Abstract: CONTEXT: Chronic pain and depression are highly comorbid conditions, yet little is known about the neurobiological basis of pain processing in major depressive disorder (MDD). OBJECTIVE: To examine the neural substrates underlying anticipation and processing of heat pain in a group of unmedicated young adults with current MDD. DESIGN: Functional magnetic resonance neuroimaging data were collected during an event-related factorial experimental pain paradigm. Painful and nonpainful heat stimuli were applied to the left volar forearm while different color shapes explicitly signaled the intensity of the upcoming stimulus. SETTING: University brain imaging center. Patients Fifteen (12 female) young adults with current MDD and 15 (10 female) healthy subjects with no history of MDD were recruited and matched for age and level of education. The Structured Clinical Interview for DSM-IV was administered to all participants by a board-certified psychiatrist. Main Outcome Measure Between-group differences in blood oxygen level-dependent functional magnetic resonance neuroimaging signal change to anticipation and processing of painful vs nonpainful temperature stimuli. RESULTS: Subjects with MDD compared with healthy controls showed (1) increased activation in the right anterior insular region, dorsal anterior cingulate, and right amygdala during anticipation of painful relative to nonpainful stimuli, (2) increased activation in the right amygdala and decreased activation in periaqueductal gray matter and the rostral anterior cingulate and prefrontal cortices during painful stimulation relative to nonpainful stimulation, and (3) greater activation in the right amygdala during anticipation of pain, which was associated with greater levels of perceived helplessness. CONCLUSIONS: These findings suggest that increased emotional reactivity during the anticipation of heat pain may lead to an impaired ability to modulate pain experience in MDD. Future studies should examine the degree to which altered functional brain response during anticipatory processing affects the ability to modulate negative affective states in MDD, which is a core characteristic of this disorder.

Strengths:
- Interesting study and design.
- Utilizes fMRI to determine brain related changes corresponding to anticipated and painful stimuli in patients with and without Major Depressive Disorder.
• Associates the same with behavioral features associated with Major Depressive Disorder such as perceived helplessness.

Weaknesses:
• Small sample size.
• Unable to generalize results to different populations with other comorbidities.

Relevance to Palliative Care: Major Depressive Disorder, and other psychological based illness, are not uncommon in patients with advanced illness. This paper contributes to the scientific understanding of the multidimensional aspect of pain expression in patients with and without major depressive disorder.