Language in schizophrenia Part 2: What can psycholinguistics bring to the study of schizophrenia…and vice versa?

Gina R. Kuperberg

‖ Department of Psychology, Tufts University, 490 Boston Avenue, Medford, MA 02155, USA

* Department of Psychiatry, Massachusetts General Hospital and MGH/MIT/HMS Athinoula A. Martinos Center for Biomedical Imaging, Bldg 149, 13th Street, Charlestown, MA 02129, USA

Abstract

This is the second of two articles that discuss higher-order language and semantic processing in schizophrenia. The companion article (Part 1) gives an introduction to language dysfunction in schizophrenia patients. This article reviews a selection of psycholinguistic studies which suggest that sentence-level abnormalities in schizophrenia may stem from a relative overdependence on semantic associative relationships at the expense of building higher-order meaning. Language disturbances in schizophrenia may be best conceptualized as arising from an imbalance of activity across two streams of processing, one drawing upon semantic relationships within semantic memory and the other involving the use of combinatorial mechanisms to build propositional meaning. I will also discuss some of the ways in which the study of schizophrenia may offer new insights into the cognitive and neural architecture of the normal language system.

This is the second of two articles that discuss higher-order language disturbances in schizophrenia. The first article gave an overview of the schizophrenia syndrome and the ways its language abnormalities have been traditionally studied and conceptualized. This article discusses the use and potential for psycholinguistic methods to further characterize language dysfunction in schizophrenia.

As explained in the companion article, two main explanations have been proposed to account for language dysfunction in schizophrenia: abnormalities in semantic memory and abnormalities in the build-up and use of 'context'. 'Context' abnormalities have often been attributed to abnormalities of working memory and/or executive function. These two explanations have usually been considered separately. There have been few attempts to link them together or to relate them to either psycholinguistic or cognitive neuroscience models of the normal language system. Ultimately, however, semantic memory and context-building

mechanisms must interact such that individual elements are combined in specific ways to build a meaningful whole. Understanding the nature of such combination and how interactions between different cognitive mechanisms break down is important in a complex disorder of higher-order thought and cognition like schizophrenia. Language is a well-studied system through which we have some idea about the rules, constraints and mechanisms that allow this type of combination (Jackendoff 2002).

In the first part of the present article, I will discuss a sample of representative studies that have taken a psycholinguistic approach to study schizophrenia (for more comprehensive reviews of language abnormalities in schizophrenia at the level of words, sentences and discourse, see Ditman & Kuperberg In press; Kuperberg et al. 2009; Kuperberg et al. In press). I then discuss some future questions and directions for psycholinguistic research in schizophrenia. Finally, I discuss some of the ways in which the study of schizophrenia may offer insights into the cognitive and neural architecture of the normal language system. More specifically, I will suggest that abnormalities of language function in schizophrenia can be conceptualized within recent frameworks holding that normal language processing is mediated by a dynamic balance between semantic memory-based and combinatorial syntactic-based mechanisms of processing.

Psycholinguistic studies of sentence processing in schizophrenia

Most of the psycholinguistic studies discussed here have used online methods which tap into representations and processes as language is built up in real time. Some have used behavioral methods, requiring participants to self-pace their way through sentences or to make lexical decisions on probe items presented immediately after a sentence. Others have employed scalp-recorded event-related potentials (ERPs)–electrophysiological activity that is time-locked to specific words and then averaged over large number of trials to produce distinct waveforms or components (Luck 2005). I will also consider studies that have used functional neuroimaging methods to yield information about the neuroanatomical basis of language abnormalities in schizophrenia.

1a. Using context in sentences and discourse

Initial online psycholinguistic studies in schizophrenia focused on whether patients were sensitive to semantic 'context' during online processing of language. These studies were inspired by the evidence that the speech of thought-disordered patients is less predictable than that of non-thought-disordered patients (see accompanying article). In an initial study, we used a paradigm developed by Marslen-Wilson and Tyler (1988) in which patients monitored targets words in spoken sentences that violated different types of semantic constraints imposed by their preceding context. We showed that patients who were thought-disordered were relatively less sensitive to such violations than patients without thought disorder and healthy controls (Kuperberg et al. 1998). This insensitivity to context was particularly prominent when the target word violated the constraints of its preceding verb (e.g., "The crowd was waiting eagerly. The man drank the guitar…") rather than the real-world pragmatic constraints of the preceding context as a whole (e.g. "The crowd was waiting eagerly. The man buried the guitar…"). Insensitivity to context also tracked with severity of thought disorder in the same individual patients over time (Kuperberg et al. 2000).

ERP studies have also examined patients' sensitivity to semantic incongruities within sentences, focusing on the N400 waveform which is evoked between 300–500ms after word onset. In healthy individuals, the N400 is evoked by words that are semantically incongruous or unexpected with their preceding context (Kutas et al. 2006). The 'N400 effect' (the attenuation of the N400 amplitude to contextually congruous versus incongruous

words) is thought to reflect the ease of mapping the meaning of a word on to the meaning of its context, with respect to information stored within semantic memory. Most sentence processing studies in schizophrenia have reported that the size of the N400 effect is normal in patients (Andrews et al. 1993; Kuperberg et al. 2006c; Nestor et al. 1997; Niznikiewicz et al. 1997; Ruchsow et al. 2003), although it can be reduced under some circumstances (Adams et al. 1993; Mitchell et al. 1991; Ohta et al. 1999; Sitnikova et al. 2002). Some studies that have introduced the incongruity on sentence-final words have noted a reduction of the N400 effect in patients, perhaps because of the relatively high processing demands as participants attempt to evaluate and 'wrap-up' the meaning of an implausible sentence as a whole. The N400 effect is also smaller in patients than controls when there is a requirement to build context over more than one sentence: Ditman and Kuperberg (2007) showed that, unlike controls, patients failed to attenuate the N400 to words that violated their discourse context, even when the critical word was semantically congruous with its immediate sentence context.

Finally, in an fMRI study comparing semantically incongruous and normal sentences, patients showed normal modulation of temporal and inferior frontal cortices. However relative to controls, they showed reduced activity within the dorsolateral prefrontal cortex (DLPFC) and inferior parietal cortex (IPC; Kuperberg et al. 2008)–regions that may be engaged when the costs of constructing an implausible overall sentence meaning are high.

