Quetiapine and Pramipexole differentially modulate emotion processing brain circuits – a pharmaco-fMRI study

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Background

The exact way how psychopharmacological agents modulate the neural circuits involved in emotion processing is only partially known. We aimed to identify emotion processing brain regions modulated by quetiapine (QP), a dopamine receptor antagonist (D1/D2, in addition 5-HT1A-receptor antagonistic effect), compared to pramipexole (PX), a dopamine D2 (and D3) receptor agonist. We used the anticipation and perception of emotional stimuli to activate emotion circuits.

Methods

• 22 healthy volunteers (11 male, mean age 26.1 +/- 6 y)
• single-blind randomized crossover pharmaco-fMRI study, single dose of QP (100 mg) vs. PX (0.5mg); 3T Philips Achieva Scanner
• Task (Fig. 1): used anticipation and perception of emotional pictures [1], either known emotional valence (positive (ps), negative (ng), neutral (nt)) or unknown valence (uk, 50% pairing).
• Analysis: repeated-measures ANOVA, main effect of treatment, interaction between task (emotional anticipation vs. nt; emotional perception vs. nt) and treatment (QP, PX), statistical threshold p < 0.005.

Results

Main effect of treatment:
• Anticipation: PX increased activity in right insula (ps, uk) and right inferior frontal gyrus (ng, uk).
• Perception: PX increased activity in left medial, inferior and middle frontal gyrus (ng, ps).

Interaction: opposite effects of PX and QP during anticipation of negative and unknown stimuli in right ventral striatum, left superior frontal and fusiform gyrus (fig. 2a), increased activation with PX in left midcingulate and precuneus during positive, but not negative perception (fig. 2b)

Discussion

The network involved in the processing of emotional information during the anticipation and perception of emotional pictures was modulated in opposite directions by the dopaminergic agonist PX and dopaminergic antagonism by QP. This could support the hypothesis of a specific dopaminergic modulating effect within this network. Interestingly, PX influenced networks during both the perception of positive pictures and the anticipation of negative stimuli, whereas QP rather dampened valence-specific activation in general. Until now, pharmaco-fMRI studies using PX have primarily focused on reward circuits, however with mixed findings (increased activation [2], decreased activation [3]). Further analyses and future studies will investigate the dopaminergic modulation of emotional networks.


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Background: The anticipation and perception of emotional stimuli is a model activating emotion processing circuits in depression and anxiety disorders. Until now, the exact way how psychopharmacological agents such as antidepressants modulate the neural circuits involved in emotion processing is only partially known. Besides serotonergic and noradrenergic pathways, dopaminergic mechanisms have come into the focus of antidepressant treatment [1]. This study aimed at identifying emotion processing brain regions modulated by quetiapine, which is a dopamine receptor antagonist (D1, D2), besides an antagonistic effect at the 5-HT1A-receptor, in comparison to pramipexole, which is an agonist at dopamine D2 (and D3) receptors.

Methods: We conducted a single-blind pseudo-randomized crossover pharmaco-fMRI study. Brain activation after ingestion of a single dose of quetiapine (100mg) is compared to a single dose of pramipexole (0.5mg) during the cued anticipation of emotional stimuli in 22 healthy participants. The emotional anticipation task comprised the cued anticipation and subsequent perception of emotional pictures of either ‘known’ emotional valence (positive, negative, neutral) or ‘unknown’ valence, that could have been positive or negative. The fMRI data were analysed with two repeated-measures ANOVA on the main effect of treatment and the interaction between the task condition (anticipation negative, unknown, positive versus neutral; perception negative and positive versus neutral) and the treatment condition (quetiapine, pramipexole). The statistical threshold was set at p<0.005 with a cluster extend threshold of 135mm3 (5 voxel à 3x3x3mm).

Results: Pramipexole increased activity in left posterior cingulate and precuneus compared to quetiapine during the perception of positive stimuli. During the perception of negative stimuli, there was no significant difference between the two pharmacological effects. The main effect of treatment showed increased activations due to pramipexole compared to quetiapine in right cerebellum and left prefrontal areas during the perception period.

During the anticipation of emotional stimuli, the two pharmacological agents differed most in the negative and the unknown condition: Pramipexole consistently increased activity in right putamen, left superior frontal gyrus and left fusiform gyrus compared to quetiapine during the anticipation of negative stimuli. Quetiapine, however, increased putamen activity during the anticipation of unknown cued, possibly negative stimuli. The main effect of treatment during the anticipation resulted in increased activations after pramipexole compared to quetiapine in right anterior insula and right inferior frontal gyrus.

Discussion: Networks involved in the processing of emotional information during the anticipation and perception of emotional pictures were modulated differently by D2 dopaminergic agonistic action by pramipexole and D1 and D2 dopaminergic antagonism by quetiapine. Interestingly, pramipexole influenced networks during the perception of positive pictures, but also during the anticipation of negative stimuli, whereas quetiapine rather seemed to dampen valence-specific activation in general. Until now, pharmaco-fMRI studies using pramipexole have primarily focused on reward circuits, however with mixed findings (increased activation [2], decreased activation [3]).

These findings could support differential clinical applications in affective disorders.


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