field of nomenclature of powder mixtures, new terms should be introduced only after careful evaluation of their actual relevance. In the past, the inconsistent use of "ordered" has caused confusion and resulted in much discussion in the literature, this has been summarized elsewhere (Egermann 1985). Hence, the authors confirm interactive and non-interactive as standard nomenclature. These terms have been increasingly accepted by the scientific community, including Thiel (1984), Soebagyo & Stewart et al (1985), Sallam et al (1986), and Schmidt & Ben (1987). In contrast, adhesive and non-adhesive mix could not be traced in the papers cited by Staniforth (Drahun & Bridgwater 1983; Thiel 1984; Soebagyo & Stewart 1985). Rather, two of them (Thiel 1984; Soebagyo & Stewart 1985) even used interactive mixture in their titles. It must be regarded as a retrograde step to change terminology which is becoming increasingly widely accepted as scientifically accurate.

Another term of questionable relevance is total mix (Staniforth 1981, 1987). Obviously, total mix may be applied synonymously to powder mix. The traditional term powder mix, however, appears to be more informative and clearer. In contrast to total mix it does not provoke uncertainties about its actual meaning.

In conclusion, we do not see that the nomenclature proposed by Staniforth is an advance in the unambiguous description of powder mixes. More accurate alternatives are already in common use. The recent past has demonstrated that imprecise terminology may present a serious source of errors. From the misleading use of 'ordered', many workers implied interactive mixes to feature a higher degree of homogeneity than that exhibited by the non-interactive random mix. In fact, plain evidence of ordered mixes still is not available and from the present state of knowledge it appears questionable if it ever will become established (Egermann 1989).

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Chronic but not acute antidepressant treatment increases pentetrazol-induced convulsions in mice

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The neurochemical basis of depression and the biochemical mechanisms of action of antidepressants are matters of intense research, especially the hypothesis linking GABA function with depression and with antidepressant effects has recently received attention (Lloyd & Pichat 1986). Thus, GABA synthesis in the frontal cortex and its levels in CSF or plasma are low in depressed patients. Moreover, several reports have shown that some GABAergic agents have antidepressant-like activity both in animal models of depression (Borsini et al 1986a; Fernández Teruel et al 1988) and in depressive patients (for a review see Lloyd & Pichat 1986).

Accordingly, an involvement of $GABA_B$ receptors in the mechanisms of action of antidepressant treatments has been suggested by the finding that both the chronic treatment with antidepressant drugs and the electroshock administration induced $GABA_B$ receptor up-regulation in rat cortex (Lloyd & Pichat 1986). On the other hand, the chronic administration of several antidepressant agents (desipramine, zimelidine, bupropion, adinazolam and maprotiline) markedly decreased the binding of [^{3}H]flunitrazepam to the benzodiazepine binding sites on the $GABA_A$ receptor complex (Suranyi-Cadotte et al 1985; Barbaccia et al 1986). Additionally, the long-term imipramine (or nomifensine) treatment reduced the binding of [^{3}H]GABA to $GABA_A$ receptors in the mouse cerebral cortex and hippocampus (Suzdak & Gianutsos 1985).

In line with these results we have recently observed that the repeated administration of the antidepressant agent imipramine was able to reduce the GABA-stimulated $^{36}Cl^-$ influx in cerebral cortex synaptoneurosomes of rats (Fernández Teruel et al, in press). Furthermore, and agreeing with these results, the effects of imipramine in the behavioural 'despair' test in rats were potentiated by the concomitant administration of sub-convulsant doses of the $GABA_A$ antagonist picrotoxin (which reduces chloride channel functionality; Fernández Teruel et al submitted).

To further test the hypothesis on the interactions of antidepressant treatment and the GABA receptor-chloride ionophore complex, we investigated the effects of imipramine and desipramine on pentetrazol-induced convulsions in mice.

Male ICO-OF1 (IFFA-CREDO) mice (Autonomous Univer-

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sity of Barcelona), 28–39 g were housed in groups of 5–6 per cage, under a controlled light-dark schedule (light on between 0800 and 2000 h.) and at constant room temperature (22 ± 2°C) with free access to food and water.

Imipramine (10, 20 and 30 mg kg^{-1}) and desipramine (10 and 20 mg kg^{-1}; kindly provided by Ciba-Geigy), and pentetrazol (40 mg kg^{-1}; Sigma), were dissolved in 0·9% NaCl. Injections were given i.p. in a volume of 5 mL kg^{-1}.