1b. Using context to resolve lexical ambiguity

A second approach has focused on the resolution of lexical ambiguity within sentences. Here, the attempt has been to explain why patients' language is dominated by semantic associations at the expense of using overall context. Most of this research comes from the study of homonyms–words that sound the same but that have more than one meaning.

There is a long history of studying homonyms in schizophrenia, going back to the early 1960s when Chapman et al. (1964) reported that, in comprehending sentences like "When the farmer bought a herd of cattle, he needed a new pen", patients were more likely than healthy adults to misinterpret "pen" in terms of its dominant meaning (a writing instrument) rather than its contextually appropriate subordinate meaning (a place where animals live). To examine the online mechanisms leading to such errors, Titone et al. (2000) asked participants to listen to sentences containing homonyms and to make lexical decisions to visually-presented target words presented after each sentence. These target words were either semantically related or unrelated to either the dominant or the subordinate meaning of the homonym. When the sentence context biased moderately towards the homonym's subordinate meaning, controls failed to show priming of the homonym's dominant meaning. This indicated that they used the moderately constraining context to suppress the homonym's dominant meaning. Patients, in contrast, showed priming of the homonym's dominant meaning suggesting that it was not suppressed by the context. Encouragingly, in the same experiment, patients were able to use a more strongly biasing context to suppress the homonym's dominant meaning.

Sitnikova et al. (2002) took a similar approach with ERPs, measuring the amplitude of the N400 waveform. In this study, participants read sentences that biased towards either the dominant meaning (e.g., "Diving was forbidden from the bridge…") or the subordinate meaning (e.g., "The guests played bridge…") of a homonym ("bridge"); the second clause introduced a critical word that was always semantically associated with the dominant meaning of the homonym (e.g., "…because the river had rocks in it"). As expected, healthy adults produced a reduced N400 to contextually appropriate versus inappropriate words in the second clause (e.g. to "river" when the initial context was "Diving was forbidden from the bridge…" versus "The guests played bridge…"). In schizophrenia patients, however, the

amplitude of the N400 to "river" was equal in both conditions: the dominant meaning of the homonym ("bridge") appeared to have inappropriately primed "river", despite the incongruous context. Critically, the same patients in the same study showed a normal N400 effect to unambiguously contextually incongruous words that, in half the sentences, were introduced towards the end of the second clause (e.g. "cracks" in "…because the river had cracks in it."). Once again, these findings were taken to indicate that patients failed to suppress the contextually inappropriate meaning of the homonym and were inappropriately dependent on semantic associations between individual words at the expense of building whole sentence context.

1c. Pitting semantic associations against syntactic structure

A third line of research has more directly probed interactions between stored lexico-semantic relationships and the build-up of meaning within clauses through syntactic mechanisms in schizophrenia. Consider the sentence (1) "Every morning at breakfast the eggs would eat…". Despite the strong semantic relationship between "breakfast", "eggs" and "eat", the rules of syntax dictate that the sentence has an impossible meaning: "eggs" is syntactically assigned as the Agent (the do-er of the central action, "eat"), even though "eggs" are inanimate and therefore do not possess the semantic properties to be able to eat. After encountering the word "eat", healthy individuals did not experience any initial cost in processing between 300–500ms (they produced no N400 effect). A few milliseconds later, however, they did show increased neural costs, as evidenced by a Late Positivity or P600 effect (Kuperberg et al. 2006a; Kuperberg et al. 2007b; Kuperberg et al. 2003b, reviewed by Kuperberg, 2007). The P600 effect may reflect increased and prolonged attempts to construct an implausible propositional meaning, particularly when there is increased need to *override* semantic relationship that match information stored within semantic memory–in this case the relationships between "eggs" and "eat".[1] In other words, despite the temporary 'semantic illusion' (the failure to produce an N400 effect to the semantic violation on "eat"), healthy individuals engage in additional processing and eventually use syntactic constraints to derive a final interpretation of the sentence, even if it is highly implausible.

Sentences such as (1) contrast with sentences like (2): "Every morning at breakfast the boys would plant…". This sentence is also incongruous with real-world knowledge, but here the incongruity does not arise from the syntactic structure of the main clause (boys can plant), but rather through relating it to words in the preceding context. In this case, healthy individuals produce an N400 effect to "plant", reflecting a relatively greater processing cost in mapping semantic relationships between incoming words on to relationships stored within semantic memory (boys are unlikely to plant at breakfast time).

We used these stimuli to examine the relationship between semantic and syntactic processing in schizophrenia (Kuperberg et al. 2006c). Schizophrenia patients produced a normal N400 response to sentences like (2), suggesting that they were able to map incoming information on to stored semantic relationships. In addition, like healthy controls, they also failed to show an N400 effect to words such as "eat" in sentences like (1). Unlike controls, however, they failed to produce a later P600 effect to these violations. Moreover, they were more likely than controls to erroneously classify these sentences as normal rather than semantically anomalous (see also Kuperberg et al. 2006b). In other words, patients failed to register the implausibility of the proposition, and both their online processing and their final interpretation of these sentences were driven by semantic relationships between the

---

[1]"eggs" and "eat" share a strong associative relationship. They also share a strong thematic relationship: although eggs cannot eat, eggs, and other inanimate things, can be eaten. Exactly what type of stored semantic relationship is critical to producing this pattern of effects is under debate (Kuperberg 2007).

individual words rather than by the combination of individual meanings of words and syntactic structure.

2. Directions for psycholinguistic research into language dysfunction in schizophrenia

Taken together, the types of findings reviewed above suggest that schizophrenia patients have difficulties in using combinatorial mechanisms to build up whole sentence meaning, particularly if it is implausible, and that their comprehension is inappropriately driven by stored semantic information about a word and its associations. As discussed below, a major question for future psycholinguistic research is whether this *imbalance* between combinatorial and semantic associative processing is a general principle that can explain the full range of language abnormalities seen in schizophrenia, as described in the companion article.

