Author's response to reviews

Title: Executive function does not predict coping with symptoms in patients with a diagnosis of schizophrenia

Authors:

Maarten Bak (m.bak@sp.unimaas.nl)
Lydia Krabbendam (l.krabbendam@sp.unimaas.nl)
Philippe Delespaul (ph.delespaul@sp.unimaas.nl)
Karola Huistra (c.huistra@sp.unimaas.nl)
Wil Walraven (w.walraven@prinsclauscentrum.nl)
Jim van Os (j.vanos@sp.unimaas.nl)

Version: 2 Date: 29 February 2008

Author's response to reviews: see over
Authors reply

To: “Executive function does not predict coping with symptoms in patients with a diagnosis of schizophrenia”, by M. Bak e.a.
MS: 2043285405170487

Referee 1.

1. It is suggested that the basic idea that cognitive problems in people with a diagnosis would lead to ineffective or maladaptive coping, should be addressed more clearly.

We have rephrased as follows:

*It has been suggested that subjects with a diagnosis of schizophrenia employ a limited repertoire of coping strategies with a preference for emotion-focused strategies [1-5] which are regarded as less effective and associated with worse outcomes [6].*

And

*Given the fact that individuals with a diagnosis of schizophrenia show deficits in executive cognitive function, it may be hypothesised that cognitive impairment in schizophrenia is associated with less effective coping responses.*

2. The referee advised to clarify differences between coping with general stress and coping with symptom related distress in more detail.

We have added to the text:

*An important difference between MACS and other coping instruments is that the focus of MACS is not on coping in general, but on coping with specific symptoms in the context of a severe psychiatric illness. In this context, coping represents an essential part of the treatment for psychotic disorder. A further difference is that the stressor, the psychotic symptom, is socially stigmatised and that the patient, in order to develop coping, must develop an accurate appraisal of the symptom.*

3. The referee questioned whether the fact that 2/3 of the sample appeared to be in symptomatic remission might explain the lack of association between cognitive dysfunction and coping.

In the limitation section, this is recognised as a limitation.

Nevertheless, whilst we understand that this argument may be raised, upon checking the data we found that symptom ratings and coping were distributed evenly across the participants; all patients reported at least one symptom and only one patient reported no coping at all. In order to clarify this point, we added to the text, in the results section:

*Twenty one (66%) subjects were in symptomatic remission (i.e. meeting the psychopathology criterion but not the time criterion of remission) as defined recently [56, 57]. However, symptomatic remission involves only six of 24 BPRS items and does not exclude residual-level
symptomatology as typically seen in chronic patients. Thus, all subjects had at least one symptom present per MACS interview. The mean number of MACS symptoms per subject was 7.0 (SD= 4.0, range 1 – 17) with a mean distress score of 4.2 (SD= 1.9, range 1-7) and a mean level of perceived control of 4.2 (SD= 1.9 range 1-7).

And later in the Results’ section:

Instances of coping were distributed across patients, only a single patient had no instances of coping at all.

And in the discussion section:

The majority of the sample was in a state of remission, but patients in symptomatic remission may display coping for residual symptoms. Thus, the analyses suggested that instances of coping were distributed across patients as only a single patient had no instances of coping at all. The fact that the majority of the sample was in remission cannot be taken to indicate that coping is not relevant in such patients; research suggests that coping strategies are typically used in chronic patients with a degree of residual symptoms, similar to the group in this study [66], and that enhancing coping skills in this group may contribute to better outcomes [67]. Although the mean BPRS score was low, it does not follow that executive function will be better and associations with coping obscured, given the fact that cognitive dysfunction is a stable feature that is not associated with symptomatology [68,69].

In order to accommodate the referee, we have changed the title to: Executive function does not predict coping with symptoms in stable patients with a diagnosis of schizophrenia

4. The referee suggests that only subjects with illness awareness were eligible for this study.

Illness awareness was not a formal inclusion criterion; it was stated that MACS can only assess coping in those people who acknowledge symptom presence and symptom related distress - page 12: “MACS assesses coping only if patients are aware of symptoms and symptom-related distress, as subjects need to recognise a symptom and the associated distress experience to undertake self-protective actions”. We speak deliberately of awareness rather than insight. This is explained in the method section.

