Author's response to reviews

Title: Can pill placebo augment cognitive-behavior therapy for panic disorder?

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Author's response to reviews: see over
RE: MS: 7116621051539254 - Can pill placebo augment cognitive-behavior therapy for panic disorder?

Dear Editors,

Thank you very much for reviewing our paper referenced above and allowing us to resubmit a revised version.

We have now revised it in accordance with your reviewer’s comments and would like to resubmit it. The details of our revisions are listed on the following pages.

We trust that these amendments adequately address the reviewer’s comments and hope that our manuscript is now acceptable for publication.

Sincerely yours,

Toshi Furukawa
REVIEWER’S COMMENTS

We thank the reviewer for his very helpful comments. Revising the manuscript gave us a precious opportunity to think over the theoretical underpinnings of the placebo effect.

MAJOR COMPULSORY REVISIONS

1. We added a paragraph on the possible theoretical explanations for the present findings in the Discussion as follows:

   The observed pill placebo effect over and above the proven psychotherapy may be explainable from both of the main theoretical models of the placebo effect, namely the classical conditioning [18] and expectancy theory [19] In the life of a modern man the beneficial experience of a pill is almost inescapable and this may have contributed to the placebo effect through pill taking in addition to the same through talk therapy. In other words, the pill has become a conditioned stimulus, eliciting a conditioned response which is placebo effect. Or alternatively, according to the expectancy theory, patients expect more from pill and talk therapy so that they respond more to pill and talk therapy. The fact that the benefit of the pill placebo appeared to wane after the treatment termination is compatible with both of these theoretical models. In fact, although they are often presented as competing perspectives, the two theories are not necessarily incompatible with each other [20].

2. Actually we had to impute the response rate for one of the three trials. We commented on this in the Discussion section where we discussed the possible shortcomings of the paper as follows:

   Thirdly, the response rate had to be imputed in one of the three studies [14] based on the panic frequency, which likely not reflect the whole panic disorder psychopathology. Deleting this study, however, did not affect the outcomes (RR=1.24, 95%CI: 1.00 to 1.54 at the end of acute phase treatment, and RR=1.28, 95%CI: 0.91 to 1.80 at 6-24 months after treatment discontinuation).

MINOR ESSENTIAL REVISIONS

3. Corrected.

DISCRETIONARY REVISIONS

4. We chose not to perform a post hoc power analysis because we thought such would be too data-driven.

5. We were unable to pool continuous outcomes from these trials because they each used varied and different outcome measures. This is a potential problem in the area of panic disorder, especially with its older studies (in distinction to major depression where the Hamilton Rating Scale for Depression or Beck Depression Inventory have become de facto standards).
6. We added a few words to make the sentences more comprehensible to the readers.