

# Semantics and N400: insights for schizophrenia

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Thought disorder is a hallmark symptom of schizophrenia, which often leads to deficits in social functioning. Some aspects of this cognitive dysfunction are the result of abnormal characteristics in the semantic processes of patients. These abnormalities exist not only at the discourse production level, but at the discourse comprehension level as well. The recording and analysis of event-related potentials has greatly advanced the investigation of the processing of linguistic information. One particular component of event-related potentials, N400, indexes semantic processing. Whereas all meaningful words elicit an N400, the amplitude of this component is much greater in response to words that are unexpected in a given context. As such, it is thought to reflect processes involved in contextual integration, which is the key to correct comprehension. N400 has been found to be abnormal in patients with schizophrenia when compared with healthy controls and, thus, may point toward the underlying cause of semantic deficits of patients with thought disorder.

Le trouble de la pensée est un symptôme caractéristique de la schizophrénie, qui entraîne souvent des déficits du fonctionnement social. Certains aspects de ce dysfonctionnement cognitif résultent des caractéristiques anormales des processus sémantiques des patients. Ces anomalies existent au niveau non seulement de la production, mais aussi de la compréhension du discours. La consignation et l'analyse de potentiels reliés à des événements a fait progresser considérablement l'étude du traitement de l'information linguistique. Un élément constituant particulier des potentiels reliés aux événements, l'élément N400, indexe le traitement sémantique. Alors que tous les mots significatifs provoquent un N400, l'amplitude de cet élément constituant est beaucoup plus grande face à des mots inattendus dans un contexte donné. C'est pourquoi on croit qu'il reflète des processus intervenant dans l'intégration contextuelle, ce qui constitue la clé de la compréhension correcte. On a constaté une anomalie de l'élément N400 chez des patients atteints de schizophrénie comparativement à des témoins en bonne santé, ce qui pourrait donc indiquer la cause sous-jacente des déficits sémantiques chez les patients atteints d'un trouble de la pensée.

## Introduction

Thought disorder in schizophrenia was first described by Eugene Bleuler<sup>1</sup> in 1911, when he depicted a disorder in which thoughts and feelings no longer functioned together normally. Since then, it has been con-

sidered a core feature of schizophrenia, though it may not be present in every patient. Thought disorder comprises several different entities, but it is typically used as an encompassing singular category rather than a plural. Thought disorder is characterized by certain language impairments, including tangentiality, bizarre

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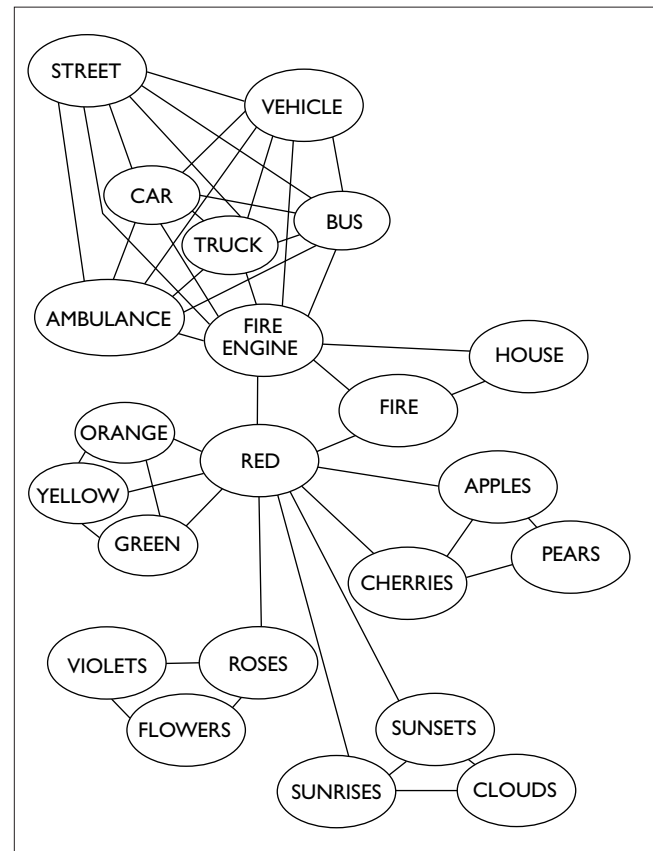
associations and disorganized speech. Associations tend to proceed along novel lines and indirect associations receive unusual significance, often resulting in strange utterances. For example, one such patient said, "I am in a switched-off fortress." Although one could find a meaning in this sentence, it is not a straightforward association. In addition, the patient could not understand why the meaning was not obvious to others. These abnormalities can lead to deficits in social functioning, such as difficulty in maintaining normal contact with other people. This symptom is sometimes found in other disorders, such as schizoaffective and bipolar disorders, and even in healthy individuals, though to a lesser extent.<sup>2-4</sup> It is much more severe in patients with schizophrenia and, in the absence of mood disorders, it is used as an important criterion for diagnosis.

