

Amphetamine analogs methamphetamine and 3,4-methylenedioxymethamphetamine (MDMA) differentially affect speech

Gina F. Marrone · Jennifer S. Pardo ·
Robert M. Krauss · Carl L. Hart

Received: 15 June 2009 / Accepted: 27 October 2009 / Published online: 17 November 2009
© Springer-Verlag 2009

Abstract

Rationale Most reports of the effects of methamphetamine and 3,4-methylenedioxymethamphetamine (MDMA) on speech have been anecdotal.

Objectives The current study used a within-participant design to assess the effects of methamphetamine and MDMA on speech.

Materials and methods Eleven recreational users of amphetamines completed this inpatient, within-participant, double-blind study, during which they received placebo, methamphetamine (20, 40 mg), and MDMA (100 mg) on separate days. Following drug administration, study participants described movies viewed the previous evening and completed mood scales.

Results Methamphetamine increased quantity of speech, fluency, and self-ratings of talkativeness and alertness, while it decreased the average duration of nonjuncture unfilled pauses. MDMA decreased fluency and increased

self-ratings of inability to concentrate. To determine if methamphetamine- and MDMA-related effects were perceptible, undergraduates listened to the participants' movie descriptions and rated their coherence and the speaker's mood. Following methamphetamine, descriptions were judged to be more coherent and focused than they were following MDMA.

Conclusions Methamphetamine improved verbal fluency and MDMA adversely affected fluency. This pattern of effects is consistent with the effects of these drugs on functioning in other cognitive domains. In general, methamphetamine effects on speech were inconsistent with effects popularly attributed to this drug, while MDMA-related effects were in agreement with some anecdotal reports and discordant with others.

Keywords Methamphetamine · Amphetamines · Ecstasy · Speech · Performance · Humans

G. F. Marrone · C. L. Hart (✉)
Division of Substance Abuse,
New York State Psychiatric Institute,
1051 Riverside Dr., Unit 120,
New York, NY 10032, USA
e-mail: clh42@columbia.edu

G. F. Marrone · C. L. Hart
Department of Psychiatry, College of Physicians and Surgeons,
Columbia University, USA

R. M. Krauss · C. L. Hart
Department of Psychology, Columbia University,
New York, NY, USA

G. F. Marrone · J. S. Pardo
Department of Psychology, Barnard College,
Columbia University,
New York, NY, USA

Introduction

The amphetamines methamphetamine and 3,4-methylene dioxymethamphetamine (MDMA) are known as “club drugs” due to their association with rave and club cultures in the 1990s. Currently, the drugs are used in a variety of social settings (Kelly et al. 2006), in part, because they are thought to increase euphoria, mood, alertness, and to facilitate speech (Halkitis et al. 2005; Rodgers et al. 2006; Semple et al. 2003). Except for speech, all of these effects have been examined in human laboratory studies (Comer et al. 2001; Gouzoulis-Mayfrank and Hermle 1998; Hart et al. 2001, 2008; Liechti et al. 2001; Vollenweider et al. 1998). Under laboratory conditions, methamphetamine (Comer et al. 2001; Hart et al. 2001, 2008) and MDMA (Liechti et al.

2001; Vollenweider et al. 1998; Tancer and Johanson 2007) increase self-ratings of sociability and talkativeness. However, no behavioral measures have been used to assess the effects of these drugs on speech.

Despite the lack of empirical information addressing this issue, anecdotal reports and clinical lore have led to the widespread belief that methamphetamine and MDMA alter speech. For example, on their website targeting young people, the US Department of Health and Human Services lists slurred speech as one indicator of club drug use (SAMHSA 2008). Findings from uncontrolled studies and case reports suggest that methamphetamine increases sociability (Halkitis et al. 2005), quantity of speech, and speech rate (Logan 1996) and, at large doses, decreases verbal fluency (McGee et al. 2004). MDMA, like methamphetamine, has been reported to increase sociability in the natural ecology (Rodgers et al. 2006). However, the limited available information about MDMA-related effects on speech is mixed. Some reports suggest that the drug enhances communication (broadly defined) when it is administered in a therapeutic environment (Greer and Tolbert 1986, 1998), whereas other reports indicate that MDMA produces slurring of speech (SAMHSA 2008). Together, these reports suggest that methamphetamine and MDMA produce both overlapping effects and divergent effects on speech.

Although these effects of methamphetamine and MDMA have not been examined empirically, there have been several studies of the effects of another amphetamine—*d*-amphetamine—on speech and social behaviors. Overall, findings suggest that *d*-amphetamine increases sociability, quantity of speech, articulation rate, and verbal fluency. Griffiths et al. (1977) showed that *d*-amphetamine dose-dependently increased speaking time in social-interaction dyads. Consistent with this finding, when participants were given the option either to converse with a partner or sit quietly and receive money, they were more likely to choose the former following *d*-amphetamine compared with placebo (Heishman and Stitzer 1989; Higgins and Stitzer 1988). In patients undergoing psychotherapy, *d*-amphetamine increased articulation rate (Natale et al. 1979) and decreased average pause duration (Jaffe et al. 1973). In interviews of healthy participants, *d*-amphetamine increased quantity of speech and syntactic complexity and decreased the frequency of filled pauses (e.g., “um”, “er”; Barch and Carter 2005). *d*-Amphetamine also increased quantity of speech in the absence of a speaking partner, suggesting that a social context may not be necessary to facilitate this effect (Higgins and Stitzer 1989; Stitzer et al. 1978). Because methamphetamine, MDMA, and *d*-amphetamine have been shown to produce similar as well dissimilar effects on human behaviors (Martin et al. 1971; Cami et al. 2000; Tancer and Johanson 2003; Johanson et al. 2006; Sevak et

al. 2009), it is not clear whether *d*-amphetamine-related effects on speech generalize to the other amphetamines.