2a. Relationships with thought disorder and language output

The inspiration for most psycholinguistic studies carried out in schizophrenia to date has been the phenomenon of 'thought disorder', in which associations between individual words dominate language output at the expense of building up sentence or discourse level context. Thought disordered language output is seen in only a subset of patients with schizophrenia. Yet, in almost all of the online psycholinguistic studies described above, abnormalities have been observed both in patients with and without clinical evidence of thought disorder at the time of testing. This suggests that they may characterize schizophrenia as a whole–an idea that was originally proposed by Bleuler (who coined the term 'schizophrenia') who saw 'loosening of associations' as a basic cognitive disturbance that could explain multiple features of the disorder (Bleuler 1911/1950). However, it raises several important questions about the link between these psycholinguistic abnormalities and the clinical phenomenon of thought disorder itself.

One possibility is that 'thought disorder' only becomes clinically manifest when an imbalance between the build-up of propositional meaning and semantic associative processing is at its extreme. Consistent with this idea, some studies have shown that, within the cohort of schizophrenia patients tested, the behavioral and neural impairments described are the most severe in the most thought-disordered patients (Kuperberg et al. 2006b; Kuperberg et al. 1998). A related possibility is that an *additional* abnormality of semantic memory function is necessary to tip the system into further imbalance and produce clinical thought disorder. One candidate might be a superimposed *automatic* overactivity within the semantic associative network which appears to be relatively specific for thought disorder (see accompanying article).

A related question is how an over-reliance on stored semantic associations affects language *production*, which is how thought disorder is clinically assessed and quantified. To date, the types of psycholinguistic paradigms used to study schizophrenia have all measured language comprehension. The underlying assumption has been that these comprehension studies tap into the same semantic associative abnormalities that affect production. However, there has been little work testing this assumption. An important direction for future psycholinguistic research in schizophrenia will therefore be to use language production paradigms to determine how and when semantic associative disturbances interact with the stages of lexical access, selection and monitoring during the production of words, sentences and discourse.

2b. Syntactic complexity

As explained in the accompanying article, there is evidence that the speech produced by schizophrenia patients is syntactically less complex than that of healthy controls. In addition, patients show some deficits in comprehending long and grammatically complex sentences. Patients' impairment in comprehending syntactically complex sentences correlates with their poor performance on a verbal working memory (WM) span task. These findings have generally been taken as evidence that syntactic impairments in schizophrenia are mediated by their WM dysfunction (Bagner et al. 2003; Condray et al. 1996; Condray et al. 2002). This conclusion, however, may be premature for several reasons. First, the correlation between poor WM function and language function may be mediated by other un-measured variables. Second, although globally impaired in comprehending syntactically complex sentences, patients show the same *relative* deficit as controls in comprehending syntactically more complex object-relative sentences, e.g., "The candidate that the governor endorsed lost the campaign", relative to less complex subject-relative sentences, e.g., "The chemist that questioned the professor discovered the cure" (Bagner et al. 2003; Condray et al. 1996; Condray et al. 2002). It is therefore possible that patients are able to engage certain syntactic mechanisms that are not reliant on general WM resources to distinguish between these two types of sentences. Their global deficits in comprehending long and syntactically complex sentences may result from deficits in combining syntactic with lexico-semantic information to assign (or reassign) thematic roles and/or in evaluating the resulting proposition for plausibility, and it may be these deficits that are mediated by their more general WM impairment (see Caplan & Waters 1999 for discussion with respect to normal language comprehension and aphasias). As discussed above, such impairments may, in turn, lead to patients' over-reliance on semantic associations between individual words for interpretation.

These ideas are fairly speculative. The dependent measure in these studies has been end-of-sentence judgments about 'who did what to whom'. This limits any inferences that can be made about the specific stages and mechanisms at which patients' deficits arise. Semantic relationships between words and plausibility have not been explicitly manipulated. The use of online psycholinguistic methods may be able to test these hypotheses more definitively.

2c. Discourse-level abnormalities and figurative language

Many of the clinical phenomena that characterize thought-disordered speech, such as tangentiality and derailment, suggest impairments in building causal and logical coherence *across* sentences. As also discussed in the accompanying article, patients' also show clear abnormalities in establishing referential coherence. Despite these observations, there are hardly any studies examining online mechanisms of discourse-level impairments in patients. This may be a particularly fruitful area of research given that, as discussed in section 2b, some current models of normal discourse processing place a large emphasis on the contributions of stored relationships within semantic memory to the buildup of coherence (see Ditman and Kuperberg, 2009, for an overall framework for studying discourse comprehension in schizophrenia).

It will also be important for future studies to determine whether an imbalance between combinatorial and semantic memory-based processes contributes to patients' problems in comprehending figurative language. Some preliminary evidence for this idea comes from a behavioral priming study by Titone et al. (2002). In this study, patients were presented with idioms which are thought to be stored within semantic memory as a whole. Some idioms such as "kick the bucket" that had both non-literal interpretations and plausible literal interpretations. These idioms effectively primed targets that were related to their literal meaning (e.g. "shovel"). Unlike in healthy controls, however, they failed to prime targets that were related to their non-literal meaning (e.g. "death"), perhaps because patients were

unable to select between the non-literal and literal interpretations which were both readily available. This pattern of findings contrasted with that seen to idioms whose literal interpretations were implausible, e.g. "be on cloud nine". These idioms did effectively prime target words that were semantically related to their idiomatic meanings (e.g. "elated"). It is possible that a relative impairment in engaging additional combinatorial processing to construct the implausible literal meaning of such idioms resulted in less conflict and increased access to the stored idiomatic meaning.

3. And vice versa?

Above, I have argued above that a psycholinguistic approach can guide research into higher-order language dysfunction in schizophrenia. I now consider the reverse perspective. Can studying schizophrenia offer new insights into the cognitive and neural architecture of the normal language system?

There are, of course, important caveats in taking this approach. Schizophrenia is a heterogeneous disorder and there is much variation in the symptoms and signs exhibited by individual patients. In addition, most patients are on psychoactive medications that further complicate the clinical and cognitive picture. Putting these concerns aside for now, however, I suggest that studying language in schizophrenia may still yield some interesting insights into the frameworks and mechanisms of normal language processing.