We added at the end of page 12 the following:

“MACS does not require insight, but awareness of the experience, similar to an interview with any instrument assessing psychopathology such as PANSS and BPRS. MACS additionally requires that the patient is able to reflect to a certain degree on what effects the symptom has on him/her but for this no insight is required.”

We have added this also as a limitation in the limitation section.

MACS requires that the patient is able to reflect to a certain degree on what effects the symptom has on him/her but for this no insight is required.

The referee questions our statement that the association between neurocognition and insight is non-linear.
We agree with the referee and changed this part in the discussion to:

*It may be argued that this latter characteristic of the MACS is relevant to the lack of any association with cognition in the current study, as reduced awareness, to the degree that it may be associated with poor insight, may be associated with neurocognitive dysfunction, especially poorer executive function [58]. Therefore, the sample may have been selected towards patients with awareness of symptoms and better cognitive function. However, comparing the neurocognitive findings with those of patients and controls in previous studies in this area revealed that mean performance in the current sample was comparable to findings in chronic patients with schizophrenia and substantially lower than performance in control subjects. This suggests that the sample was not selected towards better cognitive functioning.*

Additionally, we noted that the original description of the cognitive test procedure was not entirely accurate. Therefore we amended the description of the cognitive test section as the Zoo Map subtest, rather than the full BADS, was used in the study.

**Zoo Map (Behavioural Assessment of Dysexecutive Syndrome)**

The Zoo Map is a subtest from the BADS, a test battery designed for measurement of executive functions [42] [43, 44]. It is designed to assess difficulties due to executive deficits patients encounter in everyday life. Subjects are given a map of a zoo and a set of instructions relating to places they have to visit and rules they must follow. In the first part of the test, the subject is required to plan a route which enables them to visit all the places without breaking any rules. In the second part, the order in which places should be visited is specified. The score on the first part of the test was used, as this part involves planning and monitoring of behaviour. The Dutch version of the BADS was used [45]. The test-retest stability of this Dutch version was 0.85 [46].

In the limitation section we also added that we used a previous version of the current Groninger Intelligence Test (GIT), which resulted in an overestimation of the mean IQ in this sample. See also comment no. 5 (below). We added a phrase as follows:

(v) *The test that was used to measure intelligence (GIT) was an older version. Therefore, the normative data for this test tend to give an overestimation of IQ compared to other more recent intelligence tests (i.e. the mean IQ of 101 we reported in this sample, would be comparable with 93). This suggests we studied a representative sample of chronic patients with a diagnosis of schizophrenia.*

We added for description of the Stroop task:

*For the current analysis, the time needed to perform the third task (i.e., reading colour names printed in incongruously coloured ink) was used (hereafter: Stroop interference)*

We improved description of TMT as follows:

*………again to be connected but now the task requires switching between numbers and letters. The B/A ratio of performance in the TMT provides a measure of executive function [54] (hereafter: TMT interference).*
The referee states that persons in remission might have better neurocognition, therefore biasing our results.

See point 3 above. We added to the discussion:

Although the mean BPRS score was low, it does not follow that executive function will be better and associations with coping obscured, given the fact that cognitive dysfunction is a stable feature that is only weakly associated with symptomatology [68,69].

We have added this also as a limitation in the limitation section.

5. The referee suggests that we should only give limitations and not be defensive about them.

We have rephrased less defensively as follows:

Limitations
The results of this study should be interpreted in the light of the following limitations. (i) The number of subjects was limited and therefore the results should be seen as indications for future study rather than conclusive findings. (ii) The group was relatively homogenous. Therefore, differences in cognitive functioning present in subgroups like first-episode patients versus chronic patients or inpatients versus outpatients remained unresolved with regard to differential impact on coping properties and interactions with cognitive functioning. (iii) The mental effort people with a diagnosis of schizophrenia exhibit in test assessment, especially neurocognitive batteries, is limited [70]. We did not control for this problem in our sample. (iv) While our a priori hypothesis focussed on executive function, executive function is only one of the domains of cognitive functioning. Therefore one cannot extrapolate the results to general cognitive dysfunction and coping in people with a diagnosis of schizophrenia. (v) The test that was used to measure intelligence (GIT) was an older version. Therefore, the normative data for this test tend to gave an overestimation of IQ compared to other more recent intelligence tests (i.e. the mean IQ of 101 we reported in this sample, would be comparable with 93). This suggests we studied a representative sample of chronic patients with a diagnosis of schizophrenia. (vi) All subject were on antipsychotic medication. We did not control for the effect of antipsychotic medication, given the small sample size and the fact that the direction of association between cognition and antipsychotic medication is not consistent. (vii) We cannot exclude, on the basis of the current data, that those with better cognitive functioning are better able to comply with MACS procedures, in particular with regard to making accurate appraisals of symptoms. (viii) Although it may be argued that MACS requires that the patient is able to reflect to a certain degree on what effects the symptom has on him/her, this is not the same as requiring insight into illness or the pathological nature of symptoms. (ix) Finally, as mentioned in the discussion, the sample was characterised by stable patients with few symptoms. We cannot exclude that coping with weak symptoms requires relatively little cognitive effort so that associations between executive function and coping in the sample would remain too low to be detected. Therefore, replication in a sample with more severe symptoms is required.
Referee 2

1. The referee indicates that executive function does not equals cognition and questions whether other cognitive dysfunctions would have shown correlations with coping in persons with diagnosis of schizophrenia.

We agree with the referee. Our *a priori* hypothesis was with executive function rather than, for example, memory or attention. We have accommodated the referee by:

(i) We have replaced the general “cognitive impairment” with the specific “*executive dysfunction*” throughout the paper/

(ii) In the limitations we have added:
*While our a priori hypothesis focussed on executive function, executive function is only one of the domains of cognitive functioning (limitation number iv)*

2. It is suggested that measures are idiosyncratic or will be published in a companion article.

By mistake we suggested that some results or outcome measures were outlined in a companion article. There is no companion article and therefore the coping domains and the regrouping into two measures of coping NCS and CS was described extensively in this article (and previous work that is referenced in the paper).

We added this as follows at the end of the second before last paragraph before the method section: “Previously, it has been argued that these four coping domain could be usefully combined into one category of coping, the category of Non-Symptomatic Coping (NSC; for more detail about MACS see previous publications[15, 28, 31] or www.macsinfo.homestead.com)”

The referee advised to discuss the relationship between cognitive tests used in this paper and the MATRICS battery. However, given that we have clearly indicated that our hypothesis is on executive function and not on broad measures of cognitive impairment as assessed by MATRICS, we have not included a comparison with MATRICS measures.

3. The study population was somewhat atypical, with two third being in remission and an average high IQ for people with schizophrenia.

This was already discussed above in our reply to referee 1.

We disagree, however, that the average IQ in this sample is exceptional. IQ of people with schizophrenia do not show lower IQ by definition. In addition, we need to add that we used an older version of the GIT (Groninger Intelligence Test). An IQ of 100 on this test is comparable with 93 on current versions of the test. We therefore added the following to the limitation section:

“The GIT to measure intelligence was an older version. Therefore, the mean IQ of 101 we reported in this sample, would be comparable with 93. This suggests we collected data in a standard sample of patients with a diagnosis of schizophrenia.”
Referee 3

1. It is suggested to identify the open form of the MACS in the abstract.

This was done.

The referee indicate that type of medication as well as ratings of side-effects needs to be mentioned, because of relation with cognition.

The referee is right that medication has influence on cognitive function, and both improvement and worsening of function has been reported. This may depend on medication type and side effect profile. However, not only is this a cross-sectional study of subjects stable on medication, but also a rather small sample to study the influence of medication on cognitive function. Therefore, we chose not to explore this.

We added the following to the limitations:
All subject were on antipsychotic medication. We did not control for the effect of antipsychotic medication, given the small sample size and the fact that the direction of association between cognition and antipsychotic medication is not consistent.