The present study was part of a larger study examining the effects of methamphetamine and MDMA on a variety of behavioral measures. Previously, the effects of the drugs had not been compared within the same group of participants in a controlled setting. Anecdotal reports and individual studies of methamphetamine and MDMA suggest that the drugs produce both overlapping and divergent effects on nonverbal measures, which is consistent with anecdotal reports of their effects on speech. Both methamphetamine and MDMA increase wakefulness and euphoria and decrease food intake (Cami et al. 2000; Hart et al. 2003, 2008, in preparation; Liechti et al. 2001; Tancer and Johanson 2003). Methamphetamine improves some measures of cognitive performance (Kirkpatrick et al. 2008; Johnson et al. 2005), whereas MDMA disrupts some measures of cognitive performance (Cami et al. 2000; Kuypers and Ramaekers 2005).

The purpose of this initial study was (a) to assess empirically the effects of methamphetamine and MDMA on speech, (b) to compare these effects within participants, and (c) to determine whether these effects are perceptible to naïve listeners. Ninety minutes after drug administration, participants recorded plot descriptions of movies viewed the previous evening and completed mood scales. The plot descriptions were transcribed and coded for quantity of speech and measures of verbal fluency. In addition, listeners naïve to drug condition rated the movie descriptions for coherence and mood of the speakers. Given the complex cognitive and motor operations required to produce speech (Guenther 2006), we hypothesized that the larger dose of methamphetamine and MDMA would disrupt speech and disruptions would be apparent to naïve listeners.

Materials and method

Participants

Eleven research volunteers between the ages of 23 and 39 (mean $\pm$ SD, 29.3 $\pm$ 5.0 years) completed this study. Two participants were female (one Black, one Hispanic), and nine were male (one Asian, two Black, two Hispanic, four White). They had completed an average of 14.1 years of formal education. Prior to study entry, all passed medical and psychological screening evaluations. No participant met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for an axis I disorder other than methamphetamine abuse. All participants reported previous experience with methamphetamine and MDMA. Six participants reported current methamphetamine use

4.2±4.7 days per month; ten reported current MDMA use 2.1±1.8 days per month. Four participants also reported current cocaine use (one to four times per month), nine reported marijuana use (4.2±2.3 days per week), nine reported alcohol use (one to three times per week), and two reported ketamine use (once per month). Seven participants also reported smoking one to ten cigarettes per day. No participant was seeking treatment for her/his drug use.

Design

This 13-day inpatient study was conducted in a residential laboratory at the New York State Psychiatric Institute. The study consisted of four 3-day blocks of sessions. On the first day of each block, participants received placebo, methamphetamine (20 or 40 mg), or MDMA (100 mg); drug plasma levels were assessed before and repeatedly after drug administration. On the remaining 2 days of each block, placebo was administered to allow for sufficient drug “washout” between dosing conditions. Each participant received all dose conditions, and doses were administered in a double-blind and counterbalanced manner. Three groups of three to four individuals participated.

Speech recordings and self-ratings

On the first day of each of the four 3-day blocks, participants provided verbal descriptions of one of two movies they had viewed the previous evening. Participants were instructed to summarize the movies as if they were speaking to someone who had not seen the movies. Descriptions were recorded 90 min after drug administration, when oral methamphetamine and MDMA are known to produce peak effects (Hart et al. 2001; Liechti et al. 2001); all recordings were completed in the presence of a staff member. Following the recording session and 145 min after drug administration, participants completed a visual analog scale, which consisted of a series of 100-mm lines labeled “not at all” at one end and “extremely” at the other end (Hart et al. 2003). The lines were labeled with adjectives describing a mood (e.g., “I feel... ‘alert’”), a drug effect (e.g., “I feel... ‘high’”), or a physical symptom (e.g., “I have a... ‘headache’”). Note that only self-ratings related to speech are presented in this manuscript (i.e., “I feel... ‘alert’”, “anxious”, “focused”, “talkative”, and “I can’t concentrate”). Other self-rating data are presented in the manuscript describing the larger study (Hart et al., in preparation). In an additional session, before any study medications were administered, participants were oriented to the recording procedure. Speech was recorded using a Superscope PSD330 CD recorder with a Shure WH30 head mounted microphone.

To address potential motivational concerns, participants were informed that they were competing with fellow

participants to provide the best movie description each day. They were told that judges would listen to and rate the recordings of the descriptions; at the end of the study, winners would be announced and awarded \$40 gift cards. In reality, no feedback about participants’ performance was provided, and all participants received gift cards at the end of the study. In addition, they were compensated at a rate of US \$70 per day for completing the study.