### Organization of language processes

Language comprehension requires the activation, organization and integration of different kinds of linguistic knowledge.<sup>5</sup> In order to comprehend language successfully, a visual or auditory stimulus, such as the word "dog," is first automatically (and subconsciously) identified as a language stimulus by accessing the lexicon (the mental "dictionary"). The long-term representation of the word (its "node") is activated along with those of words that are orthographically and phonetically similar to the stimulus, though these are activated to a lesser extent. A lexical selection process focuses on the accurate node.<sup>6,7</sup> In these classic models,<sup>8</sup> links connect the various nodes and represent relations of variable strength. This ensemble of nodes and links constitutes the semantic network (Fig. 1).

Behavioural studies, for example, using lexical decision tasks (LDTs) in which subjects are required to decide as rapidly as possible whether a target letter string is a real word or a pseudo-word (e.g., "slode"), have shown shorter reaction times for words that were preceded by semantically related words than when preceded by unrelated words. These results suggest that related words benefit from facilitated processing.<sup>8-11</sup> This has been termed "semantic priming" and is thought to be accomplished via a fast-acting passive activation, referred to as automatic spreading of activation. Nodes activated by incoming stimuli automatically activate other related nodes via the links. For example, the prime word "bread" will automatically ac-

tivate the representations of associated words, for instance, "butter." Theorists propose that the spreading of activation modifies the state of semantically related word nodes, possibly by decreasing their firing threshold. This process does not require attentional capacity and begins immediately upon activation of the prime word.<sup>8,10,11</sup> More recently developed models provide a different account of the semantic priming effect.<sup>12,13</sup> These models are based on a distributed connectionist network, in which each concept corresponds to a pattern of activation of semantic features. In this framework, concepts are not assessed directly from separate memory locations as discrete local units,<sup>14</sup> as in the Collins and Loftus model. Here, semantically related words have similar patterns of activation across the meaning units: the more semantically close 2 concepts are, the more similar their patterns are. Accordingly, it becomes faster to transit from one to the other.<sup>12</sup>



**Fig. 1: Classic model: a schematic representation of concept relatedness in a stereotypical fragment of human memory (where a shorter line represents greater relatedness). Reprinted with permission from the American Psychological Association (*Psychol Rev* 1975;82:407-28).**

The activation of the lexical representation of the word also induces the activation of the so-called world knowledge<sup>15</sup> associated with the word. This set of representations is accessible by meaningful stimuli, thus including not only words, but objects and faces as well. Evidence for this multimodal access comes, for instance, from studies using rebus sentences (sentences in which pictures replace 1 or 2 concrete words). These sentences were found to be understood and recalled as well as all-word sentences, showing that the knowledge representation derived from the pictures is integrated easily into the sentence.<sup>16,17</sup> Together with other results,<sup>18,19</sup> this strongly suggests that the meanings of words are not encoded in their lexical representations, but in a postlexical conceptual system instead.

