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Reaction Time Variability and Related Brain Activity in Methamphetamine Psychosis

Catherine Fassbender, **Tyler A. Lesh**, **Stefan Ursu**, and **Ruth Salo**
Department of Psychiatry and Behavioral Sciences, University of California Davis Medical Center, Davis, California

Abstract

BACKGROUND—This study investigated the dynamics of cognitive control instability in methamphetamine (MA) abuse, as well its relationship to substance-induced psychiatric symptoms and drug use patterns.

METHODS—We used an ex-Gaussian reaction time (RT) distribution to examine intraindividual variability (IIV) and excessively long RTs (tau) in an individual's RT on a Stroop task in 30 currently drug-abstinent (3 months to 2 years) MA abusers compared with 27 nonsubstance-abusing control subjects. All subjects underwent functional magnetic resonance imaging while performing the Stroop task, which allowed us to measure the relationship between IIV and tau to functional brain activity.

RESULTS—Elevated IIV in the MA compared with the control group did not reach significance; however, when the MA group was divided into those subjects who had experienced MA-induced psychosis (MAP+) (n = 19) and those who had not (n = 11), the MAP+ group had higher average IIV compared with the other groups ($p < .03$). In addition, although control subjects displayed a relationship between IIV and conflict-related brain activity in bilateral prefrontal cortex such that increased IIV was associated with increased activity, the MAP+ group displayed this relationship in right prefrontal cortex only, perhaps reflecting elevated vigilance in the MAP+ group. Greater IIV did not correlate with severity of use or months MA abstinent. No group differences emerged in tau values.

CONCLUSIONS—These results suggest increased cognitive instability in those MA-dependent subjects who had experienced MA-induced psychosis.

Keywords

Cognitive Control; fMRI; Methamphetamine; Psychosis; RT Variability; Stroop

Address correspondence to Ruth Salo, Ph.D., University of California Davis Medical Center, Psychiatry and Behavioral Sciences, Imaging Research Center, 4701 X St, Sacramento, CA 95817; resalo@ucdavis.edu.

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DISCLOSURES
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A subset of individuals who chronically abuse methamphetamine (MA) also develop severe psychotic symptoms that are associated with high levels of psychiatric hospitalization and serious social dysfunction (1-5). Premorbid risk factors for MA psychosis include a familial history of psychiatric illness and age of first MA use (6,7), as well as abnormal measures of cognitive function early in development (8). Approximately 60% of MA abusers report a history of paranoia, delusions, and hallucinations while under the influence of the drug (2,4,8-10), with MA capable of triggering psychotic episodes in individuals with no history of psychiatric illness. (11). Early symptom descriptions of MA psychosis that hold true today include the following: 1) paranoid delusions with ideas of reference; 2) persecutory delusions; and 3) auditory and visual hallucinations that occur in a state of clear consciousness (12). The highly addictive nature of MA, as well as the ability to produce psychotic symptoms, make this drug a major public health concern (13).

Impaired attention has long been considered a marker for developing psychotic illnesses, including schizophrenia (14-18) and bipolar disorder (19-23). Sustained attention and cognitive control impairments have consistently been implicated across psychiatric disorders (24-26). Cognitive control is defined as a set of cognitive and neural operations linked to goal-driven behavior and is associated with brain regions such as the dorsolateral prefrontal cortex, anterior cingulate cortex, and the inferior parietal lobes (27-30). Disrupted cognitive control has been shown across addictive disorders (31-35) with concomitant reductions in frontal, cingulate, and parietal brain function (36-39). In the context of addiction, cognitive control can be interpreted as the inhibition of a prepotent response (e.g., habitual drug use) to carry out behaviors associated with long-term rewards and positive outcomes (e.g., abstaining from drug use).