3a. The role of semantic memory during sentence processing

Traditional models of sentence parsing have generally taken their cue from generative linguistic models which have emphasized the syntactic principles by which individually stored lexical items (words) are combined together. According to such models, the unit extracted from memory is a single word which is slotted into syntactic structure to assign theta roles around a verb, thus building up the meaning of a proposition. Classic two-stage models hold that stored *relationships* within semantic memory, and real-world knowledge, influence processing only during a second stage of processing that follows initial structure building (Ferreira & Clifton 1986; Frazier & Rayner 1982). Constraint-based models more fully acknowledge the influences of semantic relationships during the earliest stages of processing, but still assume that they act through the syntax, i.e. by modulating activity of syntactic frames (Boland & Tanenhaus 1991; MacDonald et al. 1994; Marslen-Wilson et al. 1988; Tanenhaus & Carlson 1989; Trueswell & Tanenhaus 1994; Tyler 1992). Both types of models have usually assumed that any meaning derived purely from the semantic features of words (e.g. semantic associations or other types of semantic relationships) will challenge the syntactic structure of a sentence and lead to increased processing costs only when the syntax is ambiguous or complex.

Over the past few years, this assumption has begun to be challenged. There is now strong evidence that semantic *relationships* stored within memory impact the earliest stages of processing words within sentences (Ferreira 2003; Kutas & Federmeier 2000), sometimes even operating to *predict* semantic features of upcoming words (DeLong et al. 2005; Federmeier 2007; van Berkum et al. 2005). Various types of stored semantic information have been shown to directly influence sentence processing, including lexical-associative (Van Petten 1993) and featural (Federmeier & Kutas 1999) relationships, relationships that determine the likelihood or plausibility of real-world events and states (Ferretti et al. 2001; Hagoort et al. 2004; Kuperberg et al. 2003b; McRae et al. 2005), verb-based selection restrictions (Friederici & Frisch 2000), animacy-based relationships (Frisch & Schlesewsky 2001; Paczynski & Kuperberg 2009; Weckerly & Kutas 1999) and pragmatic knowledge (Nieuwland & Kuperberg 2008; van Berkum et al. 2008). These types of prestored relationships can, at least under some circumstances, act relatively independently of syntax

in influencing the semantic processing of incoming words within sentences. I refer to them collectively as constituting a semantic memory-based stream of processing.[2]

Several sentence processing frameworks have recently been developed that incorporate this type of direct influence of stored semantic relationships, at various grains of representation, on sentence processing. Such semantic memory-based processing may operate in parallel with mechanisms by which syntactic and semantic constraints are used together to assign (or reassign) thematic roles, thereby constructing the full meaning of a proposition (Kuperberg 2007). I refer to such mechanisms collectively as constituting a combinatorial stream of processing.

In many cases, the input matches stored semantic relationships. In such cases, a semantic memory-based analysis yields representations that are plausible and 'good enough' for accurate comprehension, without requiring prolonged combinatorial analysis (Ferreira 2003). However, in some cases, semantic memory-based mechanisms may detect a match between input and stored material, but a full combinatorial analysis yields a proposition that is either syntactically unlicensed (Gunter et al. 2000), or highly semantically implausible (Hoeks et al. 2004; Kolk & Chwilla 2007; Kuperberg et al. 2006a; Kuperberg et al. 2007b; Kuperberg et al. 2003b). In such cases of conflict, the comprehender is required to override the semantic memory-based analysis and to reanalyze or continue to analyze the input combinatorially to reach an accurate interpretation, even if this interpretation is implausible (Kolk & Chwilla 2007; Kuperberg 2007).

This conception of sentence processing is a more dynamic one than classical models suggest. Both semantic memory-based and full combinatorial streams of processing are seen to function independently, and perhaps are mediated by distinct neural networks. However, they still interact closely, resting in a state of balance such that, in cases of conflict, memory-based mechanisms are usually overridden.

Seen in the light of this type of dynamic model, sentence processing abnormalities in schizophrenia may best be understood as arising from an *imbalance* in activity between semantic memory-based and combinatorial mechanisms: unlike healthy controls, patients may fail to engage in additional combinatorial processing; interpretation (and possibly production) may therefore be driven primarily by semantic memory-based processes. Understanding the precise nature of this imbalance–whether it originates from abnormalities in semantic memory-based activity, deficits in combinatorial processing, or a combination of both–may allow us to work backwards to better understand the interactions between these streams of processing in healthy individuals. In addition, studying the *types* of semantic relationships that patients can and cannot use during sentence comprehension (e.g. purely associative, categorical, those relying on particularly salient semantic features such as animacy) may yield insights into the types of relationships that are stored and drawn upon during normal language comprehension, and how they interact with one another.

3b. The role of semantic memory during discourse processing

Models of text and discourse processing have acknowledged the critical role of semantic memory mechanisms in comprehension for some time. According to many such models, incoming semantic relationships between individual words passively 'resonate' with those relationships stored within semantic memory. This resonance can facilitate the processing of upcoming information, contributing to the generation of both causal and referential coherence links across clauses (Cook et al. 1998; Kintsch 1988; Kintsch 1998; McKoon &

---

[2]It is important to recognize that semantic memory-based processing may not be unitary in nature and that the retrieval of these different types of semantic relationships may be subserved by distinct neural networks operating within the same time window.

Ratcliff 1989; Myers & O'Brien 1998; Myers et al. 1994; Sanford & Garrod 1981; Sanford & Garrod 1998).

In such discourse models, however, there remain many questions about *what types of* relationships resonate with incoming information and to what degree they can explain our ability to construct different types of relationships across sentences. While pure semantic associative relationships can account for some aspects of coherence building across clauses, they may not always be sufficient (Kuperberg et al., in press). It therefore seems likely that, just as in sentence processing, semantic relationships stored at different grains of representation are drawn upon to make sense of discourse. Once again, turning to a disorder that is characterized by both abnormalities in semantic associative processing as well as in constructing coherence relationships across clauses may yield useful insights into the interactions between these mechanisms.

3c. The role of domain-general processes

Another assumption of traditional models is that the language system is modular, drawing upon representations and cognitive operations that are unique to language (Fodor 1988). In some processing models of sentence comprehension, aspects of syntactic parsing are thought to rely on specialized working memory systems rather than more domain-general mechanisms (Caplan & Waters 1999; Grodzinsky 2006). For example, Caplan and Waters (1999) have suggested that some aspects of parsing are dependent on language-specific WM resources, while general WM resources mediate semantic-syntactic integration and the full interpretation of a proposition. On the other hand, others have argued that these systems are not so easily segregated and that both draw upon more general WM resources (Just & Carpenter 1992).

