

# Some Linguistic Signs of Ketamine-Induced Cognitive Impairment

Congzhou He Michael A. Covington  
University of Georgia

James Semple John Brown  
GlaxoSmithKline Plc

Contact: [congzhou@uga.edu](mailto:congzhou@uga.edu)

## Overview

In this study we examine, by computer analysis, the speech of volunteers influenced by sub-anesthetic doses of ketamine, which is often reported to produce schizophrenia-like cognitive impairments (e.g., Malhotra et al. 1996; Adler et al. 1998; Lahti et al. 2001).

We find that sub-anesthetic doses of ketamine have significant, measurable effects upon speech. The most prominent effect is a reduction in the number of verbs, indicating lower syntactic and semantic complexity.

The computer techniques used in this study are likely to be of more general use in psychiatric diagnosis and drug evaluation.

## Ketamine Experiment

During a placebo-controlled, double-blind experiment at Cambridge University, healthy volunteers were asked to describe some pictures from the Thematic Apperception Test (TAT, Murray 1943/1971) after two different sub-anesthetic doses of ketamine and after placebo.

Each volunteer was recorded on 3 occasions at least a week apart. Volunteers were unaware which dose they were receiving unless they felt the effects of the drug.

This study's "low dose" and "high dose" are much smaller than the usual anesthetic dose, specifically:

Low dose = 0.08 mg/kg over 10 min + 0.04 mg/kg/hr x 90 min  
High dose = 0.27 mg/kg over 10 min + 0.14 mg/kg/hr x 90 min  
Usual anesthetic dose = 1 to 4.5 mg/kg (*Physicians' Drug Hbk.* 2003).

Speech was recorded 30 minutes into the experiment.

## Computer Speech Analysis

At the time this analysis was done, 8 volunteers had been recorded successfully under all 3 conditions with the dosage regimen just mentioned. The recordings were transcribed by a linguist who was unaware of the randomized ketamine dosages.

A computer program was written in Java to tokenize the text and perform various counts. To determine part of speech (noun, verb, etc.), each word was passed to *Wordnet 2.0* (<http://www.cogsci.princeton.edu>) through its Java interface and the most common part of speech was counted. This is not strictly correct in all contexts, but hand counting showed that it was accurate enough for the present purpose.

Statistics are tabulated in the chart at the right. Although statistical significance tests are of limited value with such a small sample, *p* values were calculated against placebo with a one-tailed paired *t*-test (Microsoft *Excel*).

## Results

None of the ketamine speech samples sounded abnormal to the "naked ear." Nonetheless, computer analysis found three schizophrenia-like features.

### More nouns, fewer verbs

The most prominent result was that ketamine, even in very low doses, significantly decreased the proportion of verbs and increased the proportion of nouns. Under the influence of ketamine, speakers tended to name and describe objects without stating their actions or relations. Compare the following descriptions from one volunteer (verbs red, nouns blue):

Ketamine-influenced:  
"And a woman looking over a bridge. With, um, docks and housing in the background. With people and the docklands. And unloading a boat."

Placebo:  
"Ok, um, appear to be a sort of beach scene. And there's two women in the picture. Um looks as if there's water in the background."

