Supplementary Materials for the manuscript, *Priming Production: Neural evidence for enhanced automatic semantic activity preceding language production in schizophrenia*

Gina R. Kuperberg[1,2], Nathaniel Delaney-Busch[1], Kristina Fanucci[1] & Trevor Blackford[1]

[1]Department of Psychology, Tufts University

[2]Department of Psychiatry and the Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School

Table of Contents.

1. Mass Univariate Analysis: N400 modulation in contrasting identity related and unrelated targets

As described in the main text, in comparing identity related and unrelated targets, there appeared to be significant differences (at an alpha of $p \leq 0.05$) between the schizophrenia and the control groups in both the early N400 time window (350-450ms) and the late N400 time window (450-550ms). However, because this subdivision of the N400 increased the probability of Type I error, we also carried out a mass univariate analysis. This enabled us to determine whether the effect remained significant when separate tests were carried out at all sampling points within the 350-550ms time window at 17 contiguous electrode sites – F3, Fz, F4, FC5, FC1, FC2, FC6, C3, Cz, C4, CP5, CP1, CP2, CP6, P3, Pz, P4 – in each participant, using a cluster-level correction to account for multiple comparisons (Groppe, Urbach & Kutas, 2011). This approach explicitly accounts for multiple comparisons while retaining the ability to localize ERP effects on the scalp surface (Luck, 2014). Indeed, recent simulations in our lab show that, for relatively widespread effects, when used in combination with a cluster mass test, it does not sacrifice power to detect ERP effects (Fields, 2017, chapter 3).

To carry out this analysis, we used the Mass Univariate ERP Toolbox (Groppe, Urbach & Kutas, 2011) and the Factorial Mass Univariate ERP Toolbox (Fields, 2017). We first carried out a 2 (Group: between-subject factor) x 2 (Relatedness: within-subject factor) ANOVA that compared the identity related and unrelated targets at all sampling points between 350-550ms at each of the 17 electrode sites. Consecutive data points at electrodes within 8cm of one another (assuming a head diameter of 56cm) that exceeded a pre-set uncorrected p-value of 0.05 or less were considered clusters. The individual F-statistics within each cluster were summed to yield a cluster-level test statistic -- the cluster mass statistic.

Next, we randomly re-assigned the values across the four conditions at each sampling point at all 17 electrode sites within each participant, and calculated cluster-level statistics as described above. This was repeated 10,000 times. For each randomization, we took the largest cluster mass statistic, and, in this way, created a null distribution for the cluster mass statistic. Then we compared our observed cluster-level test statistic against this null distribution. Any clusters falling within the top 5% of the distribution were considered significant. This test revealed a cluster that was significant at $p = 0.002$, and which included 17 sites, with a spatial cluster mass peak at Fz, a temporal extent from 370-550ms and a temporal cluster mass peak at 480ms.

We then carried out planned follow-up repeated measures ANOVAs that directly compared ERPs evoked by the identity related and unrelated targets in the control and schizophrenia groups separately, again using a mass univariate approach (see Fields, 2017, for discussion for why an F- rather than a t-tests are more appropriate for these follow-ups), with tests carried out within the same spatial and temporal region with similar parameters. In the control group, this revealed a significant cluster ($p = 0.009$) that included all sites except FC5, with a cluster mass peak at Fz, a temporal extent from 435-550ms and a temporal cluster mass peak at 480ms. This cluster reflected the larger amplitude N400 to the unrelated than the identity related targets in the control group. In the schizophrenia group, the analysis revealed a significant cluster ($p = 0.044$) that included all sites except P4, with a cluster mass peak at FC5, a temporal extent between 415-550ms and a temporal cluster mass peak at 480ms. This cluster reflected the opposite pattern of modulation in the schizophrenia group — a larger negativity to the identity related than the unrelated targets.

2. Exploratory correlations between ERP effects of interest and clinical measures within the schizophrenia group

We carried out exploratory post-hoc analyses examining relationships between N400 effects and SAPS summed scores of bizarre behavior, delusions and hallucinations, as well as total positive symptoms (summed SAPS scores), total negative symptoms (summed SANS scores), and medication dosage (in chlorpromazine equivalents, calculated following Gardner et al., 2010). The N400 effects were captured by subtracting activity to the semantically related or identity related targets from their corresponding unrelated targets, each averaged across a three-electrode central region (C3, Cz, C4) over the late N400 time window (450-550ms). We examined Spearman's correlations.

We found inverse correlations between the magnitude of the semantic N400 priming effect and (a) SAPS bizarre behavior (Spearman's $r = 0.62$, $p < 0.01$); (b) SAPS delusions (Spearman's $r = 0.71$, $p < 0.002$) and (c) total SAPS (Spearman's $r = 0.554$, $p < 0.026$): in all cases, the more severe the symptom, the smaller the semantic N400 effect. There were no correlations between the magnitude of the semantic N400 priming effect and SAPS hallucinations, negative symptoms, or medication level, all ps > 0.5.

There were also no correlations between any of these clinical measures and the magnitude of the identity priming effect within the schizophrenia group (all ps > 0.08).

References

Fields, E.C., 2017. Chapter 2: Toward an understanding of the late positive component of the ERP to emotional stimuli (Event-related potential and functional MRI studies of emotion and self relevance). Department of Psychology - Chapter 2: Toward an understanding of the late positive component of the ERP to emotional stimuli; p. 22-81. Tufts University, Medford, MA.

Fields, E.C., 2017. Factorial Mass Univariate ERP Toolbox [Computer software]. Github, https://github.com/ericcfields/FMUT/releases.

Gardner, D.M., Murphy, A.L., O'Donnell, H., Centorrino, F., Baldessarini, R.J., 2010. International consensus study of antipsychotic dosing. American Journal of Psychiatry 167, 686-693.

Groppe, D.M., Urbach, T.P., Kutas, M., 2011. Mass univariate analysis of event-related brain potentials/fields I: a critical tutorial review. Psychophysiology 48, 1711-1725.

Luck, S.J., 2014. Online Chapter 13: The Mass Univariate Approach and Permutation Statistics (An introduction to the event-related potential technique). MIT press, MIT Press Online.