

S33-01

NEUROBIOLOGY OF AFFECTIVE DISORDERS - INSIGHTS FROM PET IMAGING

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Recent brain imaging studies indicate subtle functional and also structural brain changes in affective disorders. We report specific neurotransmitter receptor findings in vivo in major depression testing directly the 'old' monoamine and also newer peptide neurotransmitter hypotheses of unipolar major depression.

Positron Emission tomography imaging demonstrates relatively consistently a widespread reduction of brain serotonin 5-HT-1A receptors in drug-free or never-treated patients with clinical depression. The reduction of 5-HT-1A receptors is not confined to frontal or temporal cortex but seem to be widespread including multiple brain regions. Our data shows that the 5-HT-1A receptor finding seems to be robust even in primary care patients with mild/moderate depression. Pilot findings in our laboratory suggest that this alteration can be 'normalized' with a psychotherapeutic intervention. Substance P NK1 receptors appear not to be altered in never-medicated MDD patients. However, HAM-D total scores correlated positively with NK1 receptor binding in neocortical as well as limbic brain areas suggesting a modulatory role for NK1 receptors in major depression.

Our results indicate specific neurotransmitter changes in clinical depression that could also represent therapeutic targets but the specificity of these findings e.g. in relation to anxiety disorders (or comorbid conditions) needs to be explored further.

References:

Hirvonen et al *Psychopharmacology* (Berl). 2008 May;197(4):581-90. , Hirvonen et al *Int J Neuropsychopharmacol*. 2008 Jun;11(4):465-76, Nyman et al NK1 receptors in never-medicated patients with major depression, submitted.