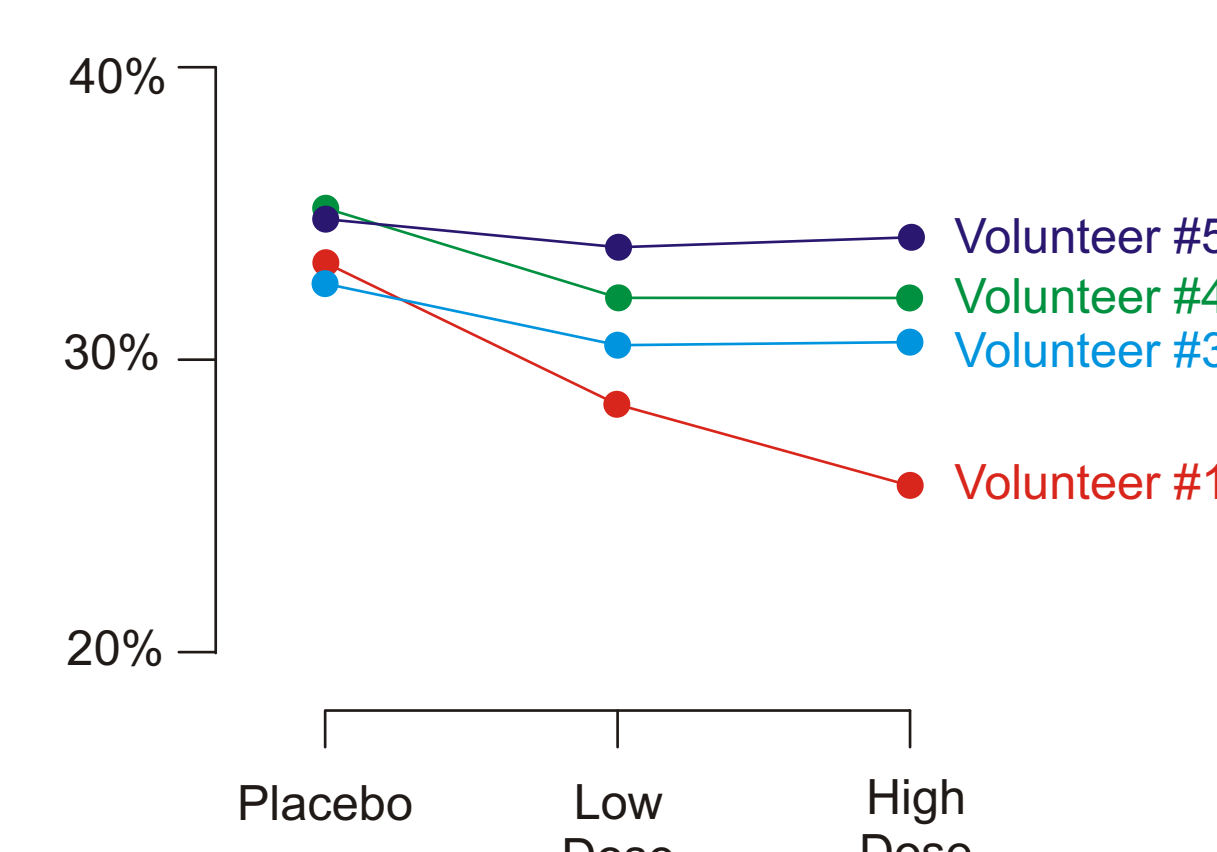
### More fillers

Ketamine significantly increased the frequency of fillers like *um*, *uh* in speech.