As discussed above, patients with schizophrenia have poor working memories and also show impairments in producing and comprehending syntactically complex sentences. From the perspective of schizophrenia research, the main question asked has been to what degree such general cognitive dysfunction can explain language dysfunction. Here I suggest that this question can be turned around: that the study of schizophrenia may yield insights into the role of such domain-general functions in the normal language system. Indeed, extending an 'individual differences approach' to schizophrenia patients may be a particularly fruitful given the large heterogeneity in WM and language function within this population. For example, if, as suggested in section 2b, online measures do show that some stages of language processing are spared in schizophrenia, but that other stages of comprehension are impaired, and if the latter but not the former can be explained by patients' WM deficits, this would provide compelling evidence for some specialization of language processes. It will also be important to extend this approach to the level of discourse where individual differences in WM capacity pattern with individual differences in a wide range of functions, including the establishment of co-reference and causal inferencing (Just & Carpenter 1992; Nieuwland & van Berkum 2006; Singer & Ritchot 1996).

Finally, there has been relatively little work in healthy individuals examining relationships between specific psycholinguistic processes and specific types of executive mechanisms such as inhibition, selection and monitoring. As discussed in the companion article, patients with schizophrenia perform poorly on most neuropsychological tasks of executive function and there has been move towards defining the more specific executive mechanisms that are spared or impaired in schizophrenia. Integrating this more specific approach to understanding patients' executive deficits with a psycholinguistic approach may have implications for understanding the relationships between specific stages of language processing and specific types of executive function in healthy individuals.

3d. Links to non-verbal comprehension, thought and behavior

Finally, and perhaps most speculatively, a deeper understanding of language in schizophrenia may provide a window into relationships between the language system and non-verbal higher-order thought, comprehension and behavior. As highlighted above, traditional linguistic models have generally regarded language as an insular system composed of its own sets of unique representations and processes. Again, however, such notions have been theoretically challenged with the idea that many aspects of higher-order thought, non-verbal comprehension and behavior may rely on representations and combinatorial processes that are analogous to those drawn upon in the language system (Jackendoff 2007). In addition, recent experimental evidence from our lab suggests that that the comprehension of simple visual events may engage some of the same types of neurocognitive mechanisms as those which mediate language comprehension: in a series of studies using silent non-verbal video-clips, Sitnikova et al. (2008) showed that clips depicting events that were possible to execute, but incongruous (versus congruous) with their context evoked an N400 effect. In contrast, clips depicting events that were impossible to execute in semantically constraining contexts (e.g. shaving with a rolling pin following a context in which a man applies shaving cream to his face in a bathroom) additionally evoked a P600 effect, similar to that seen to impossible linguistically-described events (e.g. …the eggs would eat…, see section 2c).

As reviewed in the accompanying article, the clinical language disturbances in schizophrenia co-occur with many other abnormalities of thought and behavior. For example, symptoms of language disorganization are often seen together with a disorganization of behavior, while negative thought disorder co-occurs with impairments of goal-directed behavior. Although there has been little work exploring the neurocognitive basis of relationships between verbal and non-verbal symptoms in schizophrenia, a recent study from our lab suggests that they may share some common neural mechanisms. Using the silent video-clip paradigm described above, Sitnikova et al. (2009) found that, within a group of schizophrenia patients, the magnitude of the N400 attenuation to congruous (versus incongruous) video-clips correlated with severity of behavioral disorganization. It is therefore possible that, just as increased activity within semantic memory networks may lead to the inappropriate intrusion of semantically associated lexical items into speech, it may also lead to inappropriate intrusions of semantically related actions or entities into ongoing behavior (Andreasen 1984). In contrast, the magnitude of the P600 effect was abnormally attenuated in patients, and its smaller magnitude was associated with clinical ratings of poor goal-directed behavior. Thus, distinct neurocognitive abnormalities may underlie disorganization and goal-directed behavior deficits in schizophrenia.

This type of work is in its infancy but it begins to show how it may be possible to draw links between symptomatology of schizophrenia and mechanisms of language and non-verbal higher order thought and behavior.

3e. Cognitive neuroscience of language processing

At first glance, it may not be immediately obvious how studying schizophrenia can inform our understanding of the functional neuroanatomy of language processing in the brain. The classic, neurolinguistic models of language processing and production were inspired by the study of aphasic patients with discrete lesions. They held that specific language modules were localized to distinct regions around the perisylvian fissure. Schizophrenia, by contrast, is a disorder characterized by subtle but widespread structural (Kuperberg et al. 2003a) and functional (Bullmore & Fletcher 2003; Ford et al. 2002; Friston 1998; Kuperberg et al. 2008; Wolf et al. 2007) abnormalities across cortical and subcortical regions.

However, an overview of the aphasia and functional neuroimaging literature suggests that language processing is not confined to perisylvian regions (Osterhout et al. In press). Rather, it is widely distributed across cortical and subcortical networks, engaging not only the perisylvian cortex, but also the inferior, anterior and medial temporal lobes, the parietal cortex, and subcortical regions including the basal ganglia and thalamus (Dick et al. 2001; Kaan & Swaab 2002; Osterhout et al. In press; Vigneau et al. 2006)

An important question in cognitive neuroscience is how exactly these networks work together to build meaning. Is it possible to neuroanatomically dissociate language networks engaged in different types of psycholinguistic operations? How and at what stage do these networks interact? Are these neural mechanisms reciprocally linked such that an over-engagement of one network is necessarily accompanied by an under-engagement of another? The study of language processing in a widespread functional disorder such as schizophrenia may help us begin to address some of these questions.

As discussed in the accompanying article, there is evidence that schizophrenia patients show abnormal increases in activity within temporal and anterior inferior frontal cortices to semantically associated versus non-associated word-pairs (Kuperberg et al. 2007a). As discussed in section 1a of the present article, patients also show abnormally reduced activity within the DLPFC and IPC to semantically implausible sentences (Kuperberg et al. 2008). I have suggested that, in healthy individuals there is a tight interaction and balance between combinatorial and semantic memory-based mechanisms of language processing, and that this balance is awry in schizophrenia patients: in patients, a failure to engage in additional combinatorial processing to make sense of highly implausible propositions may lead to an increased dependence on semantic associations, and conversely an increased reliance on semantic associations may bias away from additional combinatorial processing in cases of conflict. If this is the case, then it may be possible to fully dissociate activity across temporal-inferior frontal and DLPFC-IPC networks across patients and controls within the same paradigm.

