

# Anxiety Disorders



- Anxiety disorders affect 19 million US citizens annually
- Current therapies (e.g. benzodiazepines, buspirone, SSRIs) have significant limitations
  - Side-effects including sedation, nausea, muscle relaxation, memory impairment
  - Development of tolerance, dependence and withdrawal symptoms
  - Slow onset of action for buspirone and SSRIs
- Need for an anxiolytic that has a rapid onset and does not cause sedation and memory impairment or induce dependence
- Registration trials require large numbers of patients due to placebo effects
- Potential for Experimental Medicine studies to select best compound(s) for late stage trials

# Fear Potentiated Startle



- In animals and humans sudden intense sensory stimuli elicit a cascade of involuntary responses, including a short-latency skeletal muscular response ('eyeblink startle response')
- Startle responses are enhanced when subjects anticipate an aversive event compared to periods when subjects are resting ('fear potentiation')
- Diazepam can suppress fear-potentiation of the eyeblink startle response in human volunteers
- Recently researchers in Oxford have assessed whether the SSRI citalopram (20 mg/day) and the selective noradrenaline reuptake inhibitor reboxetine (8 mg/day) for seven days can effect fear potentiated startle

# Emotion Potentiated Startle



Neutral

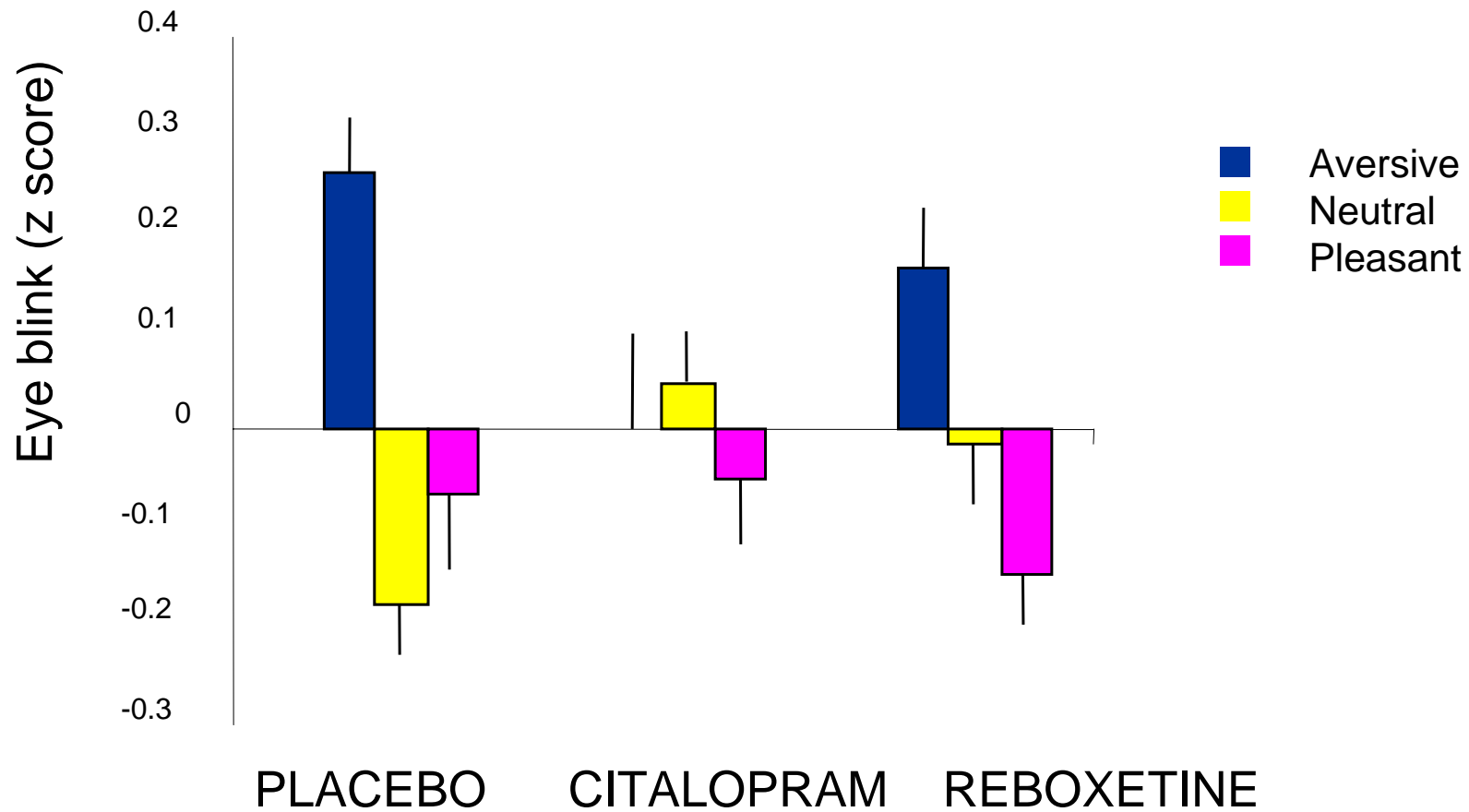


Pleasant



Aversive

Citalopram abolishes the increased startle response found in the context of negative affective images.



# Summary



- Two different types of antidepressant increased the relative processing of positive to negative information in healthy volunteers
- Citalopram appeared to have wider effects on the processing of threat related stimuli
- Direct actions on emotional processing provide another mechanism by which antidepressants may exert their therapeutic effects.

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