Finally, the knowledge activated by the word will be integrated into a global representation including the knowledge activated by the previous words. This global representation, which encompasses the meaning of the entire situation depicted by the text, is termed a situational representation.<sup>20</sup> This stage of processing, which, like knowledge activation, is postlexical, is influenced by the subject's awareness of the informational content of the discourse. It is a more controlled process that requires a greater amount of attentional resources than does the automatic stage of lexical access.<sup>21</sup>

### Event-related potentials and language

The recording of the electrical activity of the brain from the scalp has revolutionized the study of language processes, being neither intrusive nor "after the fact," as are measures of response times.<sup>22</sup> In a defined epoch of the recording that is time-locked to the presentation of a stimulus, there are voltage changes that are specifically related to the brain activity triggered by this stimulus. These voltages constitute the event-related potentials (ERPs). They represent net electrical fields associated with the activity of sizeable neuronal populations, within which the individual neurons must be synchronously active.<sup>23</sup> They are principally a reflection of postsynaptic excitatory or inhibitory potentials. When the difficulty of a task is increased or when it is manipulated so that an additional process is necessary, larger negative ERP components, or an additional negative peak, are generally observed.<sup>24</sup> In contrast to metabolic functional brain imaging methods, such as functional magnetic resonance imaging (fMRI), which provide good spatial resolution, ERPs allow a real-time

measure of brain activity, the temporal resolution of which approaches the millisecond. They also often give a first approximation of the localization of the activity.

Five ERP components involved in language processing have now been identified.<sup>5</sup> The earliest component is the phonological mismatch negativity (PMMN). It is elicited by contextually unexpected phonemes in language tasks.<sup>25</sup> The second is a left-anterior negativity (LAN), which is elicited about 200–500 ms after word onset. This component seems to be involved in processes of working memory, as well as in the activation and processing of syntactic word-category information (whether the word is acting as a subject, a verb or an adjective, etc., in the sentence).<sup>26–28</sup> The third, the N400 component, which is a negative waveform that develops between 300 and 500 ms after word onset, is related to the processing of the meaning of the stimulus in its context, or semantic processing.<sup>29</sup> Note that this wave includes a centro-parietal component and, in several tasks, an additional frontally distributed component with a slightly different functional significance.<sup>30</sup> The fourth component is the P600, a positive waveform that occurs about 500–700 ms after word onset. It belongs to the P3b family of components.<sup>31</sup> P3b components are large, positive peaks elicited in response to a wide variety of stimuli. For simple laboratory stimuli, such as tones or coloured dots, they can peak as early as 275 ms post onset. For complex stimuli, such as words, they peak at 600 ms. They can be delayed up to 2000 ms, depending on the difficulty of the task. Nevertheless, they can still be considered to belong to the same family of P3b components because their maximum remains over parietal scalp sites and because their amplitude can be modulated by the same independent variables (e.g., the probability of the occurrence of a particular stimulus<sup>32</sup>). P3b components are thought to reflect the end of the stimulus evaluation process. The greater the amount of information that has been consciously extracted from the presentation of the stimulus, the greater their amplitude.<sup>33–36</sup> Interestingly, several studies have shown that unexpected syntactic anomalies<sup>37–39</sup> elicit a large, positive and parietal component also peaking at 600 ms post onset. Their authors have thus claimed that the P600 elicited by words in normal discourse reflects a type of syntactic processing, such as "second-pass parsing,"<sup>40</sup> and as such it would not be a component of the P3b family. However, they have not yet convinced all authors.<sup>35,41,42</sup> The fifth ERP component observed during

language processing, the slow positive shift, develops throughout the span of a sentence. It has been related to the construction of a representation of the overall meaning of the sentence.<sup>5</sup>

