Published in final edited form as:

Int J Psychophysiol. 2010 February ; 75(2): 63–65. doi:10.1016/j.ijpsycho.2009.12.009.

Psychophysiology of Language Processes in Psychopathology: An Overview of the Special Issue

Stuart R. Steinhauer and Ruth Condray

Department of Psychiatry, University of Pittsburgh School of Medicine VA Pittsburgh Healthcare System Pittsburgh, PA USA

Aberrations in linguistic communication are informative in elucidating the mechanisms that underlie neuropsychiatric disorder. Perhaps foremost among such language dysfunctions are the speech disturbances associated with states of psychopathology, especially the psychotic disorders. As noted by Maher (1991), Bleuler (1911/1950) employed the language utterances of schizophrenia patients to gauge the loss of connectivity among inner associational processes that, at the time, could not be assessed more directly. Modern psychophysiological approaches provide windows into the psychological and neurophysiological systems that serve to encode and access language representations, and thereby provide objective assessments of functional activity. In this special issue, researchers who have probed aspects of linguistic and semantic function in psychopathological disorders present a compendium of recent research findings and reviews of prior work that provide working models for understanding and tracking aspects of language disorder associated with psychiatric illness.

Psychophysiological approaches have been especially powerful in providing evaluation of various aspects of language comprehension processes, ranging from the responses to simple words and meaningful symbols to the evaluations of complex semantic relationships. Many of the early studies of verbal processing employed recordings of event-related potentials (ERPs) to single words. Though Lifshitz (1966) did not find differential effects to word stimuli in his single subject, Begleiter et al. (1969) were able to demonstrate an enhanced positivity (using an occipital electrode, O₂) to visually-presented words that were “taboo” – that is, negative or aversive – in comparison to neutral words or flashes. In the latter study, the effect was maximal on the component occurring between 337 and 350 ms, and appearing to index P300. Subsequent work verified the lateralized electrophysiological effects of meaningful versus nonsense word stimulation (M. Buchsbaum and Fedio, 1969).

A conceptual shift occurred when Kutas and Hillyard (1980a, 1980b) demonstrated that semantic incongruity elicits an enhanced ERP negativity between 250 and 500 ms following the terminal word in a sentence – named the *N400*. Key to their conceptualization was the recognition that not only language, but also semantic, processing is reflected in this scalp negativity (Kutas and Hillyard 1984). This ERP component thereby provides a reliable neurophysiological index of the degree to which a word fits its proximal semantic context, as seen in the *N400*s generated to sentence constructions such as, “The boy wanted cheese on his *hamburger*” versus “The boy wanted cheese on his *bicycle*.” The *N400* elicited by ‘*bicycle*’ is typically more negative than the *N400* generated to ‘*hamburger*.’ The same principle applies

Corresponding author. Tel.: +1-412-954-5366; fax: +1-954-5366; sthauer@pitt.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

to the small units of context established by single words, so that the word pair '*dog-cat*' typically elicits a smaller N400 than does the word pair '*dog-pencil*.' Subsequent research has investigated both the N400 and a late positive component, often seen as a distinct P300 or P600 component, in studies of both healthy processing activities and dysfunction and deficit in psychopathological groups.

Multiple neuroimaging and electrophysiological approaches are now being applied to the investigation of language and semantic processes, including functional magnetic resonance imaging (fMRI), complex frequency analyses of the EEG (Pulvermüller et al., 1995), and magneto-encephalography (MEG), which are represented in the papers comprising this special issue. Deviations in patient performance can be observed in various paradigms, ranging in this issue from the evaluation of single words and pairs of words to the processes elicited by the semantic relationships portrayed in sentences and complex visual scenarios.

Contributions to the issue include comprehensive reviews as well as new experimental findings. Kuperberg and colleagues have provided a critical evaluation of how ERP studies have contributed to an understanding of processes related to disturbance in semantic relationships in schizophrenia and to difficulties related to the functioning of discourse structure. They argue that these types of deficits are interrelated, and are particularly impaired in the presence of clinical thought disorder. In examining fMRI contributions to the evaluation of semantic relationships, Han and Wible note a number of methodological problems that have been considered and overcome. They emphasize that careful parametric manipulations in the fMRI paradigms provide the strongest evidence for impairments in the connectivity and access of the lexical network in schizophrenia.