Drug

Methamphetamine hydrochloride (Desoxyn, Abbott Laboratories, North Chicago, IL, USA) and MDMA hydrochloride (manufactured and provided by Dr. David Nichols of Purdue University) were packaged by the Pharmacy Department of the New York State Psychiatric Institute by placing each tablet and appropriate amount of hydrochloride into a white #00 opaque capsule and adding lactose filler. Placebo consisted of white #00 capsules containing only lactose. The dose levels employed in this study were based on previous studies showing that 20–40 mg of methamphetamine and 100 mg of MDMA consistently increased ratings of euphoria and sociability (Hart et al. 2002, in preparation).

Speech ratings

A total of 40 native English speakers from the undergraduate subject pool of Columbia University provided ratings of the movie descriptions. All reported themselves to be free of hearing or speech abnormalities. To keep the task under 1 h in duration, the recordings were grouped to create four different testing protocols, which randomly presented recordings from all four dosing levels for each talker in a group. Each testing protocol was presented to ten listeners, yielding within-subject ratings for each dose level for each talker overall. On each trial, a listener heard a complete movie description and then rated the description on six seven-point scales: coherence of description, talker’s anxiety, focus, happiness, sociability, and speed. The materials were presented over headphones in a quiet room using PsyScope (Cohen et al. 1993), and listeners entered their ratings via the keyboard.

Data analysis

Movie descriptions were transcribed verbatim and marked for silent pauses (≥ 250 ms), filled pauses, and disfluencies. A log transformation was applied to the data for number of syllables, which were positively skewed. Disfluencies were sorted into five categories: (1) self-corrections, (2) false starts, (3) verbatim repetitions, (4) filled pauses, and (5) problems remembering a name or word.

Spontaneous speech typically contains a variety of pauses. Pauses may be filled (“er”, “um”, “uh”, etc.) or silent; either

type of pauses may occur at clause junctures or within the body of a clause. Generally speaking, juncture pauses can result from a variety of ongoing processes and functions (e.g., cognitive planning, conceptualization, rhetorical effects, problems in word finding, etc.). Nonjuncture pauses, on the other hand, are more likely to be associated with problems in lexical retrieval. Pauses were coded as juncture or non-juncture, for duration, and for frequency. Frequencies of pauses and disfluencies were converted to a rate per 100 syllables. The coder was blind to condition; a second coder, also blind to condition, transcribed and marked 10% of the speech recordings. Interrater reliability was $r=0.91$ ($p<0.01$).

Repeated measures analyses of variance with planned comparisons were used to determine the effects of methamphetamine and MDMA on speech. The dependent measures were analyzed using drug condition (placebo, methamphetamine (20 and 40 mg), and MDMA (100 mg)) as the main effect factor. The following comparisons were performed: placebo vs. all active doses, 20 vs. 40, 20 vs. 100, and 40 vs. 100 mg. Data were considered statistically significant at $p<0.05$. Product-moment correlations were calculated between relevant measures of speech, self-ratings, listener ratings, and drug plasma levels. Drug plasma levels drawn immediately after participants provided verbal descriptions (approximately 95 min postdrug administration) were correlated with speech measures, and plasma levels taken 175 min postdrug administration were correlated with self-ratings, which were completed 145 min after dosing.

Results

Quantity of speech

Figure 1 (left panel) shows that syllable count was significantly increased by methamphetamine ($F(3, 30)=5.06$, $p<0.01$). The drug (20 and 40 mg) increased quantity of speech relative to placebo and MDMA ($p<0.04$). Although methamphetamine doses increased the number of syllables produced during movie descriptions, only the 40-mg dose significantly increased self-ratings of “talkative” compared with placebo and MDMA ($p<0.04$; Fig. 1, right panel). The number of syllables produced and self-ratings of “talkative” following MDMA were not significantly different from placebo, but these measures were significantly correlated ($r=0.90$, $p<0.01$).

Verbal fluency

Figure 2 illustrates that the total number of disfluencies with all categories combined was significantly affected

by drug condition ($F(3, 30)=4.32$, $p<0.02$). Participants’ speech was significantly less disfluent following the 40-mg methamphetamine dose compared with all other drug conditions ($p<0.05$). There were no significant effects on the individual types of disfluencies. Listener ratings of the speakers’ movie descriptions indicate that the increase in verbal fluency following the 40-mg methamphetamine dose was perceptible. Descriptions following this dose were rated to be more coherent than those following other dosing conditions ($p<0.05$; Fig. 2, right panel). There were no significant correlations between listener ratings of coherence and rates of disfluencies in any of the drug conditions.

Filled pauses, concentration, and alertness

Figure 3 (left panel) shows that the average duration of filled pauses (e.g., ‘um’, ‘er’) was significantly affected by drug condition ($F(3, 30)=4.64$, $p<0.01$). Relative to all other drug conditions, MDMA significantly increased filled pauses duration ($p<0.05$). Similarly, the drug also increased self-ratings of “can’t concentrate” ($p<0.02$; Fig. 3, right panel). There was a significant correlation between duration of filled pauses and self-ratings of “can’t concentrate” ($r=0.86$, $p<0.01$).

Compared with other dosing conditions, both methamphetamine doses significantly increased self-ratings of “alert” ($p<0.05$), and listeners rated descriptions following the 40-mg dose as significantly more focused ($p<0.04$; Table 1). Correlations between these methamphetamine-related effects were not significant. On the other hand, although self-ratings of “alert” and listener ratings of “focused” following MDMA were not significantly different from placebo, they were significantly correlated ($r=0.85$, $p<0.01$).