Chronic experiment (Exp. 1). Animals received seven injections (twice daily, at 0900 and 1900 h.) of imipramine, desipramine or vehicle. One hour after the seventh injection (fourth day) of antidepressant, the mice were injected with pentetrazol or vehicle. The number of animals presenting anterior myoclonic and/or generalized myoclonic convulsions during the 30 min following the administration of pentetrazol (or vehicle) was recorded. Experimental groups were, PTZ (repeated vehicle + pentetrazol); IMI10, IMI20 and IMI30 (repeated imipramine 10, 20, 30 mg kg^{-1}, respectively + vehicle); IMI10 + PTZ, IMI20 + PTZ and IMI30 + PTZ (repeated imipramine 10, 20, 30 mg kg^{-1}, respectively + pentetrazol); DMI10, DMI20 (repeated desipramine 10 and 20 mg kg^{-1}, respectively + vehicle); DMI10 + PTZ, DMI20 + PTZ (repeated desipramine 10, 20 mg kg^{-1}, respectively + pentetrazol).

Acute experiment (Exp. 2): Animals received only one injection of imipramine (IMI, 30 mg kg^{-1}), desipramine (DMI, 20 mg kg^{-1}) or vehicle. One hour later the mice were injected with pentetrazol (PTZ, 40 mg kg^{-1}). Anterior myoclonic convulsions and generalised myoclonus were also recorded. Experimental groups were, PTZ, IMI30, IMI30 + PTZ, DMI20 and DMI20 + PTZ.

As shown in Table 1, chronic antidepressant pretreatment increased convulsant activity of pentetrazol. Thus, seven administrations of imipramine 30 mg kg^{-1}, or desipramine 20 mg kg^{-1} significantly increased the percentage of animals convulsing ($P < 0·02$, Fisher's exact test) compared with the PTZ group. This effect was dose-related, since lower doses of antidepressants were less effective in increasing convulsions. On the other hand no significant effect on convulsions was observed when antidepressants were acutely administered (Exp. 2).

Table 1. Effect of chronic and acute administration of imipramine (IMI) or desipramine (DMI) on the pentetrazol (PTZ)-induced convulsions in mice. The 'number of animals showing convulsions/number of animals studied' are represented. *$P = 0·07$ vs the respective PTZ group (Fisher's exact test). **$P < 0·02$ vs the respective PTZ group (Fisher's exact test).

	Number of animals showing convulsions	
Chronic experiment (Exp. 1)	Anterior myoclonic	Generalised myoclonus
PTZ	1/10 (10%)	1/10 (10%)
IMI10	0/5	0/5
IMI20	0/5	0/5
IMI30	0/5	0/5
DMI10	0/5	0/5
DMI20	0/5	0/5
IMI10 + PTZ	1/5 (20%)	1/5 (20%)
IMI20 + PTZ	3/5 (60%)*	3/5 (60%)*
IMI30 + PTZ	4/5 (80%)**	4/5 (80%)**
DMI10 + PTZ	0/5	0/5
DMI20 + PTZ	4/5 (80%)**	2/5 (40%)
Acute experiment (Exp. 2)		
PTZ	3/6 (50%)	2/6 (33·3%)
IMI30	0/6	0/6
DMI20	0/6	0/6
IMI30 + PTZ	4/6 (66·6%)	3/6 (50%)
DMI20 + PTZ	1/6 (16·6%)	0/6

Our present results show that repeated imipramine or desipramine treatment significantly increased the incidence of pentetrazol-induced convulsions in mice, whereas no significant effect was observed on convulsions when mice were acutely treated with the antidepressants before the administration of pentetrazol.

Since pentetrazol is a convulsant drug which decreases GABA function by acting at the $GABA_A$ receptor-chloride ionophore complex (inhibits [^{35}S]t-butylbicyclophosphorothionate binding; Ticku & Ramanjaneyulu 1984) the data are in line with the contention that chronic antidepressant treatment reduces GABAergic function (Borsini et al 1986b; Fernández Teruel et al, in press).

Although earlier experimental studies have shown that high doses of antidepressants are able to induce convulsions by themselves (Hughes & Radwan 1979) in rabbits, this was not the case in the present study.

To summarize, the proconvulsant activity of the two antidepressants tested is in agreement with previous reports (Trimble et al 1977), and the fact that this effect was observed only after chronic administration appears to be in line with recent findings showing that repeated antidepressant treatment reduces the GABA-stimulated chloride uptake in rats (Fernández-Teruel et al, in press).

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