Author's response to reviews

Title: Reduced Duration Mismatch Negativity in Adolescents with Psychotic Symptoms: further evidence for Mismatch Negativity as a possible biomarker for vulnerability to psychosis

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Author's response to reviews: see over
Reviewer's report

Title: Reduced Duration Mismatch Negativity in Adolescents with Psychotic Symptoms: further evidence for Mismatch Negativity as a possible biomarker for vulnerability to psychosis

Version: 3 Date: 4 January 2013

Reviewer: Margaret Niznikiewicz

Reviewer's report:

This is a much improved manuscript. I have two remaining comments:

1. I disagree with the explanation that the current statistical model is correct - it really is not OK to include the same variable twice in one statistical model and this is what the authors have done. I suggest a simple solution to this issue: 1. re-run the stats using only region and group as factors: looking at the grand averages - and the stats results - it does not look like there is a laterality effect anyway and the results from the region and group model will be powerful enough. 2. If the authors really feel strongly that they would love to have laterality effect analyzed, please do so by using a separate ANOVA model: thus, there will be two ANOVAs used per component: ANOVA with group and region and ANOVA with group and laterality -- the number of electrodes for each factor will remain the same. The authors can choose which approach they prefer. As I said previously, I do believe that the observed MMN amplitude reductions are real.

• In response to the reviewer’s suggestions, we ran separate ANOVA for the analyses; one 2x4 ANOVA for RegionXGroup and a second 2x2 ANOVA for LateralityXGroup. Instead of entering each electrode into the ANOVA, we averaged the three electrodes for each region (i.e. FP1, FPz & FP2 were averaged and entered into the ANOVA as “Frontalpolar” and so on).
• For amplitude, a 2x4 ANOVA incorporated Region (frontalpolar, frontal, frontocentral & central) and Group (at-risk, control) as factors and the second 2x2 ANOVA incorporated Laterality (electrodes TP9 & TP10) and Group as factors. The same statistics were re-run for latency. The results of which are now included in the manuscript and are outlined below:

• Page 11 in the Statistical Analyses section: “Mixed factorial ANOVA compared the groups on MMN amplitude and latency. A 2x4 analysis of variance (ANOVA) was conducted where the between groups factor was Group (At risk, Control), and Region (Frontal polar, Frontal; Frontocentral and Central) served as the within groups factor. A subsequent 2x2 ANOVA was also conducted where the between groups factor was Group (at-risk, controls) and the within groups factor was Laterality (left TP9, right TP10).”

• Page 12 in the Results section: “For mean amplitude measures, a 2x4 ANOVA with Group (At risk, Controls) as the between subjects factor with Region (frontal polar, frontal, frontocentral and central) as the within groups factor revealed a main effect of Group \( [F (1, 34) = 6.235, p = .018] \). An interaction effect of Region*Group \( [F (3, 102) = 5.091, p= .014] \) was also found. Follow up analyses compared the groups at each region and revealed reduced mean MMN amplitude in the at risk group at the frontal polar region \( [t (34) = -3.086, p= .004] \).”

• Page 12: “A 2x2 ANOVA with Group as the between subjects factor and Laterality (TP9, TP10) as the within groups factor also revealed a significant group difference over temporo-parietal areas \( [F (1, 34) = 6.323, p=.017] \). Follow up independent t-tests revealed reduced MMN amplitude in the at risk group over the right temporo-parietal electrode TP10 in comparison to the Control group \( [t (34) = 2.660, p=.012] \).”
Page 12: “For latency measures, a 2x4 ANOVA with Group (At risk, Controls) as the between subjects factor with Region (frontal polar, frontal, frontocentral and central) as the within groups factor was also conducted. A main effect of Region \([F (3, 102) = 5.085, p = .006]\) was found which demonstrated delayed processing over frontal polar regions. The groups did not differ in MMN latency in any region. A 2x2 ANOVA was conducted for Laterality (TP9, TP10) and Group which revealed no significant differences.”

*Note: Table 3 has now been removed from the manuscript.

2. There is still confusion about how to report measuring of the MMN amplitude:

Currently the authors say:

"Mismatch negativity was defined as a difference waveform obtained by subtracting the standard tone ERP waveforms from the deviant tone ERP waveforms over an epoch length of 80-130ms. Latency was defined as the most negative data point within the x-y msec latency." This truly does not make any sense. When I wrote the sentence about latency defined as the most negative data point within the x-y latency, I meant this as an example of an approach and not as a statement to quote verbatim.

Therefore, to avoid further problems, this is what I propose to write instead (this time, please do quote verbatim):

Mismatch negativity was measured from a difference waveform obtained by subtracting the standard tone ERP waveforms from the deviant tone ERP waveforms. MMN amplitude and latency were measured as the most negative data point within the 80-130 ms latency window, post-stimulus onset.
• The previous statement has been replaced on pages 9 & 10 of the manuscript to include the reviewer’s suggestion: “Mismatch negativity was measured from a difference waveform obtained by subtracting the standard tone ERP waveforms from the deviant tone ERP waveforms. MMN amplitude and latency were measured as the most negative data point within the 80-130 ms latency window, post-stimulus onset.”

I hope I have adequately addressed all remaining concerns from the reviewer and that this manuscript is now acceptable for publication.

Kind regards,

Jennifer Murphy