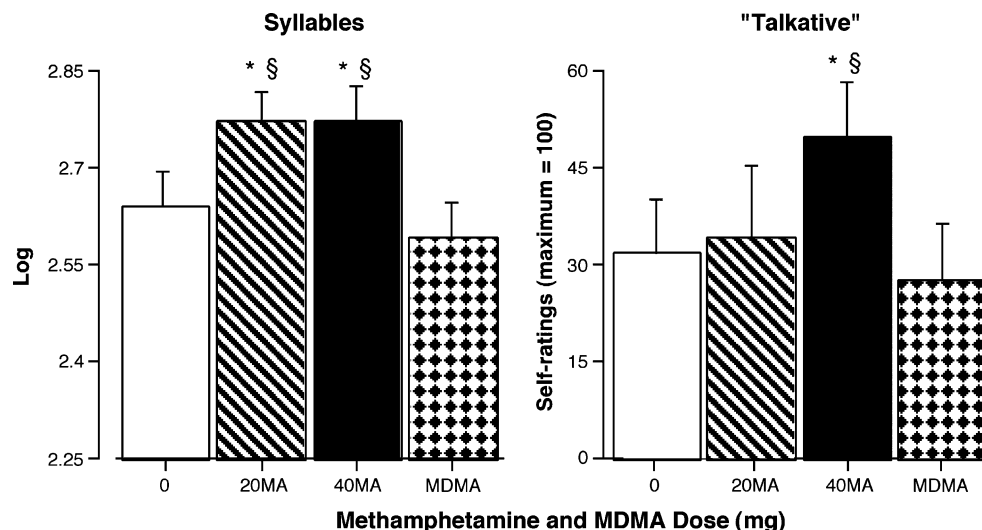
Silent pauses and speech rate

Relative to placebo, both methamphetamine doses decreased the average duration of nonjuncture silent pauses ($p<0.02$); MDMA had no effect on this measure. The frequency of pauses and articulation rate (syllables/s not including pauses) was not significantly altered by any of the drug conditions. Consistent with these findings, there were no significant differences among the four conditions in perceived speech rate.

Correlation between drug plasma concentrations and speech measures

When the relationship between drug plasma concentrations and speech measures was examined, the number of syllables produced and disfluencies were significantly

Fig. 1 Amount of syllables and self-ratings of “Talkative” as a function of dosing condition. Error bars represent one SEM. An * indicates significantly different from placebo ($p < .05$). An § indicates significantly different from 100 mg MDMA ($p < .05$). 20MA = 20 mg methamphetamine; 40MA = 40 mg methamphetamine; MDMA = 100 mg 3,4-methylenedioxymethamphetamine



correlated with methamphetamine plasma concentrations following the 40-mg dose ($r = -0.65$, $p < 0.05$ and $r = -0.58$, $p < 0.05$, respectively). Self-ratings were not significantly correlated with drug plasma concentrations.

Discussion

We hypothesized that the larger methamphetamine dose (40 mg) and MDMA would produce speech disruptions. This prediction was only partially confirmed as the present data show that methamphetamine increased both the fluency and quantity of speech, whereas MDMA produced some disruptions of fluency. Consistent with objective observations, self-ratings of alertness and talkativeness

were increased by methamphetamine, while ratings of inability to concentrate were increased by MDMA. In general, the methamphetamine-related effects we found were consistent with previous results from investigations of the effects of *d*-amphetamine on speech (e.g., Barch and Carter 2005). In addition, some effects produced by the larger methamphetamine dose were so pronounced that they were detectable by naïve listeners. Listeners judged participants to be more coherent and focused following methamphetamine than following other dosing conditions. This finding is inconsistent with our hypothesis that *disruptions* would be perceptible to listeners. These are the first data demonstrating that methamphetamine had some positive effects on speech and that these effects are apparent to naïve listeners.

