

P-800 - HOW DO ANTIDEPRESSANTS WORK? A POSITRON EMISSION TOMOGRAPHY (PET) STUDY OF BRAIN SEROTONIN LEVELS AND AFFECT REGULATION

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Background: Serotonin (5-HT) is thought to be critical for affect regulation in the brain and many antidepressants are thought to primarily work by altering 5-HT levels. However there has not been a validated means of directly imaging of endogenous 5-HT levels in humans. The main aims of this project are to image the effect of Citalopram on brain endogenous 5-HT levels and to determine the relationship between brain 5-HT and affect regulation.

Methods: Thirteen healthy volunteers (mean age 50.9yrs, range 35-63) underwent two Positron Emission Tomography (PET) scans with [¹¹C]-CUMI, a highly selective 5-HT_{1A} agonist radioligand. Subjects received either a slow intravenous infusion of citalopram 10mg or saline starting 45 minutes before each PET scan in a randomized design. All subjects had a functional MRI emotion processing task (block design) known to activate the amygdala on a separate day.

Results: The citalopram infusion induced 6-11% increases in [¹¹C]-CUMI binding potential in anterior cingulate, insula and cortical brain regions ($p < 0.05$ corrected for repeated measures).

BOLD response to fearful vs neutral faces in the left amygdala inversely correlated with baseline dorsal raphe BP (Pearson $r^2 = -0.90$, $p < 0.001$) and directly correlated with dorsal raphe BP changes ($r^2 = 0.51$, $p = 0.07$).

Conclusion: The increase in [¹¹C]CUMI-101 availability would be consistent with a decrease in endogenous 5-HT availability in certain terminal regions. The relationship between brain emotion processing and [¹¹C]-CUMI binding in the raphe indicates the 5-HT levels at presynaptic receptors regulate emotional processing and suggests presynaptic 5-HT as a treatment target for affective disorders.