Conclusion

Schizophrenia is a highly complex disorder that affects many aspects of higher-order thought and meaning. Language is a highly complex system. Both, arguably, are unique to humans and there has even been some speculation that their evolution may be linked (Crow 2000). Understanding the relationships between the two is clearly extremely challenging. What I have argued in this review is that, because language is a well-studied system through which we have some insights into how we construct higher-order meaning, and because its processing is dependent on fast, interactive, and widely distributed neural networks, psycholinguists and cognitive neuroscientists of language have an important perspective to offer schizophrenia research. While I certainly do not conceive of schizophrenia as serving as a well-understood model to study normal language processing, I do suggest that examining the two systems alongside one another may lead to new insights into the architecture of the normal language system.

Acknowledgments

References

Adams J, Faux SF, Nestor PG, Shenton M, Marcy B, Smith S, McCarley RW. ERP abnormalities during semantic processing in schizophrenia. Schizophrenia Research. 1993; 10:247–257. [PubMed: 8260443]

Andreasen, NC. The Scale for the Assessment of Positive Symptoms (SAPS). Iowa City, IA: The University of Iowa; 1984.

Andrews S, Shelley A, Ward PB, Fox A, Catts SV, McConaghy N. Event-related potential indices of semantic processing in schizophrenia. Biological Psychiatry. 1993; 34:443–458. [PubMed: 8268329]

Bagner DM, Melinder MR, Barch DM. Language comprehension and working memory deficits in patients with schizophrenia. Schizophrenia Research. 2003; 60:299–309. [PubMed: 12591591]

Bleuler, E. Dementia Praecox, or the Group of Schizophrenias. New York: International Universities Press; 1911/1950.

Boland, J.; Tanenhaus, MK. The role of lexical representation in sentence processing. In: Simpson, GB., editor. Understanding Word and Sentence. Amsterdam: North Holland; 1991. p. 331-366.

Bullmore E, Fletcher P. The eye's mind: Brain mapping and psychiatry. The British Journal of Psychiatry. 2003; 182:381–384. [PubMed: 12724239]

Caplan D, Waters GS. Verbal working memory and sentence comprehension. Behavioral and Brain Sciences. 1999; 22:77–94. discussion 95–126. [PubMed: 11301522]

Chapman, LJ.; Chapman, JP.; Miller, GA. A theory of verbal behaviour in schizophrenia. In: Maher, BA., editor. Progress in Experimental Personality Research. San Diego, CA: Academic Press; 1964. p. 49-77.

Condray R, Steinhauer SR, van Kammen DP, Kasparek A. Working memory capacity predicts language comprehension in schizophrenic patients. Schizophrenia Research. 1996; 20:1–13. [PubMed: 8794488]

Condray R, Steinhauer SR, van Kammen DP, Kasparek A. The language system in schizophrenia: Effects of capacity and linguistic structure. Schizophrenia Bulletin. 2002; 28:475–490. [PubMed: 12645679]

Cook AE, Halleran JG, O'Brien EJ. What is readily available during reading? A memory-based view of text processing. Discourse Processes. 1998; 26:109–129.

Crow TJ. Schizophrenia as the price that homo sapiens pays for language: A resolution of the central paradox in the origin of the species. Brain Research Reviews. 2000; 31:118–129. [PubMed: 10719140]

DeLong KA, Urbach TP, Kutas M. Probabilistic word pre-activation during language comprehension inferred from electrical brain activity. Nature Neuroscience. 2005; 8:1117–1121.

Dick F, Bates E, Wulfeck B, Utman J, Dronkers N, Gernsbacher M. Language deficits, localization, and grammar: Evidence for a distributive model of language breakdown in aphasic patients and neurologically intact individuals. Psychological Review. 2001; 108:759–788. [PubMed: 11699116]

Ditman T, Kuperberg GR. The time course of building discourse coherence in schizophrenia. An ERP investigation. Psychophysiology. 2007; 44:991–1001. [PubMed: 17666031]

Ditman T, Kuperberg GR. Building coherence: A framework for exploring the breakdown of links across clause boundaries in schizophrenia. Journal of Neurolinguistics "Language in Schizophrenia," Special Issue. In press.

Federmeier KD. Thinking ahead: The role and roots of prediction in language comprehension. Psychophysiology. 2007; 44:491–505. [PubMed: 17521377]

Federmeier KD, Kutas M. A rose by any other name: Long-term memory structure and sentence processing. Journal of Memory and Language. 1999; 41:469–495.

Ferreira F. The misinterpretation of noncanonical sentences. Cognitive Psychology. 2003; 47:164–203. [PubMed: 12948517]

Ferreira F, Clifton C Jr. The independence of syntactic processing. Journal of Memory and Language. 1986; 25:348–368.

Ferretti T, McRae K, Hatherell A. Integrating verbs, situation schemas, and thematic role concepts. Journal of Memory & Language. 2001; 44:516–547.

Fodor, J. The Modularity of Mind: An Essay on Faculty Psychology. Cambridge: The MIT Press; 1988.

Ford JM, Mathalon DH, Whitfield S, Faustman WO, Roth WT. Reduced communication between frontal and temporal lobes during talking in schizophrenia. Biological Psychiatry. 2002; 51:485–492. [PubMed: 11922884]

Frazier L, Rayner K. Making and correcting errors during sentence comprehension: Eye movements in the analysis of structurally-ambiguous sentences. Cognitive Psychology. 1982; 14:178–210.

Friederici A, Frisch S. Verb argument structure processing: The role of verb-specific and argument-specific information. Journal of Memory and Language. 2000; 43:476–507.

Frisch S, Schlesewsky M. The N400 reflects problems of thematic hierarchizing. NeuroReport. 2001; 12

Friston KJ. The disconnection hypothesis. Schizophrenia Research. 1998; 30:115–125. [PubMed: 9549774]

Grodzinsky, Y. A blueprint for a brain map of syntax. In: Grodzinsky, Y.; Amunts, K., editors. Broca's Region. New York: Oxford University Press; 2006.

