Article: 0022
Topic: S04 - Symposium 04: Serotonin: studies on reward, emotion, social cognition, and relevance to mood and anxiety disorders

The Effect of 5-HT2A/1a Agonist Treatment On Social Cognition, Empathy, and Social Decision-making

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Social cognition is a crucial factor influencing development, progress, and treatment of psychiatric disorders. However, social cognition skills are insufficiently targeted by current treatment approaches. In particular, patients suffering from depression show an increased negative reaction to social exclusion and deficits in empathy. The 5HT-1A/2A receptor agonist psilocybin has previously been shown to reduce the neural response to negative emotional stimuli. However, it is not known if this extends to negative social interaction and whether 5HT-1A/2A receptor stimulation induces changes in empathy. Given the clear need for improved treatment of socio-cognitive functioning in psychiatric disorders, it is important to better understand the neuronal and neuromodulatory substrates of social cognition.

In a double-blind, randomized, cross-over design we therefore investigated the neural response to ostracism after the acute administration of psilocybin (0.215mg/kg) and placebo in healthy volunteers using fMRI. Furthermore, we assessed cognitive and emotional empathy using the Multifaceted Empathy Test.

The neural response to social exclusion in the ACC – a brain region associated with 'social pain"- was reduced after psilocybin administration compared to placebo. Furthermore, emotional empathy was enhanced after treatment with psilocybin while no significant differences were found in cognitive empathy.

These results show that the 5HT-1A/2A receptor subtypes play an important role in the modulation of socio-cognitive functioning and therefore may be relevant for the treatment of social cognition deficits in psychiatric disorders. In particular, they may be important for the normalization of empathy deficits and increased negative reaction to social exclusion in depressed patients.