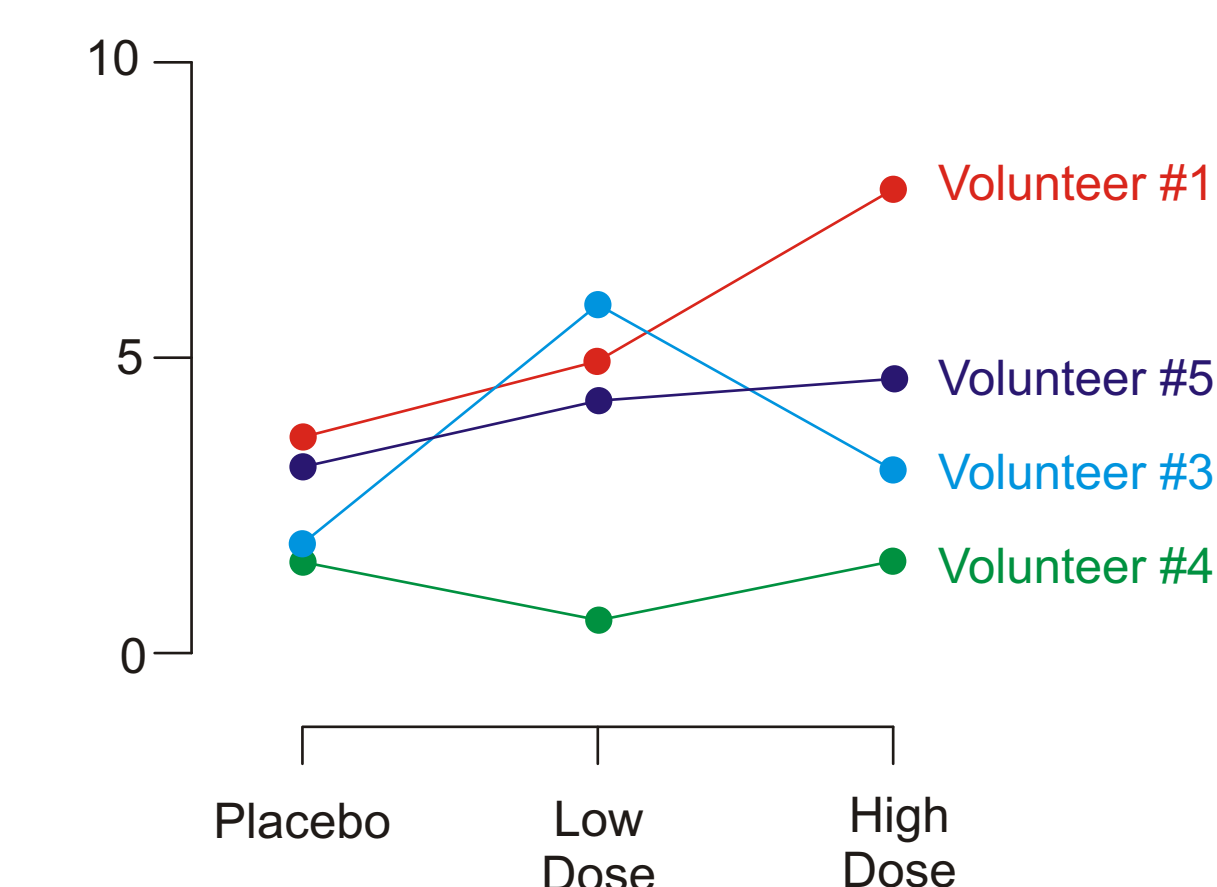
### Questions and self-reference

Although results are not entirely clear, ketamine may have slightly decreased the percentage of questions asked by the subject and increased the frequency of first person pronoun *I*.

### Percentage of Words that are Verbs (first 4 subjects only)



### Number of Filled Pauses (um, uh, etc.) Per 100 Words (first 4 subjects only)



### Statistical measures of speech with high, low, or placebo doses of ketamine

#### More nouns, fewer verbs:

Volunteer	Percentage of words (tokens) that are nouns			Percentage of words (tokens) that are verbs			
	Placebo	Low Dose	High Dose	Placebo	Low Dose	High Dose	
1	16.97	23.69	25.78	33.16	28.51	25.78	
3	25.66	24.58	26.67	32.74	30.51	30.67	
4	19.79	20.42	19.08	4	35.29	32.1	32.08
5	14.81	18.37	18.98	5	34.22	34.08	34.72
7	19.51	20.96	23.46	7	32.97	30.54	30.45
9	15.32	22.16	20.75	9	36.49	33.76	31.7
10	18.28	20	19.83	10	33.1	29.57	29.44
11	18.69	21.77	16.01	11	33.23	28.63	33

p= (relative to placebo)      **0.012**    **0.038**      p= (relative to placebo)      **0.0004**    **0.007**

#### Filled pauses (hesitations):

Volunteer	Filled pauses (um, uh, etc.) per 100 words		
	Placebo	Low Dose	High Dose
1	3.65	4.82	7.76
3	1.77	5.93	3.11
4	1.61	0.53	1.73
5	3.17	4.29	4.56
7	4.96	3.59	3.7
9	0.61	2.06	3.77
10	3.45	4.13	5.22
11	3.86	5.65	7.26

p= (relative to placebo)      **0.075**    **0.014**

#### Self-centeredness or awareness of cognitive difficulty:

Volunteer	Occurrences of I per 100 words			Questions in entire speech sample		
	Placebo	Low Dose	High Dose	Placebo	Low Dose	High Dose
1	0.79	0.4	0.7	1	0	2
3	1.33	2.12	1.78	3	2	0
4	0.54	1.59	0.87	4	0	0
5	1.06	0.82	1.37	5	0	0
7	2.47	2.7	2.88	7	2	0
9	0.2	0	0.19	9	0	0
10	0.69	1.96	2.71	10	0	1
11	0.89	0	0.66	11	0	0

p= (relative to placebo)      **0.239**    **0.076**      p= (relative to placebo)      **0.114**    **0.299**

## Discussion

Ketamine-influenced subjects exhibited impaired verbal retrieval, a tendency to repeat and grope for nouns, and a tendency to name objects without describing their actions. Verbs are inherently more complex than nouns because of their associated argument structures and less imageability. Other brain pathologies show similar lexical impairment, such as dementia (Silveri et al. 2003, Bak et al. 2001), Alzheimer's disease (Kim and Thompson 2004), and aphasia (Berndt et al. 2002). Lowered verb percentage is also an indication of reduced syntactic complexity commonly found in schizophrenic speech (Morice & Ingram 1982, Fraser et al. 1986).

