Fear versus anxiety: sex, drugs and neural pathways

*De Jongh R**, Groenink L*, Van der Gugten J*, Olivier B*/**
*Dept of Psychopharmacology, Utrecht University, Utrecht, **Dept of Psychiatry, Yale University School of Medicine, New Haven, CT, USA

In the 'fear-potentiated startle paradigm' (FPS), the acoustic startle response is increased by presenting the startle-eliciting noise in the presence of a cue previously paired with footshock. More recently, it was shown that the startle response can also be increased by bright light (the so-called 'light-enhanced startle paradigm', or LES), an unconditioned anxiogenic stimulus in rats.
Although both paradigms are sensitive to a range of anxiolytic agents, they differ markedly in both their eliciting stimuli and the time course of the response. The specific threat stimulus and the rapid onset and offset of the response, suggest that the FPS models fear. In contrast, the potential threat (for a nocturnal animal in daylight, there is the potential risk of being attacked by a predator) and the slow onset and offset of the response suggest that the LES could model anxiety. Moreover, we have also shown that the potentiations of the startle response in the FPS and LES appear to be mediated by different brain regions.
Experiments have provided evidence for the predictive validity of the LES as an animal test for anxiety. Due to the use of an unconditioned anxiogenic stimulus (light), the LES offers several benefits over animal models that depend on conditioning. Drug effects can be ascribed more directly to effects on anxiety, as opposed to memory retrieval and non-specific drug effects can easily be detected, without the interference of contextual fear.
Observed sex differences in terms of startle potentiation effects add to the validity of both the FPS and LES as animal paradigms of fear and anxiety. These findings indicate that the paradigms can also be used to study the biological basis of sex differences in fear and anxiety.

Reinoud de Jongh, Department of Psychopharmacology, Utrecht University, Sorbonnelaan 16, 3584 CA Utrecht, t 030-2537382, e-mail reindejongh@yahoo.com

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