P06.06

Changes in regional cerebral blood flow in response to acute vagus nerve stimulation in depressed patients and association with clinical response

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Background: Stimulation of the vagus nerve (VNS) via implanted electronic device has anticonvulsant efficacy. In epilepsy studies VNS increased brain activation in some regions (medulla, thalamus, and postcentral gyrus) and decreased it in others (amygdala). Using positron emission tomography (PET), this study examined changes in regional cerebral blood flow (rCBF) with acute VNS in depressed patients and the relation to clinical response to VNS.

Methods: Using labeled 15O2 water PET, four brains were scanned four times in succession, twice during a burst of VNS and twice at rest. Patients then received chronic VNS therapy for 6 months, with Hamilton Rating Scale for Depression (HAM-D) at baseline 3 and 6 months.

Results: Statistical parametric mapping will be done to measure acute rCBF differences in the medulla, thalamus, postcentral gyrus, and amygdala, as well as cingulate, prefrontal, and basal ganglia regions.

Anticipated Conclusions: Acute VNS in depressed subjects will cause a similar pattern of brain metabolism alteration as seen in epilepsy. Additional brain areas (anterior cingulate, prefrontal, and basal ganglia regions) will undergo metabolic change. Antidepressant response will be predicted by this activation.

P06.07

Trends in BOLD response during processing emotional cues in depression

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Objectives: We investigated cortical response correlates to the processing of emotional facial expressions of varying intensity in major depression.

Methods: 9 patients in acute state of unipolar depression and 9 normal controls participated at event-related fMRI experiments. The subjects were asked to recognize the sex of individuals presenting different facial expressions, i.e., happy and sad. The intensity of facial expressions varied from neutral to 50% and 100%. We employed orthogonal polynomial trend analysis and compared the trends between the groups using voxel- and cluster-wise ANCOVA.

Results: Relative to controls, the patients demonstrated significantly stronger trends of activation in response to increasing intensity of sad expressions which were observed in visual cortical areas (BA19/37). Conversely, the patients had significantly weaker than normal trends to activate visual cortex (BA19/37) in response to processing of increasing intensity of happy expressions.

Conclusions: Greater than normal cortical modulation related to the processing of sad emotional expressions and weaker than normal modulation related to the happy expressions could represent a part of the mechanism of a mood-congruent bias in depression.

P06.08

Cerebral blood flow in bipolar disorder measured with PET: I trait effects at rest and after mood induction

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Objective Examination of resting state regional cerebral blood flow (rCBF) of remitted bipolar patients with Positron Emission Tomography (PET) is one approach for identifying functionally vulnerable brain regions that may be involved in mediating relapse. In addition, the known sensitivity of BD patients to external stressors may trigger new episodes. Imitating such stressors by exposing these patients to a sad stimulus may help to further identify aberrant functional responses. Method rCBF was measured in 9 remitted patients with BD and 8 healthy controls at rest and after induction of transient sadness using 15O-water PET . Results At baseline, BD patients, relative to controls showed bilateral decreases in dorsolateral prefrontal (DLPF, BA 9), inferior parietal (Par, BA 40) and left orbitofrontal cortex (OF, BA 11), increases in left inferior temporal cortex (BA 21), right anterior insula and left hippocampus. Common changes seen with induction of transient sadness in patients and controls included increases in premotor cortex, insula, and cerebellum and decreases in DLPF and Par. Exaggeration of baseline abnormalities in BD patients were characterized by further increases in anterior insula, and further decreases in medial frontal/DLPF, OF, Par and OF. Sadness-induced increases in regions with previously normal baseline function occurred in anterior cingulate (BA 24) and the striatum. Increased rCBF in subgenual cingulate uniquely distinguished sadness in controls from that in patients. Conclusions Although clinically well, basal brain activity in remitted bipolar patients deviates from the expected "normal" pattern, suggesting ongoing subclinical symptoms and risk for new episodes. Mood induction appears to further unmask areas of potential vulnerability. The stabilization of these regions with therapeutic measures may be an important step towards relapse prophylaxis in BD.

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Effects of VNS on regional cerebral blood flow in depressed subjects

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Objective: Vagus nerve stimulation (VNS) has shown promising antidepressant effects in patients with treatment-resistant depression. This study employed SPECT imaging to determine if there were changes in regional cerebral blood flow (rCBF) after VNS in patients with treatment-resistant depression.

Method: Six subjects underwent SPECT imaging at baseline, post implant (before stimulation), and after 10 weeks of VNS. Image data were transformed into Talairach space and submitted to voxel-based analyses to investigate rCBF changes before and after VNS treatment. Comparisons to normal controls were also performed.

Results: When compared to normal controls, VNS patients at baseline had reduced rCBF to left dorsolateral prefrontal, anterolateral temporal, and perisylvian temporal structures, including posterior insula. These patients, after 10 weeks of VNS , had increased rCBF in cingulate gyrus, bilateral thalamic activation, and

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