Frontolimbic serotonin 2A receptor binding in healthy subjects is associated with personality risk factors for affective disorder

**Background:** Serotonergic dysfunction has been associated with affective disorders. High trait neuroticism, as measured on personality inventories, is a risk factor for major depression. In this study we investigated whether neuroticism is associated with serotonin 2A receptor binding in brain regions of relevance for affective disorders.

**Methods:** Eighty-three healthy volunteers completed the standardized personality questionnaire NEO-PI-R (Revised NEO Personality Inventory) and underwent [F-18]altanserin positron emission tomography imaging for assessment of serotonin 2A receptor binding. The correlation between the neuroticism score and frontolimbic serotonin 2A receptor binding was evaluated by multiple linear regression analysis with adjustment for age and gender.

**Results:** Neuroticism correlated positively with frontolimbic serotonin 2A receptor binding \( r(79) = .24, p = .028 \). Post hoc analysis of the contributions from the six constituent traits of neuroticism showed that the correlation was primarily driven by two of them: vulnerability and anxiety. Indeed, vulnerability, defined as a person's difficulties in coping with stress, displayed the strongest positive correlation, which remained significant after correction for multiple comparisons \( r = .35, p = .009 \). Conclusions: In healthy subjects the personality dimension neuroticism and particularly its constituent trait, vulnerability, are positively associated with frontolimbic serotonin 2A binding. Our findings point to a neurobiological link between personality risk factors for affective disorder and the serotonergic transmitter system and identify the serotonin 2A receptor as a biomarker for vulnerability to affective disorder.