

A single dose of Fluoxetine modulates emotional processing in young healthy volunteers

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Background

- Depression in adolescents is frequent and associated with high levels of morbidity and recurrence
- However treatment is complex since serotonergic antidepressants (SSRIs), other than fluoxetine, are not recommended for adolescent depression
- Pre-clinical data suggests that SSRIs may have age dependent effects^[1]
- Cognitive neuropsychological studies in adults suggest early effects of antidepressants on emotional processing which are seen before therapeutic effects emerge^[2]
- The current study aimed to explore early effects of fluoxetine in young people on measures of emotional processing

Aim

- Investigate the early psychological mechanisms underlying fluoxetine action in young adults

Methods

- 39 young healthy volunteers (18-21 years) were randomised to receive a single oral dose of fluoxetine (20mg) or placebo
- 6-hours after administration, participants completed the **Facial Expression Recognition Task (FERT)** and the **Emotion Potentiated Startle (EPS)**
- The groups were matched for age, gender, verbal IQ and trait anxiety scores
- Self-rating scales measuring mood, anxiety, energy levels and side-effects were administered pre- and post-drug/placebo
- Statistical analyses conducted: mixed repeated measures ANOVA with emotion/picture valence and group as within and between subject factors. Significant interaction effects further explored using pairwise comparisons or separate repeated measures ANOVAs.

Results

Subjective mood ratings

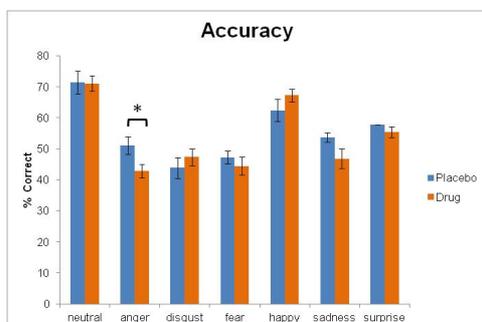
- There was no significant effect of acute fluoxetine on any of the subjective measures administered

Facial Expression Recognition Task (FERT)

- Participants are asked to identify different facial expressions (neutral, anger, disgust, fear, happy, sadness and surprise) presented at different intensities

Accuracy

Trend for an interaction between face emotion and group [F(6,222)=2.050, p=0.08], driven by a decreased accuracy in the recognition of angry faces in the fluoxetine group (*p<0.05)



Reaction Times

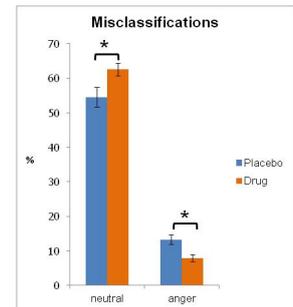
Significant interaction between face emotion and group [F(6,222)=2.707, p=0.027], with the fluoxetine group being slower to identify angry faces (*p<0.05)

Facial Expression Recognition Task (cont.)

Misclassifications

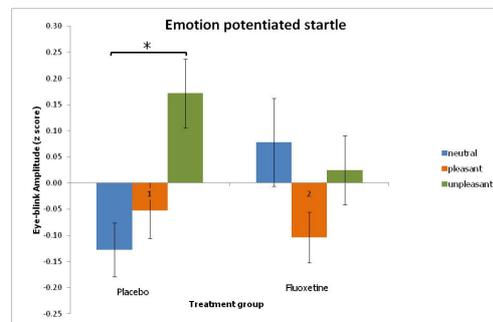
Significant face emotion x group interaction [F(2,666)=3.847, p=0.015]

Fluoxetine group misclassified more faces as being neutral and less as angry (*p<0.05)



Emotion potentiated startle (EPS)

- Neutral, pleasant and unpleasant stimuli are presented along with acoustic probes, and eye-blink amplitudes are recorded
- Human analogue of the fear potentiated startle used in animals to screen for anxiolytic/anxiogenic drug effects



Trend for significant interaction between picture valence and group [F(2,52) = 2.822, p = 0.065]

Separate repeated measures ANOVAs revealed an effect of picture valence in the placebo group (p=0.015), but not in the fluoxetine group (p=0.295)

Conclusions

- After **fluoxetine** treatment, participants were less accurate and slower to identify angry faces, showing a **decreased negative bias**
 - Irritability is a distinctive symptom of adolescent depression^[3]; however, there is a lack of studies exploring how this symptom affects emotional processing
 - A decrease in irritability and aggressive behaviour after acute or sub-chronic fluoxetine administration has been reported in both human and pre-clinical animal models^[4,5]
 - This specificity in targeting anger/irritability may help explain why fluoxetine is an effective SSRI for adolescent depression
- Fluoxetine abolished the normal emotion potentiated startle effect found in the placebo group, suggesting an **anxiolytic-like mechanism**
 - This is not consistent with clinical reports of increased anxiety seen early in treatment with fluoxetine; however, this anxiogenic effect may be mediated by other cognitive processes or be specific to depressed and younger populations
- Future studies are needed in order to fully characterise the psychological mechanisms underlying fluoxetine action, including the dissociation between anxiolytic vs. anxiogenic effects and their specific time course of action/reversal

References

- ^[1] Homberg JR et al (2011) *PLoS ONE* 6: e16646
^[2] Browning M et al (2007) *J Psychopharmacol* 1: 684-690
^[3] Crowe M et al (2006) *Int J Ment Health Nurs* 15: 10-8
^[4] Fava JM et al (2003) *Am J Psychiatry* 150: 1158-1163
^[5] Fuller RW (1996) *Neuropsychopharmacol* 14: 77-81.

This poster does not have a conflict of interest.