The semantic priming paradigm has been widely used to investigate the organization and access of linguistic representations stored in memory. In this class of experimental designs, pairs of words are varied in terms of their degree of semantic relationship (*dog-cat versus dog-pencil*), and the behavioral response and ERP elicited by the second word in the pair normally reflect the degree of relatedness in meaning. The priming paradigm has also been used to estimate the relative contributions of automatic activation and controlled attention to semantic processing (Neely, 1991). Because psychopathologies such as schizophrenia are additionally associated with disturbance to attention, it was hypothesized early that an attentional deficit might account for the language problems associated with this psychiatric disorder (Schwartz, 1978). Studies of semantic processing in schizophrenia have therefore incorporated experimental conditions that are believed to bias responding in the direction of these functional mechanisms. One such manipulation involves the use of shorter versus longer interstimulus intervals (stimulus onset asynchronies, SOA) between prime and target words, which, respectively, reveal the influence of automatic activation and controlled attention. Additional strategies believed to bias responding toward either automatic or controlled processing include varying the proportions of semantically associated word pairs and using behavioral tasks that differ with respect to resource demand and level of processing.

The four papers by Condray, Kiang, Mathalon, and Niznikiewicz all address the question of how semantic memory processes in schizophrenia are influenced by automatic activation. Findings from these studies converge to suggest the presence of semantic disturbance for this patient population even when their responding is biased toward primary or automatic processing.

In the study reported by Condray and colleagues, an incidental semantic priming paradigm was used, in which semantic relatedness and word frequency were varied. The behavioral task was resource demanding, independent of the psycholinguistic factors of interest, and biased toward a shallow (orthographic) level of processing. The N400 priming effect elicited by this paradigm

was therefore assumed to reflect primarily automatic processing. Word frequency is also a critical aspect of lexical processing. How often speakers and writers use a particular word provides information about its psychological importance and salience. Condray et al. demonstrated that as word frequency decreases, N400 increases parametrically in healthy individuals but not in patients with schizophrenia. Rather, the patients were characterized by a deficit in semantic access reflected in a larger N400 to high-frequency words. They also noted a similar pattern of N400 priming for patients receiving either typical or atypical antipsychotics. An interesting finding in the Condray et al. study is that the distribution of the N400 priming effect was more anterior in schizophrenia patients than in healthy controls.

Kiang and colleagues examined the association between semantic processing and schizotypal personality characteristics in healthy volunteers. This domain of character traits includes eccentricities of behavior and distortions in cognition and perception. Lexical decisions were made about word pairs that were directly, indirectly, or not related semantically. Presentation rates (SOAs) were rapid and relatively slow. The magnitude of N400 to target words showed the typical decrease as the degree of semantic relatedness increased. Of importance, N400 priming was correlated with responses on a questionnaire that measures schizotypal personality traits. In particular, the N400 direct priming effect, elicited at both SOAs, was correlated with the score on the cognitive-perceptual scale: A smaller magnitude of direct priming was associated with scores indicating the presence of distortions in cognition and perception. The authors interpreted their findings as support for the hypothesized roles of semantic activation and inhibition processes in the development of unusual beliefs.

Mathalon and co-workers also used a short SOA to capture automatic semantic processing. N400 was recorded to picture-word pairs that provided either an identity match or a non-match. Of interest, non-matching pairs were varied to create a semantic gradient by using exemplars from within versus outside semantic categories. Controls were characterized by a larger N400 priming effect, compared to patients, and groups also differed in their response to the category levels of non-matching target words. Patients' N400 was more negative to matching (primed) words, while controls' N400 was more negative to non-matching (unprimed) words. Moreover, patients and controls differed in their response to the semantic gradient: Controls were characterized by an enhanced N400 to outside category words, but patients' N400 did not differentiate category levels. The authors interpreted the pattern observed for patients as reflecting an overly broad spread of semantic activation, as well as a deficient use of context. Finally, patients with more severe negative symptoms showed a smaller difference in N400 between the within and outside category non-match conditions.

Creating a bias toward automatic activation by employing both a short SOA and a low proportion of semantically-related primes, Niznikiewicz et al. observed the typical N400 priming effect for healthy controls, but the absence of N400 priming for schizophrenia patients. Of interest, the absence of N400 priming for patients paralleled an absence of behavioral priming as well. Moreover, the source of the group difference in N400 priming appeared to be due to patients' reduced N400 amplitude to semantically-unrelated target words. The investigators interpreted the pattern of findings for patients as evidence for an abnormality in early inhibition processes.