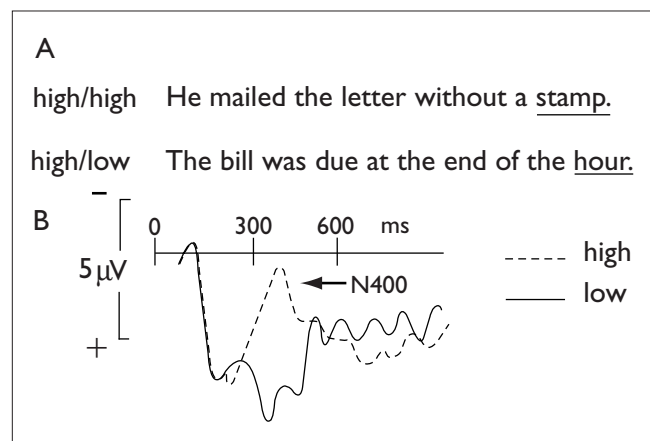
### N400 and semantic processing

N400 was first discovered in a landmark study<sup>43</sup> in which ERPs were recorded in response to incongruous sentence endings (e.g., "He takes his coffee with cream and dog"). Semantically deviant words were followed by a large negative waveform, peaking about 400 ms after the onset. Kutas and Hillyard<sup>43</sup> first speculated that this N400 indexes a "second look" process by which subjects try to derive a meaning from nonsensical sentences. This hypothesis was quickly discarded with the discovery that N400 could be evoked by congruous sentence endings. In these conditions, its amplitude is inversely proportional to the degree of expectancy of the word ending the sentence,<sup>44</sup> which is measured as a function of the Cloze probability. This probability is determined by having people supply words that have been deleted from highly constraining sentences ("He takes his coffee with cream and ...") and poorly constraining sentences ("He was soothed by ..."). The Cloze probability of the word "wind," for instance, is the percentage of people who used it to complete the sentence frame. High Cloze probability word endings (e.g., "He takes his coffee with cream and *sugar*") elicit minimal or no N400s, whereas low Cloze probability words (e.g., "He was soothed by the gentle *wind*") elicit large N400s. Thus, words that are easier to process because they are expected in a context, or words that are semantically related to earlier words, elicit N400s of smaller amplitudes than words out of context or words that are weakly related. One study<sup>44</sup> found a very high inverse correlation ( $r = 0.94$ ) between the N400 amplitude at right parietal electrode sites and Cloze probability (Fig. 2).

It was soon discovered that sentences are not needed to elicit N400s but that single words are sufficient, provided that the task does not focus on physical characteristics of words (such as deciding whether words are written in upper or lower case letters).<sup>21</sup> Thus, in lexical decision tasks (LDTs), for instance, prime words that are semantically related to the target words reduce the amplitudes of the N400 to these target words.<sup>21,45-47</sup> In order to determine whether the N400 is reflective of mechanisms in the automatic stage or in the postlexical

stage of processing, Holcomb<sup>48</sup> used a semantic priming protocol with degraded target words (formed by deleting a random 33% of the pixels from each letter). The reaction time data indicated a greater amount of behavioural priming in the degraded compared with the nondegraded condition. Meanwhile, there was no greater effect on the N400 in the former case. He thus concluded that reaction times and N400s must depend on 2 independent and therefore different stages of processing.<sup>49</sup> The use of an interaction to infer the unicity of a stage of processing has been criticized<sup>50</sup> in the case of the entire chain of information processing. But it is very relevant when applied to a single ERP component. Because it is well-established that reaction times reflect lexical processes,<sup>9</sup> Holcomb proposed that the N400 indexes postlexical processes.

This new perspective appeared to be consistent with studies showing that the amplitudes of the N400s elicited by the words of an isolated sentence decrease with the increasing fit between the individual word and its sentence context.<sup>46</sup> Thus, words located at the beginning of a sentence evoke the largest N400s because of weaker contextual restraints. It is also consistent with the fact that N400s depend on global, discourse-level constraints as well.<sup>51-53</sup> For example, the discourse "As agreed upon, Jane was to wake her brother at five o'clock in the morning. But the brother had already washed himself and had even got dressed," was fol-



**Fig. 2:** An example of sentences with a high degree of contextual constraint and with varying degrees (high/low) of Cloze probability of the sentence-ending word (A). Grand average event-related potentials (ERPs) from the Pz electrode in response to sentence-ending words show a large N400 in response to low Cloze probability words and no N400 to high-probability words (B). Adapted with permission from Macmillan Publishers (*Nature* 1984;307:161-3. [www.nature.com](http://www.nature.com)).

