EFFECTS PRODUCED BY SINGLE AND REPEATED DOSAGES OF FIPRONIL ON THE EEG OF LONG-EVANS RATS.

D F Lyke[1], K L McDaniel[1], V C Moser[1], and D W Herr[1].
[1]NB/TAD/NHEERL, ORD, US EPA, RTP, NC, USA.

We have previously reported that various classes of pesticides have different effects on the non-stimulus driven EEG after acute treatment, including fipronil (25 or 50 mg/kg) (Lyke *et al.*, *Toxicologist*, 2010, 2011, 2012, 2013). In this study, we compared the effects of single and repeated treatment with fipronil on the EEG. Fipronil is a member of the phenylpyrazole class of compounds that inhibits GABA receptors. Pilot studies indicated that 6 hours post dosing was the time of peak effect for neurological signs. Dosages for repeated treatments were chosen based on weight loss, regain, and neurological signs during pilot studies. Adult male Long-Evans rats were implanted with epidural screw electrodes. After about 1 week recovery, single exposure animals were dosed for 2 days with 1 ml/kg corn oil vehicle and then tested to allow acclimation to the procedures. On the third day, animals were dosed with corn oil, 5, or 10 mg/kg Fipronil and tested 6 h later. Animals in the repeated dosing group were dosed for 14 consecutive days with corn oil, 5, or 10 mg/kg/day Fipronil. Transient weight loss and occasional tremors were observed in the high dosage group, but these effects resolved after about 1 week. On days 12 and 13, animals had EEG recorded prior to dosing. On day 14, the rats were dosed 6 h prior to testing. Single treatment with these lower dosages did not significantly alter the EEG. However, repeated dosing with 5 or 10 mg/kg/day resulted in increases in the amplitude of the Delta (34 and 30% respectively) and Theta bands (41, 47%), and the area of the Theta band (30, 39%) compared to control. The area of the Gamma band was decreased at 5 (20%) and 10 mg/kg/day (22%) when recorded between the visual and frontal cortex, compared to control. The data confirm that fipronil alters CNS activity as measured by EEG. Additionally, dosages that were ineffective with a single treatment produced significant changes with repeated dosing. *This is an abstract of a proposed presentation and does not necessarily reflect EPA policy.*