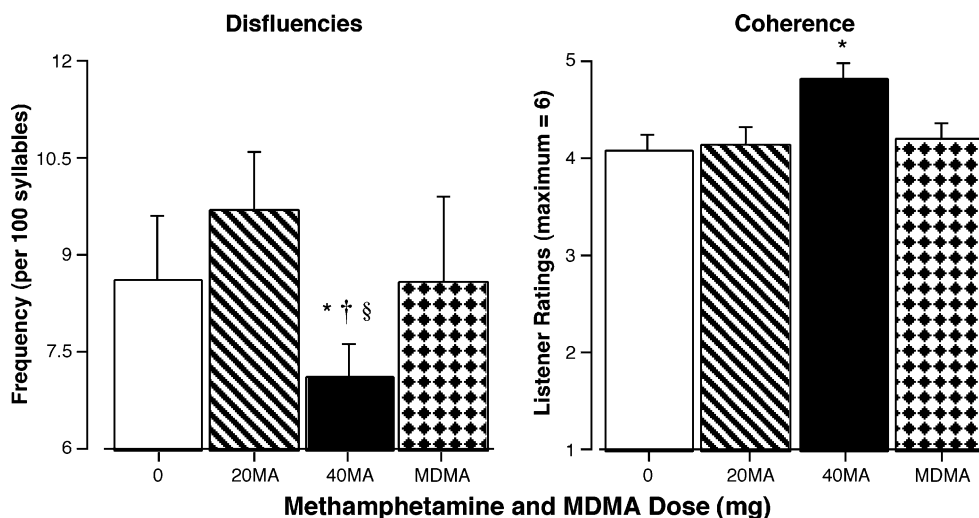
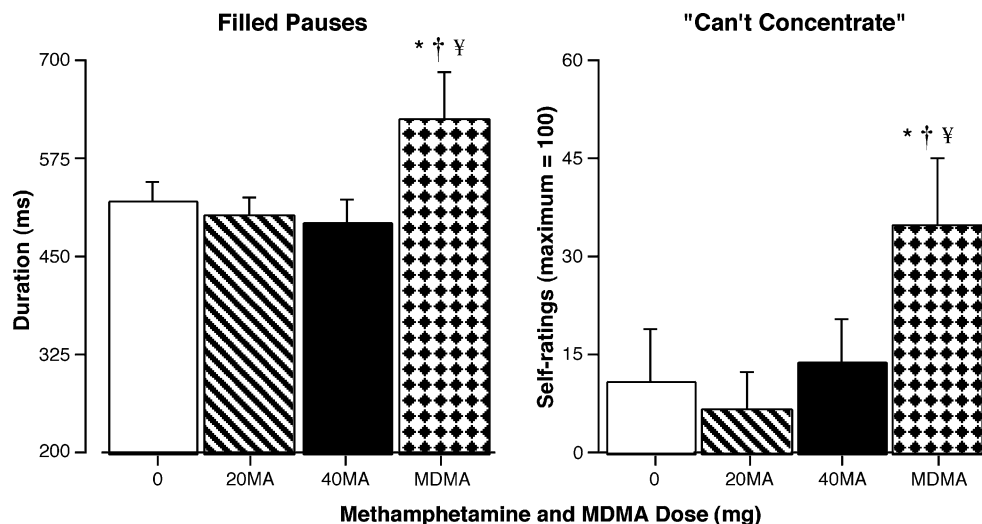


Fig. 2 Frequency of disfluencies and Listener ratings of speakers' coherence when describing the movie as a function of dosing condition. Error bars represent one SEM. An * indicates significantly different from placebo ($p < .05$). An † indicates significantly different

from 20 mg methamphetamine ($p < 0.05$). An § indicates significantly different from 100 mg MDMA ($p < .05$). 20MA = 20 mg methamphetamine; 40MA = 40 mg methamphetamine; MDMA = 100 mg 3,4-methylenedioxymethamphetamine

Fig. 3 Duration of filled pauses and self-ratings of “Can’t concentrate” as a function of dosing condition. An * indicates significantly different from placebo ($p < .05$). An † indicates significantly different from 20 mg methamphetamine ($p < .05$). An ¥ indicates significantly different from 40 mg methamphetamine ($p < .05$). 20MA = 20 mg methamphetamine; 40MA = 40 mg methamphetamine; MDMA = 100 mg 3, 4-methylenedioxymethamphetamine



In this study, participants summarized a film viewed the previous evening. While this task seems deceptively simple, it actually is quite complex. First, participants had to retrieve details of the film from long-term memory. Then they had to devise a narrative of the film’s plot, formulate specific sentences to communicate the narrative, and finally, articulate coherent speech. The complex cognitive and motor operations involved in this process require a large portion of the cerebral cortex (Guenther 2006). Given the complexity of the task and anecdotal accounts of speech difficulties following methamphetamine use (e.g., Logan 1996), we predicted that methamphetamine would produce speech disruptions. This hypothesis was not borne out; the data show that the drug (40 mg) improved fluency without deleteriously impacting other measures.

Because this is the first published investigation of acute methamphetamine-related effects on speech, it is difficult to relate the present findings to those of previous research. Nevertheless, the current data are consistent with results from studies assessing the effects of methamphetamine on cognitive and psychomotor performance. A burgeoning database demonstrates that acute methamphetamine

improves performance in multiple domains including learning and memory (Hart et al. 2002), attention (Silber et al. 2006), reaction time (Hart et al. 2008), and metacognition of agency (Kirkpatrick et al. 2008).

In contrast, MDMA produced fluency disruptions; it increased the average duration of filled pauses (e.g., “um”, “er”). Some of these effects were apparent to the research participants as indicated by their increased self-ratings of “can’t concentrate”. These findings are consistent with our prediction that MDMA would produce speech disruptions. Furthermore, six of 13 participants spontaneously reported that the quality of their performance had deteriorated following MDMA administration. There were no such reports after methamphetamine. Although anecdotal reports suggested that MDMA broadly enhances communication (Greer and Tolbert 1986, 1998), there are limited reports in the scientific literature indicating that enhanced serotonergic activity contributes to speech dysfunction (Patterson et al. 1997; Maguire et al. 1999). This is consistent with previous findings showing that the drug produced performance decrements in other cognitive domains. For example, Kuypers and Ramaekers (2005) reported that acute

