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Letter to the Editor

When context is difficult to integrate: Cortical measures of congruency in schizophrenics and healthy relatives from multiplex families

Language disorders have classically been considered the hallmark of schizophrenia (Andreasen, 1979). Contextual semantic integration processes seem to play a fundamental role in this disorder. In event related potential (ERP) research, N400 can be considered a cortical marker of semantic integration (Hagoort, 2008). N400 amplitude increases in response to an unrelated semantic target presented following a semantic context. Recently, a frontal N400 has been reported (Ibáñez et al., 2006, 2010). If schizophrenic patients have semantic integration deficits, then congruent targets should require a similar amount of post-lexical retrieval to that required by incongruent targets. Consequently, the N400 from congruent trials should elicit enhanced N400 amplitude similar to incongruent trials.

In patients, several studies have reported N400 deficits (review: Kuperberg et al., 2010). In relatives, there are also preliminary reports of contextual semantic integration impairment (Guerra et al., 2009; Riveros et al., 2009). However, no study has directly assessed these deficits using different degrees of contextual congruency. Thirteen clinically-stable medicated schizophrenia patients, thirteen healthy first-degree relatives from multiplex families, and thirteen controls subjects, matched by age, gender and educational level (see Supplementary data 1), performed a passive listening task with four degrees of congruency (Ibáñez et al., 2006; see Fig. 1B and Supplementary data 2 and 6).

EEG signals were recorded using a 129-channel system from an EGIs amplifier (for recording details and data analysis, see Supplementary data 3–4). No group differences were observed regarding intellectual capabilities, speed processing (TMT-A) and executive function performance (TMT-B; see Table 1, Supplementary data).

Fig. 1A illustrates the ERP group effects from the left frontal ROI. The ANOVA yielded an effect of Context ($F(3,108) = 26.01, p < 0.001$) and an interaction effect of Context \times Group ($F(6,108) = 5.5, p < 0.001$). Post hoc comparisons (Group \times Context; $MS = 2.60, df = 139.8$) evidenced that in the control group, the Incongruent 3 category presented more negative N400 amplitude compared to Incongruent 1 ($p < 0.01$), Incongruent 2 ($p < 0.01$), and congruent categories ($p < 0.01$). In Relatives, only congruent category compared to all other incongruent categories ($p < 0.05$ all conditions) yields signif-

icant N400 differences. No differences were observed among incongruent categories. ERPs from probands presented pronounced N400 deficits, showing no amplitude differences amongst levels of contextual discrimination. In addition, congruent category in relatives was more negative than in controls ($p = 0.03$) and even more negative in probands than in controls ($p < 0.001$). Fig. 1C shows the Group \times Context interaction. See Supplementary data 5 for more details.

In brief, N400 from relatives only discriminated between congruent and incongruent targets but not partially incongruent targets. When compared to controls and relatives, N400 from probands unsuccessfully discriminated between categories.

Failure in building up and using contextual information to construct meanings (Cosmelli and Ibáñez, 2008) has been proposed as an underlying primary cognitive deficit in schizophrenia (Cohen et al., 1992). Our results support an impaired brain processing in schizophrenia and relatives. The reduction of the congruent category amplitude in relatives and probands compared to controls suggests integration deficits. Congruent (in probands), and partially incongruent stimuli (in probands and relatives), require equivalent amounts of post-lexical retrieval as incongruent stimuli, since the amount of negativity in all cases is similar. In contrast, N400 amplitude from controls seems to require less contextual retrieval for congruent stimuli.

Future studies using larger samples are needed. Additionally, it will be necessary to investigate the relationship of the N400 to other cognitive deficits in schizophrenia, such as attention and executive function (Weinberger et al., 2001, see Supplementary data 7). Based on these results, we argue that there is empirical evidence for a deficient neural integration of degrees of congruency indexed by N400 in schizophrenia and first degree relatives.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.schres.2010.04.008](https://doi.org/10.1016/j.schres.2010.04.008).

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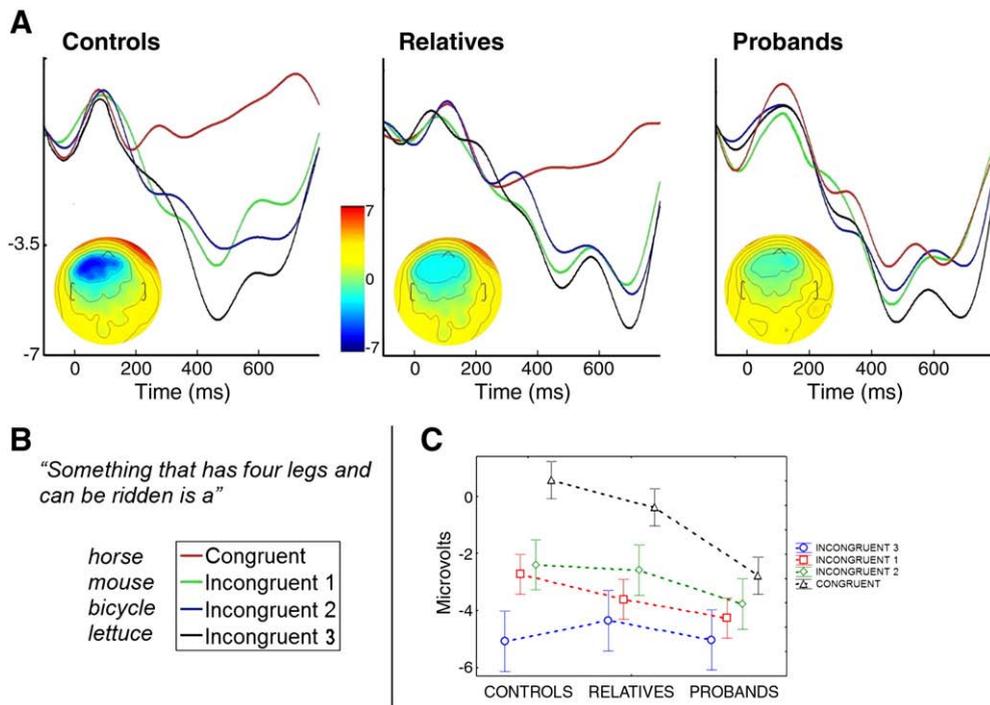


Fig. 1. A) ERP waveforms from each group (Controls, Relatives and Probands) at Left Frontal Region (ROI centered over F3 electrode) showing the N400 amplitude in each condition. B) Examples of the four categories. C) ERP mean amplitude values for the interaction between group and context. Vertical bars denote 0.95 confidence intervals.

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