Schizophrenia as a disorder of thought, or language? Evidence from brain and behavioral investigations

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Outline

• Big questions, and why this is fun and interesting

• Some background:
  – Schizophrenia
  – Semantic priming
  – MEG and brain/behavior dissociations

• An experiment, and some preliminary results
Language & other systems

• The language faculty is part of the overall structure of the mind/brain

• Interface properties of language systems are imposed by properties of external systems – that is, the systems amongst which language is embedded set constraints on the nature of language

• So, language has the structure it has (whatever that is) because of
  – Internal properties
  – Response to requirements of external systems
Language & other systems

- What happens if these systems are profoundly disturbed?
- A broadly “modular” approach to the investigation of language and its relations with cognitive systems
- The cognitive disorders in schizophrenia are often referred to as “thought disorders”
- The nature of the “language disorder” in this genetically-determined disorder has been less thoroughly investigated
http://www.snowcrystals.com
Schizophrenia

- profound disruption in cognition and emotion
- language, thought, perception, affect, and sense of self

**Positive symptoms:**
- Delusions
- Hallucinations
- Disorganized Thinking
- Disorganized Behavior

**Negative symptoms:**
- Withdrawal, Loss of Motivation and Ambivalence (Avolition)
- Loss of Feeling or an Inability to Experience Pleasure (Anhedonia)
- Poverty of Speech (Alogia)
- Flat Presentation (Affective Flattening)
Semantic Priming

- ACTIVATION
- COMPETITION
- INHIBITION

Stimulus: NURSE

Facilitation

Word recognition

Level of activation

Stimulus: DOCTOR

...etc

HOSPITAL
INJECTION

Stimulus: NURSE

DOCTOR

Stimulus: DOCTOR
Semantic priming in schizophrenia

• Studies of semantic priming in schizophrenia have yielded mixed results, consistent with semantic memory and lexical access being amongst many cognitive systems affected in this heterogeneous disorder. Findings include:
  – **enhanced priming** in schizophrenia (e.g. Spitzer et al 1993, Manschreck et al 1988)
  – **no differences** in priming between controls and schizophrenics (e.g. Blum & Friedes 1995)
  – **impaired priming** in schizophrenia (e.g. Henik et al 1992, Ober et al 1997)
Semantic priming in schizophrenia

• This heterogeneity has given rise to a variety of hypotheses concerning the nature of the underlying impairments in schizophrenia, including:
  – An impairment affecting early processes, especially activation: too many representations are activated, competition and inhibition processes break down as a result (Pizzagali et al 2001)
  – An impairment affecting competition and inhibition: activation of (lexical, conceptual) representations is normal, but inhibition of competitors fails (Titone et al 2000)
MEG

- Magnetic fields associated with current flow within neurons induce a current in a detection coil (magnetometer) at the scalp
- To detect these very small signals, the detection coils are coupled to a superconducting device (maintained at very low temperatures) within a magnetically shielded room
M350: an MEG index of lexical activation

By kind permission: Liina Pylkkanen
http://psych.nyu.edu/pylkkanen/
Brain vs Behavior

• Separation between apparently intact behavior and clearly disordered brain responses
• Validates the addition of neurological measures to behavioral investigations of language
The research question

The M350 is localized to the superior temporal gyrus – a brain region known to show volumetric abnormalities in many individuals with schizophrenia.

Lexical activation can be facilitated in control subjects: a faster M350 is shown when words are preceded by other words that are related in meaning - E.g. doctor primes nurse.

Question:

can we observe facilitation of the M350 in the same way in schizophrenic brains?

Investigation of this issue could permit us to distinguish between hypotheses about the underlying nature of the impairment in schizophrenic thought and language:

Hyperactivation

too many words and ideas are activated, competition and inhibition processes break down as a result

E.g. Pizzagalli et al 2001

→ Abnormalities at M350 predicted

Hypoinhibition

activation of words and ideas is normal, but the inhibition of inappropriate competing representations fails

E.g. Titone et al 2001

→ No abnormalities at M350 predicted
Participants

– **SZ**: Six adults with a clinical diagnosis of schizophrenia, all stable outpatients managed on medication, at least ten years from the time of their first episode. All right handed, three male, mean age 44;10 (range 37-49 years), mean years of education 14;10.

– **Controls**: six adults with no history of neurological or psychiatric disorder, five right handed, three male, matched to schizophrenic participants for age (mean 44;3, range 39-52 years) and years of education (mean 15;4).
Experimental Procedure

Example trials

"quilt"

blanket

Response collected

"zipper"

*REPEAT*

Time

Spoken response
Experimental procedure

Magnetoencephalographic data were concurrently acquired via a 160-channel whole-head gradiometer system (KIT/MIT MEG Lab), sampling at 1kHz, with High Pass filtering at DC and Low Pass at 200Hz. A 60 Hz notch filter was applied.
Behavioral results: reaction times & accuracy

Mean RTs (lines) and mean % correct responses (bars); error bars show ± 1 SD
Results: localization task

SZ: 87 msec

Controls: 93 msec
Control subjects: M350 results

Grand-averaged data for controls, showing M350 peak and field distribution
Schizophrenic subjects: M350 results

Related

Unrelated

RMS peak with approximate M350 distribution; latency is longer to unrelated than related items
Schizophrenic subjects: M350 results

Reversed field pattern, steady state from 200-560 msec; field is switched in Unrelated condition.
Schizophrenic subjects: M350 results

**Related**

**Unrelated**

Multiple dipolar activations in region of interest
How can these results be interpreted?

• The variability in the brain data resists interpretation at anything but an individual level
• Further work will examine the possibility of subgrouping schizophrenic adults on the basis of M350 differences:
  – some have an M350 which approximates to normal and is sensitive to the priming manipulation, suggesting that the early stages of lexical access are not impaired
  – some show an M250 field pattern, but by the M350 time window there are abnormalities, suggesting that deficits in early processes may have downstream effects on lexical processing
  – some have a normal M350 in the Unrelated condition only, possibly indicating that priming is impaired, but that unprimed lexical processing is not
More questions

• Initial examination of other variables (performance IQ, antipsychotic medications, time since onset, performance on language assessments) found no predictive factor correlating with M350 abnormalities

• Current results show a dissociation between behavior which approximates to that of control subjects, and highly variable abnormalities in a brain component known to index (some) processes which underpin performance on the present task

• This suggests that semantic knowledge is available to the schizophrenic adults who took part in our study; we must look at the mechanisms for retrieval of such knowledge to determine possible underlying causes for the language-related deficits in SZ
More questions

• Returning to the bigger question: abnormalities which affect cognitive systems and processes with which language must interface – semantic memory – would appear to impact on how linguistic systems respond and are structured

• This research raises more questions than it answers
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