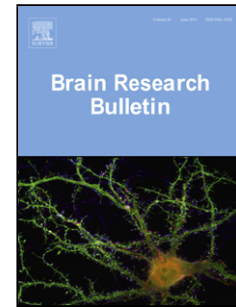


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## The contribution of contextual fear in the anxiolytic effect of chlordiazepoxide in the fear-potentiated startle test

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### Highlights

- Chlordiazepoxide reduces both contextual and cued conditioned fear in the absence of non-specific drug effect.
- The context-independent overall reduction in startle following treatment with zolpidem confirms its non-specific drug effects and lack of anxiolytic effect.
- Training and testing rats in different contexts makes it possible to distinguish between cued, contextual and non-specific drug effects.
- This approach using two contexts could be a valuable addition to the standard preclinical screening of anxiolytic compounds.

### Abstract

This study evaluated the extent to which a reduction in contextual fear contributes to the anxiolytic effect of benzodiazepines in the fear-potentiated startle response. To this end, chlordiazepoxide, an anxiolytic often used as positive control in preclinical drug studies, and zolpidem, known to have sedative properties and to be devoid of anxiolytic effects, were tested in two contexts: the same context as training had taken place and an alternative context. In addition, the level of muscle relaxation was assessed in a grip strength test. Chlordiazepoxide (2.5-10 mg/kg) decreased the fear-potentiated startle response, confirming its anxiolytic activity. In addition, it dose-dependently decreased the overall startle response in the same, but not the alternative context, and did not affect grip strength, indicating that chlordiazepoxide inhibits contextual fear in the absence of non-specific drug effects. Zolpidem (1.0-10 mg/kg) reduced the overall startle response in both contexts equally and decreased grip strength, indicating that its effects on fear-potentiated startle are due to non-specific drug effects, and not anxiolytic effects. The present findings show that chlordiazepoxide reduces contextual conditioned fear in the absence of non-specific drug effects. In addition, they show that training and testing rats in different contexts makes it possible to distinguish between cued, contextual and non-specific drug

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