Gunter TC, Friederici AD, Schriefers H. Syntactic gender and semantic expectancy: ERPs reveal early autonomy and late interaction. Journal of Cognitive Neuroscience. 2000; 12:556–568. [PubMed: 10936910]

Hagoort P, Hald L, Bastiaansen M, Petersson KM. Integration of word meaning and world knowledge in language comprehension. Science. 2004; 304:438–441. [PubMed: 15031438]

Hoeks JCJ, Stowe LA, Doedens G. Seeing words in context: The interaction of lexical and sentence level information during reading. Cognitive Brain Research. 2004; 19:59–73. [PubMed: 14972359]

Jackendoff, R. Foundations of Language: Brain, Meaning, Grammar, Evolution. New York: Oxford University Press; 2002.

Jackendoff, R. Language, Consciousness, Culture: Essays on Mental Structure. Cambridge, MA: MIT Press; 2007.

Just MA, Carpenter PA. A capacity theory of comprehension: Individual differences in working memory. Psychological Review. 1992; 99:122–149. [PubMed: 1546114]

Kaan E, Swaab TY. The brain circuitry of syntactic comprehension. Trends in Cognitive Sciences. 2002; 6:350–356. [PubMed: 12140086]

Kintsch W. The role of knowledge in discourse comprehension: A construction-integration model. Psychological Review. 1988; 95:163–182. [PubMed: 3375398]

Kintsch, W. Comprehension: A paradigm for cognition. New York: Cambridge University Press; 1998.

Kolk HHJ, Chwilla DJ. Late Positivities in unusual situations. Brain and Language. 2007; 100:257–262. [PubMed: 16919324]

Kuperberg GR. Neural mechanisms of language comprehension: Challenges to syntax. Brain Research, Special Issue: Mysteries of Meaning. 2007; 1146:23–49.

Kuperberg GR, Broome MR, McGuire PK, David AS, Eddy M, Ozawa F, Goff D, West WC, Williams SC, Van Der Kouwe AJ, Salat DH, Dale AM, Fischl B. Regionally localized thinning of the cerebral cortex in schizophrenia. Archives of General Psychiatry. 2003a; 60:878–888. [PubMed: 12963669]

Kuperberg GR, Caplan D, Sitnikova T, Eddy M, Holcomb P. Neural correlates of processing syntactic, semantic and thematic relationships in sentences. Language and Cognitive Processes. 2006a; 21:489–530.

Kuperberg GR, Deckersbach T, Holt D, Goff D, West WC. Increased temporal and prefrontal activity to semantic associations in schizophrenia. Archives of General Psychiatry. 2007a; 64:138–151. [PubMed: 17283282]

Kuperberg, GR.; Ditman, T.; Kreher, DA.; Goldberg, TE. Behavioral and electrophysiological approaches to understanding language dysfunction in neuropsychiatric disorders: Insights from the

study of schizophrenia. In: Wood, SJ.; Allen, NB.; Pantelis, C., editors. The Neuropsychology of Mental Illness. New York: Cambridge University Press; 2009. p. 67-95.

Kuperberg GR, Kreher DA, Ditman T. What can event-related potentials tell us about language, and perhaps even thought, in schizophrenia? International Journal of Psychophysiology. Special Issue on Language and Psychophysiology. In press.

Kuperberg GR, Kreher DA, Goff D, McGuire PK, David AS. Building up linguistic context in schizophrenia: Evidence from self-paced reading. Neuropsychology. 2006b; 20:442–452. [PubMed: 16846262]

Kuperberg GR, Kreher DA, Sitnikova T, Caplan D, Holcomb PJ. The role of animacy and thematic relationships in processing active English sentences: Evidence from event-related potentials. Brain and Language. 2007b; 100:223–238. [PubMed: 16546247]

Kuperberg GR, McGuire PK, David A. Reduced sensitivity to linguistic context in schizophrenic thought disorder: Evidence from online monitoring for words in linguistically-anomalous sentences. Journal of Abnormal Psychology. 1998; 107:423–434. [PubMed: 9715577]

Kuperberg GR, McGuire PK, David AS. Sensitivity to linguistic anomalies in spoken sentences: a case study approach to understanding thought disorder in schizophrenia. Psychological Medicine. 2000; 30:345–357. [PubMed: 10824655]

Kuperberg GR, Sitnikova T, Caplan D, Holcomb PJ. Electrophysiological distinctions in processing conceptual relationships within simple sentences. Cognitive Brain Research. 2003b; 17:117–129. [PubMed: 12763198]

Kuperberg GR, Sitnikova T, Goff D, Holcomb PJ. Making sense of sentences in schizophrenia: Electrophysiological evidence for abnormal interactions between semantic and syntactic processing. Journal of Abnormal Psychology. 2006c; 115:243–256.

Kuperberg GR, West WC, Goff D, Lakshmanan B. fMRI reveals neuroanatomical dissociations during semantic integration in schizophrenia. Biological Psychiatry. 2008; 64:407–418. [PubMed: 18504037]

Kuperberg GR, Paczynksi M, Ditman T. Establishing causal coherence across sentences: An ERP study. Journal of Cognitive Neuroscience. In press.

Kutas M, Federmeier KD. Electrophysiology reveals semantic memory use in language comprehension. Trends in Cognitive Sciences. 2000; 4:463–470. [PubMed: 11115760]

Kutas, M.; Van Petten, C.; Kluender, R. Psycholinguistics electrified II: 1994–2005. In: Traxler, M.; Gernsbacher, MA., editors. Handbook of Psycholinguistics. New York: Elsevier; 2006. p. 659-724.

Luck, S. An Introduction to the Event-Related Potential Technique. Cambridge: MIT Press; 2005.

MacDonald MC, Pearlmutter NJ, Seidenberg MS. The lexical nature of syntactic ambiguity resolution. Psychological Review. 1994; 101:676–703. [PubMed: 7984711]

Marslen-Wilson WD, Brown C, Tyler LK. Lexical representations in language comprehension. Language and Cognitive Processes. 1988; 3:1–17.

McKoon G, Ratcliff R. Semantic associations and elaborative inference. Journal of Experimental Psychology: Learning, Memory, and Cognition. 1989; 15:326–338.