Table 1 Listener ratings during each drug condition

Listener ratings	Placebo Mean (SEM)	Methamphetamine (20mg) Mean (SEM)	Methamphetamine (40mg) Mean (SEM)	MDMA (100mg) Mean (SEM)
Anxious	3.15 (.14)	3.39 (.17)	3.10 (.15)	3.47 (.16)
Coherence	4.13 (.12)	4.15 (.14)	4.75 (.14)*	4.19 (.13)
Focus	4.35 (.12)	4.10 (.12)	4.67 (.09)*	4.06 (.15)
Happiness	4.45 (.11)	4.36 (.12)	4.54 (.11)	4.13 (.13)
Sociability	4.58 (.15)	4.61 (.15)	4.68 (.14)	4.40 (.14)
Speed	3.62 (.11)	3.70 (.12)	3.65 (.11)	3.70 (.09)

Maximum ratings=6

* $p < .05$ (indicates significantly different from all other groups)

MDMA (at a dose comparable to the one used here) disrupted immediate and delayed recall on a verbal learning task. While both MDMA and methamphetamine release monoamine neurotransmitters, methamphetamine is approximately a 30-fold more potent releaser of dopamine (DA) than serotonin (5-hydroxytryptamine, 5-HT). By contrast, MDMA is about a six- to sevenfold more potent releaser of 5-HT than of DA (Rothman et al. 2001). It is tempting to speculate that MDMA-related effects on 5-HT contributed to the current speech findings, but additional research is needed to address this issue.

The finding that methamphetamine decreased the average duration of nonjuncture silent pauses is consistent with previous results of the effects of *d*-amphetamine on speech (Jaffe et al. 1973). The mechanism by which these drugs accomplish this effect is unclear. Although one popular stereotype portrays the amphetamine user as speaking rapidly and incoherently, our data provide little support for such a characterization. Pause frequency, pause duration, and articulation rate determine perceived speech rate, with articulation rate being most important (Grosjean and Lane 1976). Neither methamphetamine nor MDMA affected pause frequency or articulation rate, and not surprisingly, speech following the administration of these drugs was not perceived by naive judges to differ in rate from speech following placebo. Thus, our findings failed to confirm anecdotal reports that the drugs increase speech rate and highlight the importance of examining this issue under controlled conditions.

It should come as no surprise that the drugs we studied affected speech, but the effects were for the most part not the ones popularly attributed to them. Although alcohol has profound effects on both the cognitive and motor aspects of speech production (Pisoni et al. 1986; Klingholz et al. 1988; Pisoni and Martin 1989), the most reliable effects are not the ones an actor would use to portray a stereotypical “drunk”. In a clever experiment, Hollien and colleagues (1998) recorded the speech of actors simulating intoxication. They also recorded the same actors when they were actually inebriated and trying to speak normally. Listeners judged the actors to be more intoxicated when they were simulating intoxication than when they were actually intoxicated.

Only one dose of MDMA was examined in this study. Although the MDMA dose tested is well within the range typically used by recreational users to produce euphoria and other desired effects, a more general understanding of the effects of this drug on speech would require a broader range of doses. A related concern is that single low doses of methamphetamine were administered via the oral route. Anecdotally, the drug is abused in a binge pattern (multiple doses administered repeatedly) via routes other than oral and at doses larger than those employed here (e.g., Cho et

al. 2001). Conceivably, speech would be disrupted following larger methamphetamine doses administered repeatedly. Also, there is substantial inter- and intrasubject variability in spontaneous speech, and more reliable estimates of the influence of drugs on speech would require a greater number of participants than is typically found in studies of the pharmacological effects of drugs. In addition, because speech was elicited and not spontaneous, this study does not address whether methamphetamine and MDMA alter tendency to talk versus remaining silent. Finally, our speech samples were collected in a highly controlled environment that differs in many ways from the settings in which recreational drug use occurs and were confined to a particular circumscribed topic. It would be useful to ascertain whether the effects we observed are found when setting and topic are varied. A number of studies have demonstrated that the effects of stimulants can be modified by environmental contingencies (e.g., Silverman et al. 1994; Comer et al. 1996; Jones et al. 2001; Stoops et al. 2005a, b). For example, amphetamine, cocaine, and methylphenidate have been shown to function as reinforcers under conditions that required vigilance but not under relaxation conditions (Silverman et al. 1994; Jones et al. 2001; Stoops et al. 2005a).

Despite these limitations, this study provides the first evidence from a well-controlled study that the cognitive effects of methamphetamine and MDMA are manifest in speech. Moreover, these effects are discernible by naive listeners. Methamphetamine and MDMA produced different effects on speech. Importantly, methamphetamine improved fluency without causing disruptive effects on other measures, whereas MDMA disrupted fluency and increased the duration of filled pauses. For the most part, methamphetamine-related effects were not the ones that are popularly attributed to the drug. The effects of MDMA, on the other hand, are consistent with anecdotal reports suggesting the drug produces temporary speech disruptions. However, MDMA-related effects are discordant with reports indicating the drug enhances communication.

Acknowledgements This research was supported by a grant from NIDA (Hart, R01 DA03746) and served as Gina Marrone’s undergraduate honor’s thesis project at Barnard College. We gratefully acknowledge Isabel Cajori Jay, Chantal Sowemimo-Coker, and Christina Perry for their help collecting listener-rated data. We also thank Drs. Stephen Heishman, David Epstein, and Peter Balsam for their comments on earlier versions of the manuscript.