The modulation of N400 in relation to strong and weak associations of words, which is typically found for healthy individuals, is impaired among schizophrenia patients, who tend to misinterpret subordinate meanings. To examine this bias further, Salisbury utilized short sentences that included an initial homograph or ambiguous noun whose meaning was made unambiguous by the final word in the sentence, such as "The *toast* was *battered*." His findings for healthy individuals included graded N400 amplitudes to sentence terminal words, ranging from smaller N400 amplitudes elicited by dominant or strong associations to enhanced N400

amplitudes produced by weak or subordinate associations. Patients failed to show these variations in N400. Salisbury argued that, unlike healthy individuals, schizophrenia patients appear to pre-select dominant meanings of the initial words, which may indicate deviations in the associative networks of semantic memory.

Difficulties in the modulation of attention to semantic versus non-semantic task requirements pose a particular difficulty for patients with cognitive disorders. Laurent et al. demonstrated that semantic difficulties were reflected in the ERPs of schizophrenia patients diagnosed with formal thought disorder, even while their processing of the physical characteristics of lexical stimuli appeared to be normal. The N400 priming effect was observed for healthy controls, but not for patients during the lexical decision task. However, when subjects were instructed to attend to non-semantic characteristics of word stimuli (color of the word, not the meaning), both control and patient groups showed responsiveness of the P300 component.

The hypothesis that impairment in the processing of context is a key factor underlying language disturbance in schizophrenia was addressed by Debruille and colleagues. These investigators reasoned that a purer measure of semantic processing can be obtained if the deficit in context processing is controlled or 'circumvented.' To achieve that control, they established context by using only one experimental prime word ("*animal*"), which was repeated throughout the task and was followed by target words that varied in semantic relatedness to that single category prime. Participants were required to decide whether a target word matched the preceding context or prime word ("*animal*"), or simply to pay attention to the target word following a cue word ("*inaction*") indicating that no decision response should be made. Consistent with their hypothesis, Debruille et al. did not observe a priming difference between schizophrenia patients and healthy controls in an ERP window of 320 to 500 ms. In the group of patients, they observed both a deficit in inhibiting responses when no action was required and impaired response preparation when action was required.

An early contribution to research on language function was made by Molfese et al. (1979). They showed that early ERP components reflect phonemic discrimination, which is further associated with semantic processing. Whether disturbance in such early linguistic processing is associated with schizophrenia is an important question that was addressed by Dale and colleagues. Using variations of syllables that differed for voice onset time or place of articulation, these investigators examined the early MEG response, M100, to pairs of syllables. Their results suggest that early phonological processing of the initial syllables of language stimuli is not impaired in schizophrenia. Instead, early phonological processing may be deficient in these patients only when background noise is increased as they listen to successive syllables. Across patients and controls, the magnitude of M100 elicited by successive syllables was correlated with their performance on tests of general intelligence and verbal learning and memory. These findings by Dale et al. are generally consistent with a recent reconceptualization of phonological memory as the integration of neural processes that serve speech perception and production (B.R. Buchsbaum and D'Esposito, 2008). We anticipate that the growing inclusion of MEG approaches to the study of linguistic processes will add substantially to our knowledge of linguistic-based problems in schizophrenia.

The same lexical decision and semantic priming paradigms that have revealed impressive neurophysiological deficits for schizophrenia have shown less abnormality for patients suffering from depression and related mood disorders. Klumpp and Deldin carefully evaluated this literature, with particular attention to hemispheric differences and regional activations. In an additional contribution to the volume, Klumpp and colleagues have provided evidence across three samples of depressed patients that N400 was not differentiated from control levels for sentence terminal words that varied with respect to emotional valence. In contrast, N400

was exaggerated to negative terminal words for their small comparison sample of schizophrenia patients.

Klumpp and Deldin, in their review, also emphasized the importance of the modulation of emotional information, which may be of greater significance in depression than in other psychiatric disorders. Complementary findings favoring this latter emphasis are reported in the paper by Siegle et al., who examined sustained gamma band activity in patients diagnosed with either depression or schizophrenia. Of particular interest is that while lexical identification was not abnormal for the group of depressed patients, they showed exacerbation of gamma band activity when valence judgments were required, in comparison to schizophrenia patients and healthy individuals. It is noteworthy that wavelet analyses allowed examination of sustained gamma activity over a period of many seconds.

Although schizophrenia patients exhibit a preserved 'old-new effect' that is reflected in greater midline parietal positivity to old versus newly presented words, they have been shown to exhibit reduced lateral parietal P300 source activity. Expanding on their previous findings, Kayser and coworkers employed visual stimuli that included words or faces presented in a visual recognition paradigm. Using current source density (CSD) analyses of multielectrode data, they demonstrated that long-latency left parietal old/new effects were reduced in patients over lateral/temporal, but not over midline, electrodes. The working memory deficits observed by Kayser et al. for schizophrenia patients were associated with the recognition of common words but not with the recognition of facial stimuli.