lowed by "Jane told her brother that he was exceptionally quick/slow." The coherent ending ("quick") elicited a smaller N400 when the sentence was preceded by the discourse than when the sentence was presented as an isolated, but valid, sentence.<sup>53</sup> This suggests that N400 indexes a process that integrates the meaning of a word into the higher-order situational representation. When the integration of a word's meaning into a local context is easier, there is a reduction in the N400 amplitude, giving rise to the idea that N400 reflects "contextual integration." The N400 modulations that had been obtained with isolated words in LDTs were then taken as an indication that contextual integration is an automatic, though not irrepressible, process that occurs even when no sentence syntax is present. This can be illustrated by the following famous series of words: "Women, Fire, and Dangerous Things," the title of a George Lakoff book.<sup>54</sup> The overwhelming majority of readers automatically wonders whether it means that women, like fire, are dangerous things.

Consistent with the idea that the knowledge representations of the postlexical stage of processing can be activated by meaningful stimuli other than words, N400 is also evoked in response to meaningful nonlinguistic stimuli, such as line drawings of objects,<sup>55</sup> photographs,<sup>56</sup> faces<sup>57,58</sup> and environmental sounds.<sup>59</sup> For each type of stimulus, similar N400 modulations are observed as with linguistic stimuli. For example, pictures of faces (e.g., that of Canadian Prime Minister Paul Martin) can prime (i.e., decrease) the amplitude of the N400 evoked by another face (e.g., that of former Canadian prime minister Jean Chrétien).<sup>58,60</sup>

The temporal and amplitudinal features of N400 are similar across all the stimulus modalities. However, its distribution across the scalp varies with stimulus modality, implying that the N400 is not reflective of an amodal semantic process but, rather, that "semantic memory may consist of featural mosaics distributed across multiple, higher-order perceptual and motor processing areas,"<sup>29</sup> each one contributing to the semantic representation of a single concept.

## N400 and schizophrenia

It has been suggested that language impairments in schizophrenia, such as thought disorder, could be the result of an increased automatic spread of activation in the semantic store<sup>8</sup> as compared with controls, or of a more diffuse pattern of activation in terms of the dis-

tributed accounts of the semantic priming.<sup>12-14</sup> This idea was supported by studies employing indirect priming LDTs, in which prime words (e.g., "lion") are related to target words (e.g., "stripes") through mediating associated words (e.g., "tiger") that are not presented to the subject. Under these conditions, in which subjects are not conscious of semantic relations between words, there is a greater priming effect on reaction times in patients with schizophrenia<sup>61,62</sup> when compared with healthy controls. The exaggerated activation responsible for this greater indirect priming effect may be a plausible cause of the bizarre associations that appear in patients' discourses.