References

- Carter BDM, Carter CS (2005) Amphetamine improves cognitive function in medicated individuals with schizophrenia and in healthy volunteers. *Schizophr Res* 77:43–58

- Cami J, Farre M, Mas M, Roset PN, Poudevida S, Mas A, San L, de la Torre R (2000) Human pharmacology of 3, 4-methylenedioxymethamphetamine (“ecstasy”): psychomotor performance and subjective effects. *J Clin Psychopharmacol* 20:455–466
- Cho AK, Melega WP, Kuczenski R, Segal DS (2001) Relevance of pharmacokinetic parameters in animal models of methamphetamine abuse. *Synapse* 39:161–166
- Cohen J, MacWhinney B, Flatt M, Provost J (1993) PsyScope: an interactive graphical system for designing and controlling experiments in the psychology laboratory using Macintosh computers. *Behav Res Meth Instr Comp* 25:257–271
- Comer SD, Haney M, Foltin RW, Fischman MW (1996) Amphetamine self-administration by humans: modulation by contingencies associated with task performance. *Psychopharmacology (Berl)* 127:39–46
- Comer SD, Hart CL, Ward AS, Haney M, Foltin RW, Fischman MW (2001) Effects of repeated oral methamphetamine administration in humans. *Psychopharmacology* 155:397–404
- Gouzoulis-Mayfrank E, Hermle L (1998) Are the “entactogens” a distinct psychoactive substance class? The contribution of human experimental studies to the classification of MDMA and other chemically related methylenedioxyamphetamine derivatives. *Heftler Rev Psych Res* 1:46–51
- Greer G, Tolbert R (1986) Subjective reports of the effects of MDMA in a clinical setting. *J Psychoact Drugs* 18:319–327
- Greer GR, Tolbert R (1998) A method of conducting therapeutic sessions with MDMA. *J Psychoact Drugs* 30:371–379
- Griffiths RR, Stitzer M, Corker K, Bigelow G, Liebson I (1977) Drug-produced changes in human social behavior: facilitation by d-amphetamine. *Pharmacol Biochem Behav* 7:365–372
- Grosjean F, Lane H (1976) How the listener integrates the components of speaking rate. *J Exp Psychol Hum Percept Perform* 4:538–543
- Guenther FH (2006) Cortical interactions underlying the production of speech sounds. *J Commun Disord* 39:350–365
- Halkitis PN, Fischgrund BN, Parsons JT (2005) Explanations for methamphetamine use among gay and bisexual men in New York City. *Subst Use Misuse* 40:1331–1345
- Hart CL, Ward AS, Haney M, Foltin RW, Fischman MW (2001) Methamphetamine self-administration by humans. *Psychopharmacology* 157:75–81
- Hart CL, Haney M, Foltin RW, Fischman MW (2002) Effects of the NMDA antagonist memantine on human methamphetamine discrimination. *Psychopharmacology* 164:376–384
- Hart CL, Ward AS, Haney M, Nasser J, Foltin RW (2003) Methamphetamine attenuates disruptions in performance and mood during simulated night shift work. *Psychopharmacology* 169:42–51
- Hart CL, Gunderson EW, Perez A, Kirkpatrick MG, Thurmond A, Comer SD, Foltin RW (2008) Acute physiological and behavioral effects of intranasal methamphetamine in humans. *Neuropsychopharmacology* 33:1847–1855
- Heishman SJ, Stitzer ML (1989) Effect of d-amphetamine secobarbital and marijuana on choice behavior: social versus nonsocial options. *Psychopharmacology (Berl)* 99:156–162
- Higgins ST, Stitzer ML (1988) Time allocation in a concurrent schedule of social interaction and monetary reinforcement: effects of d-amphetamine. *Pharmacol Biochem Behav* 31:227–231
- Higgins ST, Stitzer ML (1989) Monologue speech: effects of d-amphetamine secobarbital and diazepam. *Pharmacol Biochem Behav* 34:609–618
- Hollien H, DeJong G, Martin CA (1998) Production of intoxication states by actors: Perception by lay listeners. *J Forensic Sci* 43:1153–1162
- Jaffe J, Dahlberg CC, Luria J, Chorosh J (1973) Effects of LSD-25 and dextroamphetamine on speech rhythms in psychotherapy dialogues. *Biol Psychiatry* 6:93–96
- Johanson CE, Kilbey M, Gatchalian K, Tancer M (2006) Discriminative stimulus effects of 3, 4-methylenedioxymethamphetamine (MDMA) in humans trained to discriminate among d-amphetamine, meta-chlorophenylpiperazine and placebo. *Drug Alcohol Depend* 81:27–36
- Johnson BA, Roache JD, Ait-Daoud N, Wallace C, Wells LT, Wang Y (2005) Effects of isradipine on methamphetamine-induced changes in attentional and perceptual-motor skills of cognition. *Psychopharmacology (Berl)* 178:296–302
- Jones HE, Garrett BE, Griffiths RR (2001) Reinforcing effects of oral cocaine: contextual determinants. *Psychopharmacology (Berl)* 154:143–152
- Kirkpatrick MG, Metcalfe J, Greene MJ, Hart CL (2008) Effects of intranasal methamphetamine on metacognition of agency. *Psychopharmacology* 197:137–144
- Kelly BC, Parsons JT, Wells BE (2006) Prevalence and predictors of club drug use among club-going young adults in New York City. *J Urban Health* 83:884–895
- Klingholz F, Penning R, Liebhart E (1988) Recognition of low-level alcohol intoxication from speech signal. *J Acoust Soc Am* 84:929–935
- Kuypers KP, Ramaekers JG (2005) Transient memory impairment after acute dose of 75 mg 34-methylene-dioxymethamphetamine. *J Psychopharmacol* 19:633–639
- Liechti ME, Gamma A, Vollenweider FX (2001) Gender differences in the subjective effects of MDMA. *Psychopharmacology (Berl)* 154:161–168
- Logan BK (1996) Methamphetamine and driving impairment. *J Forensic Sci* 41:457–464
- Maguire GA, Gottschalk LA, Riley GD, Franklin DL, Bechtel RJ, Ashurst J (1999) Stuttering: neuropsychiatric features measured by content analysis of speech and the effect of risperidone on stuttering severity. *Compr Psychiatry* 40:308–314
- Martin WR, Sloan JW, Sapira JD, Jasinski DR (1971) Physiologic, subjective, and behavioral effects of amphetamine, methamphetamine, ephedrine, phenmetrazine, and methylphenidate in man. *Clin Pharmacol Ther* 12:245–258
- McGee SM, McGee DN, McGee MB (2004) Spontaneous intracerebral hemorrhage related to methamphetamine abuse: autopsy findings and clinical correlation. *Am J Forensic Med Pathol* 25:334–337
- Natale M, Dahlberg CC, Jaffe J (1979) The effect of psychotomimetics on therapist–patient matching of speech “rhythms”. *J Commun Disord* 12:45–52
- Patterson DE, Braverman SE, Blandres PV (1997) Speech dysfunction due to trazodone–fluoxetine combination in traumatic brain injury. *Brain Injury* 11:287–291
- Pisoni DB, Martin CS (1989) Effects of alcohol on the acoustic–phonetic properties of speech: perceptual and acoustic analyses. *Alcohol Clin Exp Res* 13:577–587
- Pisoni DB, Yuchtman M, Hathaway N (1986) Effects of alcohol on the acoustic–phonetic properties of speech In: *Alcohol accidents and injuries*. Society of Automotive Engineers, Pittsburgh, PA, special paper P-173, 131–150
- Rodgers J, Buchanan T, Pearson C, Parrott AC, Ling J, Heffernan TM, Scholey AB (2006) Differential experiences of the psychobiological sequelae of ecstasy use: quantitative and qualitative data from an internet study. *J Psychopharmacol* 20:437–446
- Rothman RB, Baumann MH, Dersch CM, Romero DV, Rice KC, Carroll FI, Partilla JS (2001) Amphetamine-type central nervous system stimulants release norepinephrine more potently than they release dopamine and serotonin. *Synapse* 39:32–41

