#3071 Acute escitalopram administration increases premature responding as a function of reward magnitude in healthy male volunteers

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Objectives

Impulsivity is a multifaceted construct that involves a tendency to act prematurely with little foresight, reflection or control. Waiting impulsivity is one aspect of action impulsivity and is commonly studied in animals using tasks such as the 5-choice serial reaction time task (5CSRTT) [1]. It is neurochemically distinct from motor response inhibition defined as the ability to restrain or cancel a pre-potent motor response and measured with no-go and stop-signal tasks respectively [1]. Serotonin modulates waiting impulsivity as decreased serotonergic transmission promotes premature responding in the rodent 5CSRT and the human analogue 4CSRT task [2]. Potential mechanisms contributing to waiting impulsivity include proactive or tonic inhibition, motivational processes and sensitivity to feedback and delay [3]. Higher waiting impulsivity in response to high reward cues was previously associated with greater subthalamic nucleus connectivity with orbitofrontal cortex and greater subgenual cingulate connectivity with anterior insula [4].

Methods

We administered a clinically relevant dose of escitalopram (20mg) in healthy subjects in a double-blind, placebo-controlled, parallel-groups design study and assessed its effect on waiting impulsivity using the well-validated 4CSRT task. Compared to previous studies [2,4], we added another test block with increased potential gain to assess the interaction between premature responding and reward processing. We recruited sixty-six healthy participants who completed an extensive neuropsychological test battery assessing probabilistic reversal learning, set-shifting, response inhibition, emotional processing and waiting impulsivity. Sixty participants (N=60, 26 females, 34 males) completed the 4CSRT task with N=30 in the escitalopram and N=30 in the placebo group, due to technical errors and experienced side-effects for the remaining six participants. The results of the other cognitive tasks are reported separately [5].

Results

Escitalopram increased premature responding in the high incentive condition of the 4CSRT task, $p= .028$, $t= 2.275$, this effect being driven by male participants, $p= .019$, $t=2.532$ (for females, $p> .05$). We further show that escitalopram increased premature responses after a premature response in the same block again in male participants only, $p=.034$, Mann-Whitney $U= 61.500$. We found no correlation between premature responding in the 4CSRT task, in any test block, and the Stop-signal reaction time, the

primary measure of the stop-signal task completed by the same participants (reported in [5]).

Conclusions

We show that acute escitalopram increased premature responding in healthy male participants only in high incentive conditions potentially mediated potentially through an effect on increased incentive salience. We also show that acute escitalopram increased perseverative responding thus producing a maladaptive response strategy. We show no correlation between SSRT and premature responding in the same participants consistent with these two forms of impulsivity being neurochemically and anatomically distinct. We interpret our findings in the context of acute escitalopram decreasing serotonergic transmission in some brain areas through inhibitory actions on terminal 5-HT release mediated by auto-receptors on raphe 5-HT neurons analogous to the presumed transient reduction in 5-HT activity caused by ATD [5].
Our findings provide further insights in the relationship of premature responding and reward processing and our understanding of pathological impulse control behaviours.

References

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