Filled pauses increase the latency of response and are a sign of speech poverty — a representative negative symptom of schizophrenia. They may be either due to the difficulty in lexical retrieval, or due to poverty of content of speech, or due to drug-induced emotional withdrawal.

Changes in the frequency of questions and first person pronoun may be due to increased "self-reference" (Andreasen 1979) and impaired interpersonal communicative skills often referred to as "theory of mind" (Premack and Woodruff 1978; Corcoran, Mercer and Frith 1995, Frith 2004).

## References

- Adler, Caleb M., Terry E. Goldberg, Anil K. Malhotra, David Pickar and Alan Breier (1998) "Effects of Ketamine on Thought Disorder, Working Memory and Semantic Memory in Healthy Volunteers," *Biological Psychiatry*, 43, 811-816.
- Andreasen, Nancy C. (1979) "Thought, Language, and Communication Disorders," *Archives of General Psychiatry*, 36, 1315-1321.
- Bak, Thomas H., Dominic G. O'Donovan, John H. Xuereb, Simon Boniface and John R. Hodges (2001) "Selective Impairment of Verb Processing Associated with Pathological Changes in Brodmann Areas 44 and 45 in the Motor Neurone Disease-Dementia-Aphasia Syndrome," *Brain*, 124, 103-120.
- Berndt, Rita Sloa, Martha W. Burton, Anne N. Haendiges and Charlotte C. Mitchum (2002) "Production of Nouns and Verbs in Aphasia: Effects of Elicitation Context," *Aphasiology*, 16(1/2), 83-106.
- Corcoran, Rhiannon, Gavin Mercer and Christopher D. Frith (1995) "Schizophrenia, Symptomatology and Social Inference: Investigating 'Theory of Mind' in People with Schizophrenia," *Schizophrenia Research*, 17, 5-13.
- Fraser, W.I., King, K.M., Thomas, P., Kendell, R.E., 1986. "The Diagnosis of Schizophrenia by Language Analysis," *British Journal of Psychiatry* 148, 275-278.
- Frith, Christopher D. (2004) "Schizophrenia and Theory of Mind," *Psychological Medicine*, 34(3), 385-389.
- Kim, Mikyong and Cynthia K. Thompson (2004) "Verb Deficits in Alzheimer's Disease and Agrammatism: Implications for Lexical Organization," *Brain and Language*, 88(1), 1-20.
- Lahti, Adrienne C., Martin A. Weiler, Tamara Michaelidis, Arti Parwani and Carol A. Tamminga (2001) "Effects of Ketamine in Normal and Schizophrenic Volunteers," *Neuropsychopharmacology*, 25(4), 455-467.
- Malhotra, Anil K., Debra A. Pinals, Herbert Weingartner, Karen Sirocco, C. David Missar, David Pickar and Alan Breier (1996) "NMDA Receptor Function and Human Cognition: The Effects of Ketamine in Healthy Volunteers," *Neuropsychopharmacology*, 14(5), 301-307.
- Morice, Rodney and J. C. L. Ingram (1982) "Language Analysis in Schizophrenia: Diagnostic Implications," *Australian and New Zealand Journal of Psychiatry*, 16, 1121.
- Murray, H. A. (1971). *Thematic Apperception Test: Manual*. Cambridge, MA: Harvard University Press. (Original work published 1943.)
- Premack, D. and G. Woodruff (1978) "Does the Chimpanzee Have a Theory of Mind?" *Behavioral and Brain Sciences*, 1(4), 515-526.
- Silveri, M. C., B. L. Salvigni, A. Cappa, C. Della Vedova and M. Puopolo (2003) "Impairment of Verb Processing in Frontal Variant-Frontotemporal Dementia: A Dysexecutive Symptom," *Dementia and Geriatric Cognitive Disorders*, 16(4), 296-300.