- SAMHSA (2008) Tips for teens: the truth about club drugs. <http://ncadisamhsa.gov/govpubs/phd852/>
- Semple SJ, Patterson TL, Grant I (2003) Binge use of methamphetamine among HIV-positive men who have sex with men: pilot data and HIV prevention implications *AIDS. Educ Prev* 15:133–147
- Sevak RJ, Stoops WW, Hays LR, Rush CR (2009) Discriminative stimulus and subject-rated effects of methamphetamine d-amphetamine methylphenidate and triazolam in methamphetamine-trained humans. *J Pharmacol Exp Ther* 328:1007–1010
- Silber BY, Croft RJ, Papafiotiou K, Stough C (2006) The acute effects of d-amphetamine and methamphetamine on attention and psychomotor performance. *Psychopharmacology* 187:154–169
- Silverman K, Kirby KC, Griffiths RR (1994) Modulation of drug reinforcement by behavioral requirements following drug ingestion. *Psychopharmacology (Berl)* 114:243–247
- Stitzer ML, Griffiths RR, Liebson I (1978) Effects of d-amphetamine on speaking in isolated humans. *Pharmacol Biochem Behav* 9:57–63
- Stoops WW, Lile JA, Fillmore MT, Glaser PE, Rush CR (2005a) Reinforcing effects of methylphenidate: influence of dose and behavioral demands following drug administration. *Psychopharmacology (Berl)* 177:349–355
- Stoops WW, Lile JA, Fillmore MT, Glaser PE, Rush CR (2005b) Reinforcing effects of modafinil: influence of dose and behavioral demands following drug administration. *Psychopharmacology (Berl)* 182:186–193
- Tancer M, Johanson CE (2003) Reinforcing subjective and physiological effects of MDMA in humans: a comparison with d-amphetamine and mCPP. *Drug Alcohol Depend* 72:33–44
- Tancer M, Johanson CE (2007) The effects of fluoxetine on the subjective and physiological effects of 3, 4-methylenedioxymethamphetamine (MDMA) in humans. *Psychopharmacology* 189:565–573
- Vollenweider FX, Gamma A, Liechti M, Huber T (1998) Psychological and cardiovascular effects and short-term sequelae of MDMA (“ecstasy”) in MDMA-naive healthy volunteers. *Neuropsychopharmacology* 19:241–251