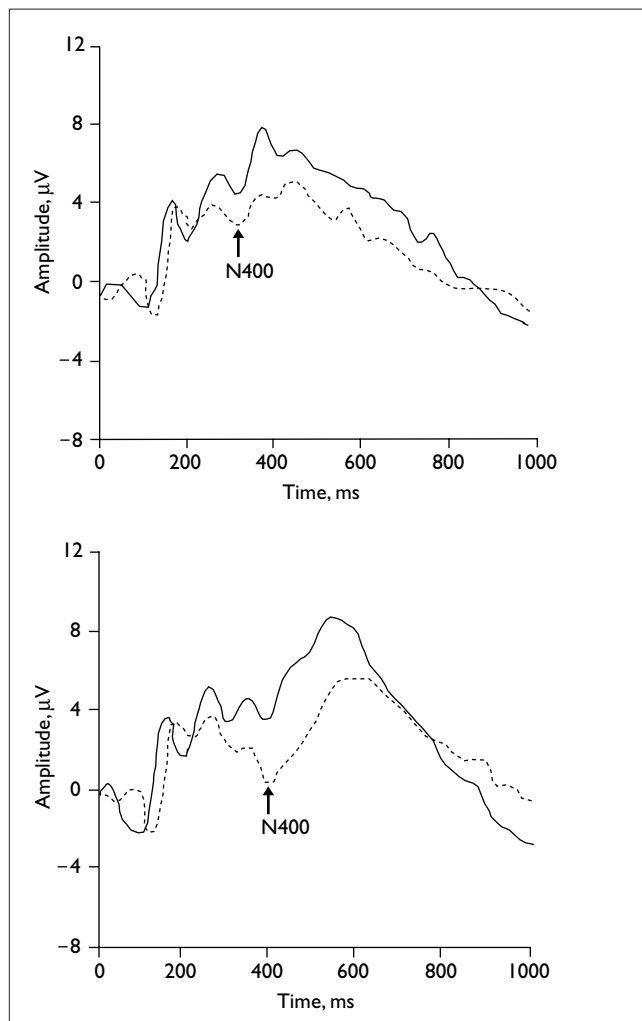
There also seem to be significant differences in N400 data. Adams et al<sup>63</sup> investigated N400 in patients with thought disorder using the sentence priming task with congruous and incongruous word endings. In this preliminary study, the group with schizophrenia showed, on average, a significant reduction in the N400 effect, that is, the difference in amplitude between the N400 in response to congruous and to incongruous words. Interestingly, only 2 of the 4 patients, those with high thought disorder scores, showed this reduction. Reduced N400 effects were replicated in several studies,<sup>64-69</sup> though most reported a delay in the N400 onset and peak as well. One study also replicated the finding that patients with high thought disorder scores had greater N400 abnormalities.<sup>70</sup> Whereas the N400 reduction is indicative of language processing abnormalities, the delay in N400 latency probably indicates that patients are slower at processing information.<sup>65</sup> This speed reduction could be disrupting, because it could lead to the disturbance of normal flow of information by the interference of stimuli that have yet to be processed.<sup>69</sup>

A problem with focusing only on the N400 effect is that the source of the amplitude differences becomes masked. The reduced N400 effect found in patients could be the result of either a reduced N400 in the unrelated conditions where there is no semantically related word, or an enhanced negativity in the related conditions, or both. Koyama et al<sup>68</sup> used the LDT protocol and discerned that in the unrelated target word and non-word conditions, there was no difference in the N400 amplitude between patients with schizophrenia and matched controls, which implies that the neural generator of the N400 is intact in patients. Meanwhile, the N400 effect was still reduced in patients, indicating a larger N400 amplitude in the *related* target word con-



dition. These findings were confirmed in studies using the sentence priming task,<sup>65,71</sup> though they showed that patients have a greater N400 negativity not only to congruous sentence endings, but to incongruous ones as well (Fig. 3).

Although the patients were not impervious to incongruity, the enhanced negativity to congruous completions suggested that their language processes are less constrained by semantic context than those of healthy subjects. In other words, patients may have more trouble in using context to generate expectancies.



**Fig. 3:** Grand average ERPs from the Pz electrode in response to sentence-ending words show an enhanced N400 in response to sentences that make sense (upper) and to nonsensical sentences (lower) in patients with schizophrenia compared with healthy controls. Dashed lines = patients with schizophrenia; solid lines = healthy controls. Adapted with permission from the American Psychiatric Association (*Am J Psychiatry* 1997;154:640-6. <http://ajp.psychiatryonline.org>).

A recent study using a picture–word verification paradigm showed that whereas N400s to primed words were normal, patients with schizophrenia had reduced N400s to *unprimed* words.<sup>72</sup> However, word stimuli and the pictures priming them were always drawn from the same category. There was, thus, a partial priming, even for “unprimed” words (e.g., the word “duck” appearing after the picture of a swan). Nevertheless, the results suggest an improper priming of the relatively distantly related words, which is in keeping with the farther automatic spreading of activation observed in patients with an indirect priming task.

