
There is a large body of evidence that the serotonergic system plays an important role in the transmission and regulation of pain. Here we used positron emission tomography (PET) with the serotonin transporter (SERT) tracer [11C]DASB to study the relationship between SERT binding in the brain and responses to noxious heat stimulation in a group of 21 young healthy volunteers. Responses to noxious heat stimuli were assessed in a separate psychophysical experiment and included measurements of pain threshold, pain tolerance, and responses to phasic noxious heat stimuli and to a long-lasting (7-minute) tonic noxious heat stimulus. PET data were analyzed using both volume-of-interest (VOI) and voxel-based approaches. VOI analysis revealed a significant negative correlation between tonic pain ratings and SERT binding in the hypothalamus ($r = -0.59; p = 0.008$), a finding confirmed by the parametric analysis. The parametric analysis also revealed a negative correlation between tonic pain ratings and SERT binding in the right anterior insula. Measures of regional SERT binding did not correlate with pain threshold or with responses to short phasic suprathreshold phasic heat stimuli. Finally, the VOI analysis revealed a positive correlation between pain tolerance and SERT binding in the hypothalamus ($r = 0.53; p = 0.02$) although this was not seen in the parametric analysis. These data extend our earlier observation that cortical 5-HT receptors co-determine responses to tonic but not to phasic pain. The negative correlation between SERT binding in the hypothalamus and insula with tonic pain ratings suggests a possible serotonergic control of the role of these areas in the modulation or in the affective appreciation of pain.