McRae K, Hare M, Elman JL, Ferretti T. A basis for generating expectancies for verbs from nouns. Memory and Cognition. 2005; 33:1174–1184.

Mitchell PF, Andrews S, Fox AM, Catts SV, Ward PB, McConaghy N. Active and passive attention in schizophrenia: An ERP study of information processing in a linguistic task. Biological Psychiatry. 1991; 32:101–124.

Myers JL, O'Brien E. Accessing the discourse representation during reading. Discourse Processes. 1998; 26:131–157.

Myers JL, O'Brien EJ, Albrecht JE, Mason RA. Maintaining global coherence during reading. Journal of Experimental Psychology: Learning, Memory, and Cognition. 1994; 20:876–886.

Nestor PG, Kimble MO, O'Donnell BF, Smith L, Niznikiewicz M, Shenton ME, McCarley RW. Aberrant semantic activation in schizophrenia: a neurophysiological study. The American Journal of Psychiatry. 1997; 154:640–646. [PubMed: 9137119]

Nieuwland MS, Kuperberg GR. When the truth isn't too hard to handle: An event-related potential study on the pragmatics of negation. Psychological Science. 2008; 19:1213–1218. [PubMed: 19121125]

Nieuwland MS, van Berkum JJ. Individual differences and contextual bias in pronoun resolution: Evidence from ERPs. Brain Research. 2006; 1118:155–167. [PubMed: 16956594]

Niznikiewicz MA, O'Donnell BF, Nestor PG, Smith L, Law S, Karapelou M, Shenton ME, McCarley RW. ERP assessment of visual and auditory language processing in schizophrenia. Journal of Abnormal Psychology. 1997; 106:85–94. [PubMed: 9103720]

Ohta K, Uchiyama M, Matsushima E, Toru M. An event-related potential study in schizophrenia using Japanese sentences. Schizophrenia Research. 1999; 40:159–170. [PubMed: 10593455]

Osterhout, L.; Kim, A.; Kuperberg, GR. The Neurobiology of sentence comprehension. In: Spivey, M.; Joannisse, M.; McRae, K., editors. The Cambridge Handbook of Psycholinguistics. Cambridge: Cambridge University Press; In press

Paczynski, M.; Kuperberg, GR. Animacy hierarchy, but not thematic role type, influences direct object argument realization in English: Evidence from event-related potentials. Paper presented at the CUNY Conference on Human Sentence Processing, UC Davis; 2009.

Ruchsow M, Trippel N, Groen G, Spitzer M, Kiefer M. Semantic and syntactic processes during sentence comprehension in patients with schizophrenia: evidence from event-related potentials. Schizophrenia Research. 2003; 64:147–156. [PubMed: 14613679]

Sanford, AJ.; Garrod, SC. Understanding Written Language: Explorations of Comprehension Beyond the Sentence. New York: Wiley; 1981.

Sanford AJ, Garrod SC. The role of scenario mapping in text comprehension. Discourse Processes. 1998; 26

Singer M, Ritchot KF. The role of working memory capacity and knowledge access in text inference processing. Memory & Cognition. 1996; 24:733–743.

Sitnikova T, Goff D, Kuperberg GR. Neurocognitive abnormalities during comprehension of real-world goal-directed behaviors in schizophrenia. Journal of Abnormal Psychology. 2009; 118:256–277. [PubMed: 19413402]

Sitnikova T, Holcomb PJ, Kiyonaga KA, Kuperberg GR. Two neurocognitive mechanisms of semantic integration during the comprehension of visual real-world events. Journal of Cognitive Neuroscience. 2008; 20:2037–2057. [PubMed: 18416681]

Sitnikova T, Salisbury DF, Kuperberg G, Holcomb PI. Electrophysiological insights into language processing in schizophrenia. Psychophysiology. 2002; 39:851–860. [PubMed: 12462512]

Tanenhaus, MK.; Carlson, G. Lexical structure and language comprehension. In: Marslen-Wilson, W., editor. Lexical Representation and Process. Cambridge: MIT Press; 1989. p. 529-561.

Titone D, Holzman PS, Levy DL. Idiom processing in schizophrenia: Literal implausibility saves the day for idiom priming. Journal of Abnormal Psychology. 2002; 111:313–320. [PubMed: 12003452]

Titone D, Levy DL, Holzman PS. Contextual insensitivity in schizophrenic language processing: Evidence from lexical ambiguity. Journal of Abnormal Psychology. 2000; 109:761–767. [PubMed: 11196002]

Trueswell, JC.; Tanenhaus, MK. Towards a lexicalist framework of constraint-based syntactic ambiguity resolution. In: Clifton, C.; Frazier, L.; Rayner, K., editors. Perspectives on Sentence Processing. Hillsdale, NJ: Erlbaum; 1994. p. 155-179.

Tyler, LK. Verb-argument structures. In: Tyler, LK., editor. Spoken Language Comprehension: An Experimental Approach to Disordered and Normal Processing. London: MIT Press; 1992. p. 107-124.

van Berkum JJA, Brown CM, Zwitserlood P, Kooijman V, Hagoort P. Anticipating upcoming words in discourse: evidence from ERPs and reading times. Journal of Experimental Psychology: Learning, Memory, and Cognition. 2005; 31:443–467.

van Berkum JJA, Van den Brink D, Tesink CMJY, Kos M, Hagoort P. The neural integration of speaker and message. Journal of Cognitive Neuroscience. 2008; 20:580–591. [PubMed: 18052777]

Van Petten C. A comparison of lexical and sentence-level context effects in event-related potentials. Special Issue: Event-related brain potentials in the study of language. Language and Cognitive Processes. 1993; 8:485–531.

Vigneau M, Beaucousin V, Herve PY, Duffau H, Crivello F, Houde O, Mazoyer B, Tzourio-Mazoyer N. Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. Neuroimage. 2006; 30:1414–1432. [PubMed: 16413796]

Weckerly J, Kutas M. An electrophysiological analysis of animacy effects in the processing of object relative sentences. Psychophysiology. 1999; 36:559–570. [PubMed: 10442024]

Wolf DH, Gur RC, Valdez JN, Loughead J, Elliott MA, Gur RE, Ragland JD. Alterations of fronto-temporal connectivity during word encoding in schizophrenia. Psychiatry Research. 2007; 154:221–232. [PubMed: 17360163]