Strandburg et al<sup>73</sup> investigated N400 activity in patients with schizophrenia by using an idiom paradigm. Idiomatic pairs of words (e.g., “vicious circle,” “square deal”) are learned as units and have no literal meaning. In these pairs, the Cloze probability of the second word is very high and the contextual link is further strengthened by familiarity and frequent use. Subjects had to judge the meaningfulness of idiomatic, literal (e.g., “vicious dog”) and nonsensical word pairs (e.g., “square wind”). An earlier study<sup>74</sup> of healthy subjects showed that, as observed by Strandburg et al,<sup>73</sup> “semantic access to an idiomatic completion of a phrase is faster and more efficient than to other semantically meaningful completions.” Here, patients showed an N400 response to nonsensical word pairs equivalent to that of controls. However, they did not show the same reduction in amplitude for idioms and literal second words as in healthy subjects, indicating that, even under conditions in which the Cloze probability is very high, the second word of an idiomatic or literal word pair is less predictable than it is for healthy individuals. Strandburg et al<sup>73</sup> suggest that the results are in accordance with the concept that “a disturbance in the internal representation of context is a core deficit in schizophrenia,” as proposed by Cohen and Servan-Schreiber.<sup>75</sup> Thus, patients may be unable to maintain the semantic constraints generated by the first word in order to interpret the second properly.

The maintenance of a vivid context in working memory requires attentional resources. The aforementioned results may thus be the result of a failure in maintaining selective allocation of these resources. To explore this idea, Andrews et al<sup>70</sup> investigated patients’ performance in a passive sentence-reading task in which subjects were not required to make any response. The sentences ended either with a congruous word, an incongruous word or an incongruous word that was related to the congruous word ending (e.g., “The pizza

was too hot to drink"). The amplitude of the N400s under all 3 sentence-ending conditions was similar for both patients and healthy individuals, a finding that was inconsistent with previous studies in which responses were required. This suggests that the N400 abnormalities found in patients may lie in the allocation of attentional resources to semantic processing. In other words, a reduction in the N400 amplitude may only become evident when the patient is required to categorize semantic information or to make responses based on such categorizations, and thus when more controlled processes, requiring greater amount of attentional resources, are needed. However, these results have not been replicated. For example, in another passive sentence-reading task,<sup>76</sup> subjects were presented with sentences that were 4 words long, some containing homographs (ambiguous words). The sentence endings delivered the meaning constraints for the proper selection of the homograph meaning (e.g., *The bank was closed/steep*). Results showed a greater N400 to all sentence endings in patients with schizophrenia. The authors concluded that there was a generalized processing dysfunction, though there was a slightly greater N400 activity to subordinate sentence endings. These results were replicated in an active version of the study,<sup>77</sup> where subjects had to judge the sentences as making sense or not.

It is important to consider overlapping waves when interpreting the N400 results. In the passive-reading study reported by Andrews et al,<sup>70</sup> the latency of the N400 *peak* was slightly delayed in patients, though the onset of the waveform itself was the same as in healthy subjects. Furthermore, the N400 difference between congruous and incongruous word endings lasted longer in the patients (more than 700 ms), whereas in healthy individuals, this difference resolved itself by 600 ms. It is possible that these 2 differences are not the result of N400 differences but of abnormalities in the P600. This component peaks later than the N400, but its onset overlaps with the N400. Therefore, it decreases the apparent size of the N400; however, the smaller the P600, the less significant this decrease. In schizophrenia, this fact is important because many teams have found smaller P600s in patients than in healthy individuals.<sup>68,70,71,76,78</sup> Therefore, in patients, the persistence of the N400 in the related condition (where there are congruous word endings or semantically related words) may be because it is less masked by the positive waveform that succeeds it. Accordingly, the real N400 could

always be smaller in patients with schizophrenia than in healthy controls. In terms of the integration hypothesis, the reduced N400 would mean less integration efforts in patients.

