Reviewer's report

Title: Neural Correlates of Individual Differences in Depressive Symptoms: A Pilot Functional Brain Imaging Study

Version: 1 Date: 6 February 2012

Reviewer: Ron Salomon

Reviewer's report:

This review will take something more along the lines of a coaching stance. The primary author is clearly in a junior role, and needs considerable mentoring before resubmitting to avoid major organizational/structural issues. Many of these are easily fixed. All should be considered major, compulsory requests for revision unless otherwise noted.

Strengths are many, especially for an early work.

Unfortunately, it was not possible to list every single problem, so often only examples are given. The entire work needs major re-writing. This means that a full checklist that would assure approval is not provided. A second revision might be necessary when the number of issues comes to a manageable set. Greater brevity will benefit the interested reader.

A resubmission is encouraged in the view of this reviewer – the work appears to have been very carefully conducted. Senior authors will be helpful in deciding which components to retain. There is interesting material in the resting data that will hopefully be brought forward.

1. ABSTRACT
   1.a. The first sentence, or actually all 3 background sentences, of the Abstract are confusing; please clarify, preferably replacing the word “linkages” and specifying whether you are examining associations among individual differences, individual symptoms, a specific brain activity, and/or some measure of variations in brain activities. Consider something such as,
   
   “Brain changes preceding the development of major mood illnesses may be informed by studies of individuals with sub-clinical depressive symptoms. Brain activity changes, previously shown to differentiate depression from healthy states, may improve predictive models of MDD onset.”

   1.b. The methods sentence would be more readable as three sentences.

2. TEXT
   2.a. The background section is organized around a list of methods that are reported later. A justification for these choices (among all the available paradigms) would help the reader understand relationships among, or independence between, the tests that were performed. How are they similar? How are they different? Do they complement each other? Are they testing
overlapping functions?

2.b. The phrase, “low frequency brain activity is active during rest” begs for revision.

Methods.

2.c. Please justify the selection of women for this study. Concerns regarding estrogen effects on fMRI have been described. Please describe any monthly variability in mood symptoms in this population, if recorded at interview. Please describe whether menstrual phase or oral contraceptive use were recorded. Please describe any effort to analyze for covariance with estrogen status.

2.d. Give the BDI version and citation here in the methods.

2.e. Please specify version(s) of SCID (I, NP, II) used.

2.f. Since the depression ratings are reported for different study days, please explain any sequence that was used in scheduling these procedures.

2.g. Please specify the high pass filter cutoff frequency in the preprocessing in the methods.

2.h Given the negative findings for several paradigms, consider a more condensed and skeletal description of the methods.

2.i. The phrase “Of central interest,...” should be used sparingly; otherwise it becomes “of many interests.” If you need to point out the central interests, you must be writing about too much extraneous stuff. Every word needs to be of central interest.

2.j Please describe any corrections performed (Bonferroni, etc.), or state that there were none.

3. Results

3.a Much of this section describes methods. Move methods into the methods section. The first phrase showing a result begins “A one-way MANOVA...,” which is about 2 pages into the results section.

3.b. Generally, try to give positive results before negative results. State the positive findings with supporting statistics, just as the statistics were presented for the negative results. For example, “Areas that showed activation included the cingulate gyrus, right supramarginal gyrus, and right lateral occipital cortex.”, should appear with statistics for each region. If some are not corrected for multiple comparisons, state so.

3.c The hypotheses stated in the introduction appear to be much narrower than the exploratory nature of the results presentation would imply. If analyses were not specific to the hypotheses, and if they were not handled differently (in terms of tails), it may be worth letting go of the initial description of the detailed hypotheses. This is an early paper in this realm, and an exploratory stance is acceptable as long as the statistics offer support.

3.d The table entry,

Occipital Cortex (Lateral, Superior) 0
This may imply that two peak clusters are observed. If these can be merged as a single larger cluster, or just one selected to tabulate, it would make sense given the relatively small N, the exploratory nature of the work, and the small distance between them.

There are several such listings. It is not clear that anything is learned from these multiple nodes; if there is a justification, please explain.

4. Discussion
4.a. A richer consideration of caveats would be helpful. Were all subjects right handed? If reported, it was missed. Controls were not reported; stratification by severity is interesting but not entirely a satisfactory replacement. Estrogen effects may be a factor in the variance. The complexity of some paradigms may be a limitation. It might be interesting to know how strongly each patient would rate their understanding of the reward system. This could be a source of variability.
4.b. The discussion needs to show the value of the findings. With text-body word limitations, this means that less critical methodology needs to be more succinctly stated

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.