Electrophysiological insights into conceptual disorganization in schizophrenia

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Abstract

Disorganized speech, or thought disorder, in schizophrenia may reflect abnormal processing of meaningful concepts. To examine whether schizophrenia involves abnormalities in how a meaningful context influences processing of concepts strongly, weakly, or not related to it, we used the N400, an event-related brain potential (ERP) index of semantic relatedness. ERPs were recorded from schizophrenia patients ($n=18$) and normal controls ($n=18$) while they viewed category definitions (e.g., *a type of fruit*), each followed by a target word that was either a high-typicality category exemplar (*apple*), low-typicality exemplar (*cherry*), or non-exemplar (*clamp*). Participants' task was to indicate via button-press whether or not the target belonged to the category. In both patients and controls, N400 amplitude was largest (most negative) for non-exemplars, intermediate for low-typicality exemplars, and smallest (least negative) for high-typicality exemplars. Compared to controls, patients showed a trend toward reduced N400 amplitude differences between non-exemplars and low-typicality exemplars. Most importantly, within patients, reduced N400 amplitude differences between high- and low-typicality exemplars were correlated with psychotic symptoms. This association of an N400 index of semantic processing with psychotic symptoms suggests that psychosis in schizophrenia may be associated with greater similarity in how concepts strongly and weakly meaningfully related to their context are processed.
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1. Introduction

"Disturbance of associations" was identified as a core feature of schizophrenia by Bleuler (1911/1950), who observed that in schizophrenic language "associations lose their continuity" and "appear odd, bizarre, distorted" or "senseless." He inferred from this that:

thinking operates with ideas and concepts which have no, or a completely insufficient, connection with the main idea…The result is that thinking becomes confused, bizarre, incorrect, abrupt.

Disorganized speech in schizophrenia has thus been thought to objectively reflect underlying conceptual disorganization, or "thought disorder."

Bleuler's (1911/1950) notion of abnormalities in "pathways of association and inhibition" presaged more recent theories proposing that schizophrenic disorganization results from abnormalities in how concepts activate one another in semantic memory (McCarley et al., 1999; Nestor et al., 1998; Spitzer, 1997). These theories assume a model of semantic long-term memory in which concepts

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are nodes in a neural network, and meaningful associations among concepts reflect connectivity among these nodes (Anderson and Pirolli, 1984; Collins and Loftus, 1975; Neely, 1977). When a concept node is activated, as by its corresponding word stimulus, this activation spreads through the network to associated nodes. The degree to which the stimulus concept activates another concept and facilitates its processing is presumably related to the strength of the links between them.

One hypothesis for how abnormal activation in semantic memory may lead to disorganized speech postulates a broader spread of activation to weakly or remotely related items. For instance, Spitzer (1997) proposed that indirect associates — those related through at least one other concept, like CAT and CHEESE (mediated by MOUSE) — activate one another more strongly in schizophrenia, thereby leading to speech containing sequences of apparently unrelated or weakly related concepts.

Some semantic priming data support this hypothesis. Semantic priming refers to the facilitation of response to a target item — e.g., faster reaction time (RT) in a lexical-decision task — when it is preceded by a meaningfully related prime stimulus rather than an unrelated one. Greater priming is thought to reflect greater activation of the target by the prime. Consistent with increased spread of activation to weak associates, an abnormally large priming effect for indirectly related words has been found in thought-disordered schizophrenia patients, although only when the prime-target interval (or stimulus-onset asynchrony (SOA)) is relatively short (≤300 ms) (Moritz et al., 2001; Moritz et al., 2003; Spitzer et al., 1993).

A different hypothesis attributes disorganized speech in schizophrenia to impaired ability to use context to activate related items, or to inhibit unrelated items (Cohen and Servan-Schreiber, 1992; McCarley et al., 1999). Importantly, this abnormality is not necessarily mutually exclusive with increased spreading activation, as they could occur in sequence. In fact, whereas RT priming evidence for increased spreading activation has come from word-pair studies employing relatively short SOAs (≤300 ms), most RT priming evidence for impaired context use has come either from word-pair studies employing longer SOAs, or from studies using sentence contexts, which also build up over a longer period. For instance, schizophrenia patients displayed less priming than normal controls for closely related words at a long SOA of 950 ms, but not at shorter (200–700 ms) SOAs (Barch et al., 1996). In a sentence-context study (Kuperberg et al., 1998), both schizophrenia patients and controls were slower to recognize a sentence-final word when it was semantically incongruent with the context than when it was congruent, but patients with high thought-disorder

ratings were delayed less than were either controls, or patients with low thought-disorder ratings — consistent with impaired use of context.

Semantic priming effects also have been investigated using the N400 component of scalp-recorded event-related brain potentials (ERPs). The N400 is a negativity occurring from approximately 200 to 500 ms, and peaking at approximately 400 ms, after presentation of any potentially meaningful stimulus such as a word or picture. N400 amplitude is reduced by factors facilitating an item's processing, such as linguistic word frequency or stimulus repetition (reviewed in Kutas and Federmeier, 2000). Of relevance here is that N400 amplitude elicited by a target stimulus is reduced (i.e., made less negative) by increasing semantic relatedness between the target and a preceding prime stimulus (Holcomb and Neville, 1990; Holcomb and Neville, 1991; Kutas, 1985; Kutas and Hillyard, 1980; Stelmack and Miles, 1990). In other words, N400 amplitude to a target is smaller (less negative) when it is more related to the prime. N400 amplitude has thus been used to measure the degree to which concepts activate one another in semantic memory, with reduced (less negative) amplitude corresponding to greater activation.

Results of N400 studies in schizophrenia have been mixed. Prime-target word pairs with SOA=450 (Kostova et al., 2005; Kostova et al., 2003) and 600 ms (Strandburg et al., 1997) were associated with larger N400 amplitudes to related targets in schizophrenia patients than in normal controls, while amplitudes to unrelated targets did not differ between patients and controls. These results suggest decreased activation of related targets in schizophrenia, consistent with the impaired context use hypothesis. In another word-pair experiment, Condray et al. (2003) reported a reduced N400 priming effect (i.e., reduced difference in N400 amplitude between related and unrelated targets) in patients versus controls, at SOAs of both 350 and 950 ms, although N400 amplitudes did not significantly differ between patients and controls for either related or unrelated targets. In contrast, Spitzer (1997) reported that N400 amplitude for indirectly related words (SOA= 200 ms) was smaller in patients compared to controls, consistent with relatively greater activation of weak associates. In a picture-word matching task (SOA= 250 ms) (Mathalon et al., 2002), target words referring to an item from the same category as the picture elicited a smaller N400 in patients than in controls, consistent with increased activation of related items. Studies with sentence-final word paradigms (Kostova et al., 2003; Ohta et al., 1999) showed larger N400 amplitudes to congruent words in patients than controls, consistent