Given that it is now thought likely that N400 taps into higher-order postlexical stages of processing, it is improbable that the N400 abnormalities in patients with schizophrenia are indicative of an overspread of automatic activation. However, this does not preclude the involvement of this overspread in the generation of abnormal N400s. It is possible that the N400 is larger in patients with schizophrenia *because of* the hyperpriming. This hyperpriming could indeed lead to difficulties in the integration of the greater-than-normal amount of activated knowledge. Another possibility lies in the inhibition hypothesis, which proposes that the N400 may actually reflect inhibitory mechanisms that usually subserve the screening out of irrelevant information.<sup>33,79,80</sup> Thus, if there is hyperpriming in patients with schizophrenia and thought disorder, their larger N400s could be reflecting the greater amount of inhibition that must occur in those conditions. Interestingly, several works, including N400 studies, suggest that inhibition or suppression mechanisms may also be deficient in patients with schizophrenia. Sitnikova et al,<sup>81</sup> for instance, presented subjects with sentences in which the first clause ended with a homograph. The second clause started with a target word that was always semantically congruent with the dominant meaning of the homograph (e.g., "The book must have had great *stories* because the *author* won an award for it" v. "The skyscraper had ninety *stories* because the *author* won an award for it"). ERPs recorded to the target words that were at the beginning of the second clause revealed an attenuated N400 to incongruent targets. This indicates that the patients failed to suppress the activation of the context-inappropriate dominant meaning of the homograph.

Whatever the nature of the deficits in these patients, it is important to consider that they may not be limited to language-based systems. In a semantic matching task that used pictures of common words and animals, results revealed a delayed N400 latency and a reduced N400 effect in patients.<sup>82</sup>

### Neurochemicals, schizophrenia and N400

Defects in chemical neurotransmission have been proposed as the underlying cause of the symptoms of

schizophrenia. Hyperactive dopaminergic transmission has often been suggested as the basis of positive psychotic symptoms.<sup>83</sup> Recent studies at the cellular level have shown that glutamate, and the *N*-methyl-D-aspartate (NMDA)-type glutamate receptor, may also play important roles in the pathogenesis of the disorder.<sup>84-87</sup> Phencyclidine, an NMDA-receptor antagonist, produces several psychotic symptoms, including thought disorder and auditory hallucinations.<sup>88</sup> Ketamine, another NMDA-receptor antagonist, has been shown to induce a similar profile of thought disorder as that found in patients with schizophrenia.<sup>89</sup> These authors reported that the mean scores on the Scale for the Assessment of Thought, Language and Communication did not differ significantly between healthy volunteers receiving ketamine and patients with schizophrenia and thought disorder. Interestingly, ketamine has been found to eliminate the typical effects that the repetition of stimulus presentation has on the N400<sup>90</sup> generator in the anterior mesial temporal lobe.<sup>91</sup> Whether the reduction in the N400 effect seen in patients with schizophrenia could index glutaminergic imbalances has yet to be determined.

## Conclusion

The diagnosis of schizophrenia remains exclusively based on clinical symptoms. However, because of its relation with a core symptom of this disorder, the N400 abnormality may help to bridge the gap between the phenomenology and the pathophysiology of this disorder. To this extent, the abnormal N400 differs from the abnormal P3b wave found in all psychiatric patients, which is due in large part to a deficit in selective attention. By further exploring the neurochemical bases of the mechanisms responsible for the N400 generation, pharmacologic treatments relevant to schizophrenia could be found.

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### 2004 Jock Cleghorn Prize

This prize, which will consist of a cheque for \$500, will be awarded by the CCNP for the best poster presentation by a research trainee (graduate student or clinical resident) at the Annual Meeting of the CCNP. Candidates wishing to have their poster presentation considered should send a covering letter and a copy of their submitted abstract to Dr. Sidney Kennedy at the address below. Those already applying for travel bursaries will automatically be considered for the Jock Cleghorn Prize. All others can contact Dr. Kennedy.

The poster presentations will be judged at the Annual Meeting by a committee consisting of at least 3 members of the Awards Committee (or substitute judges to be chosen by the Council from the CCNP membership if Awards Committee members are unable to attend the Annual Meeting). Topics on either basic or clinical aspects of neuropsychopharmacology will be considered. The poster should represent research in which the graduate student or resident is the primary investigator, and (s)he should be the first author of the submitted abstract. The winner of the award will be announced in the first newsletter after the Annual Meeting.

Please send a copy of the abstract and a covering letter to: Dr. Sidney Kennedy, Psychiatrist-in-Chief, University Health Network, 200 Elizabeth St., 8th Fl., Eaton Wing, Rm. 222, Toronto ON M5G 2C4; fax 416 340-4198; sidney.kennedy@uhn.on.ca

*Deadline for submissions: April 2, 2004*