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DIFFERENCES IN THE MODULATORY ROLE OF ESCITALOPRAM AND CITALOPRAM REVEALED BY EFFECTIVE CONNECTIVITY ANALYSIS

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Introduction: Citalopram is a widely applied SSRI in patients suffering from affective disorder. It is a racemic mixture of the S- and R-enantiomer of citalopram, consisting of equal parts of S-citalopram and R-citalopram, respectively. It has been shown that the inhibitory potency in serotonin reuptake of S-citalopram is much higher compared to R-citalopram, and it is assumed that S-citalopram is the main carrier of the antidepressant effect.

Objectives: Here we investigated the effects of the two SSRIs Citalopram (50% S-, 50% R-citalopram) and Escitalopram (100% S-citalopram) on brain networks during emotion processing using pharmacological functional magnetic resonance imaging (fMRI) and dynamic causal modelling (DCM), an advanced tool to investigate functional integration between different brain regions.

Methods: Our results are based on a placebo-controlled, randomized, double-blind, cross-over pharmacological study in 16 healthy subjects during three fMRI scanning sessions performing a facial emotional discrimination paradigm (Windischberger, Neuroimage, 2010). 32 models of pharmacological modulation within the amygdalar-parahippocampal-orbitofrontal network were analysed using Bayesian Model Averaging (BMA) as implemented in SPM8.

Results: S-citalopram showed statistically significant modulatory effects on forward amygdala-orbitofrontal and bidirectional amygdala-parahippocampal connections. No significant modulatory effects of R-citalopram were found.

Conclusions: This is the first fMRI study that showed stimulus-specific differential effects of the two enantiomers R- and S-citalopram at the neural connectivity level. Our results corroborate studies in rats where escitalopram-induced increases in extracellular serotonin levels were found attenuated when R-citalopram was coinjected. Taken together this might explain the response differences between study drugs as demonstrated in previous clinical trials.