Whereas examination of semantic effects to non-verbal stimuli was provided by Mathalon et al., and comparison of words to non-verbal stimuli in recognition memory was provided by Kayser et al., all of the studies described in this issue involve relatively static stimuli, which is the typical approach used for psychophysiological studies. An innovative approach was developed by Sitnikova et al. that enables examination of the semantic processing stimulated by dynamic scenarios depicted in movies; an overview of their work is provided in this volume. Their data implicate two complementary neurocognitive mechanisms that integrate comprehension of real-world events and their verbal descriptions. The first mechanism involves associative and semantic memory networks and appears to be encoded in the N400. This process may be hyperactive in schizophrenia patients who exhibit symptoms of disorganization. The second mechanism is associated with conceptual knowledge and the goal-related aspects of actions, which may be particularly critical in novel situations. This latter mechanism is reflected in the P600, and may indicate difficulties in real-world processing for schizophrenia patients.

It is apparent from the papers presented in this volume that the most fruitful application of psychophysiological approaches to investigating language and semantic processes has been related to the evaluation of schizophrenia-related disorders. However, there are also exemplary approaches that utilize evaluation of semantic processing to study mood disorders. There are unique aspects of the psychophysiological data that may distinguish underlying components of these psychiatric disorders, and it is likely that these various approaches may be extended to other domains of psychopathology in the future.

In preparing this special issue on language processes, our thanks are due to the reviewers of the individual papers, and, in particular, to the support of the Journal's Editor-in-Chief, Connie C. Duncan. We also note the initial encouragement for this issue by the late John L. Andreassi, former Editor-in-Chief, who was instrumental in establishing the tradition of special topic issues that have provided important resources to the psychophysiology community.

Acknowledgments

Supported by NIMH grants 55762 (SRS) and MH50631 (RC) and by the Medical Research Service of the Department of Veterans Affairs.

References

- Begleiter H, Platz A. Cortical evoked potentials to semantic stimuli. *Psychophysiology* 1969;6:91–100. [PubMed: 5820910]
- Bleuler, E. *Dementia Praecox or the Group of Schizophrenias*. International Universities Press; NY: 1950. translated from the 1911 original German language edition
- Buchsbaum BR, D'Esposito M. The search for the phonological store: From loop to convolution. *J. of Cogn. Neurosci* 2008;20:762–778. [PubMed: 18201133]
- Buchsbaum M, Fedio P. Visual information and evoked responses from the left and right hemispheres. *Electroencephal. Clin. Neurophysiol* 1969;26:266–272.
- Kutas M, Hillyard SA. Reading senseless sentences: brain potential reflects semantic incongruity. *Science* 1980a;207:204–206.
- Kutas M, Hillyard SA. Reading between the lines: event-related brain potentials during natural sentence processing. *Brain and Language* 1980b;11:354–373. [PubMed: 7470854]
- Kutas M, Hillyard SA. Brain potentials during reading reflect word expectancy and semantic association. *Nature* 1984;307:161–163. [PubMed: 6690995]
- Lifshitz K. The average evoked cortical response to complex visual stimuli. *Psychophysiology* 1966;3:55–68. [PubMed: 5942874]
- Maher, BA. Language and schizophrenia. In: Steinhauer, SR.; Gruzeliier, JH.; Zubin, J., editors. *Handbook of Schizophrenia, Vol. 5: Neuropsychology, Psychophysiology and Information processing*. Elsevier; Amsterdam: 1991. p. 437-464.1991
- Molfese, DL.; Papanicolaou, A.; Hess, TM.; Molfese, VJ. Neuroelectrical correlates of semantic processes. In: Begleiter, H., editor. *Evoked Brain Potentials and Behavior*. Plenum Press; New York: 1979. p. 89-106.
- Neely, JH. Semantic priming effects in visual word recognition: A selective review of current findings and theories. In: Besner, D.; Humphreys, GW., editors. *Basic Processes in Reading: Visual Word Recognition*. Erlbaum Associates; Hillsdale, N.J.: 1991. p. 264-336.
- Pulvermüller F, Lutzenberger W, Preissl H, Birbaumer N. Spectral responses in the gamma-band: physiological signs of higher cognitive processes? *Neuroreport* 1995;6:2059–2064. [PubMed: 8580440]
- Schwartz, S. Language and cognition in schizophrenia: A review and synthesis. In: Schwartz, S., editor. *Language and cognition in schizophrenia*. Erlbaum Associates; Hillsdale, N.J.: 1978. p. 237-276.