Cognitive paradigms, such as the Stroop paradigm, have long been used to evaluate the integrity of cognitive control processes in a variety of clinical disorders (24,40). Traditionally, the number of correct responses and number of differing reaction times (RT) across different conditions, such as the transition from congruent to incongruent stimuli in the Stroop, have been used as a measure of differing attention and control demands. Incongruent stimuli introduce competing information that taxes top-down attention control by increased demands on selective attention and working memory due to interference between competing task-relevant and taskirrelevant information (i.e., word reading versus color naming) and by activating two competing motor responses and generating response conflict (response to the word meaning versus the color ink). However, behavioral measures such as the number of correct responses and RT to different stimulus classes may stem from a variety of impairments from perceptual problems to problems with top-down control through to response preparation and response selection impairments. More recently, intraindividual RT variability (IIV) has been employed to tease apart different aspects of cognitive impairment in clinical groups. Highly variable and/or unusually long RTs (compared with mean RT to other items in a similar stimulus class) have been associated with lapses in attention or cognitive control [e.g., (41-43)]. High levels of RT variability have been associated with an inability to effectively engage cognitive control in situations of increased cognitive demands (44), sustained attention impairments (45,46), and problems in regulating energetic states (47-50). Cognitive control may bias attention in favor of task-related stimuli and reduce attention to nontask-related stimuli or thoughts, resulting in fairly

homogenous RTs, whereas poor attention control allows taskirrelevant information to interfere with performance, resulting in highly variable RT. Increased RT variability has been noted in clinical disorders associated with cognitive impairments, including attention-deficit/hyperactivity disorder (51-54), autism (55), traumatic brain injury (56-59), Alzheimer's dementia (60,61), frontal lobe damage (62), schizophrenia (63,64), and bipolar disorder with psychotic symptoms (19).

Traditional methods of measuring RT variability have recently been argued to be somewhat flawed. This is because RT distributions are not best represented by the normal curve but instead contain a right-sided tail that captures numbers of abnormally long RT. The values within this tail can skew the RT distribution, making the mean RT appear to be longer than its true value. Furthermore, the use of standard measures of RT variability in research with clinical groups may be problematic as the standard deviation of RT is highly correlated with the mean RT (65-67), which often differs significantly in clinical groups. The ex-Gaussian distribution can be decomposed into the summation of two independent components: a symmetric Gaussian component and an exponential component that captures the right-sided skew in RT data. The model permits the measurement of the mean (mu) and standard deviation (sigma) of the normal (Gaussian) component, as well as the mean and standard deviation (tau) of the exponential component. Tau is often considered to represent trials on which lapses in attention have occurred (46,68,69), whereas the standard deviation of the normal component is considered to capture response preparation/execution problems (44,70-72).

Increased RT variability has been associated with poor performance on cognitive control tasks, such as response inhibition tasks (44,73,74), as well as with increased number of omission errors to Go trials. Hyperactivity in brain regions associated with cognitive control has been linked to RT variability in healthy control subjects (44,74). The authors interpreted increased RT variability as reflecting a lack of consistency of topdown cognitive control (44) or an overreliance on higher order processes when more successful performance was associated with more automatic response patterns (74). In a recent study of RT variability and attention lapsing in a group of subjects with schizophrenia (41), we found evidence that long RTs in the Stroop paradigm were associated with increased engagement of the cognitive control network, including bilateral dorsolateral prefrontal cortex, anterior cingulate, and parietal cortex. We also found that the schizophrenia group engaged these cognitive control regions to a lesser degree than control subjects.

The goal of the present study was to investigate the dynamics of cognitive control instability in MA abuse using the Stroop task during functional magnetic resonance imaging. We sought to examine both IIV, as well as trials with uncharacteristically long RT, as measured by tau, via the ex-Gaussian distribution of RT. We hypothesized that MAdependent subjects would display both increased IIV and increased tau compared with control subjects, reflecting lapses in cognitive control. Guided by previous imaging studies of brain activity associated with RT variability (44,74), we predicted that across groups, trials with elevated IIV and tau would be associated with increased activity in prefrontal cortex (PFC) due to increased engagement of control during these trials. We also hypothesized that this engagement of cognitive control related activity would be attenuated in MAdependent

individuals. As elevated RT variability has been associated with psychosis (19,63,64,75,76), we sought to examine if RT patterns were correlated with MA-induced psychiatric symptoms (i.e., psychosis) as well as drug use patterns.

METHODS AND MATERIALS

Subjects

Two groups were studied: 30 MA-abusing subjects and 27 nonsubstance-abusing control subjects. Neuroimaging data from this cohort have been previously published, but the analyses employed in the current study are novel and have never been previously reported (77). The MA abusers met DSM-IV criteria for lifetime MA dependence determined from the Structured Clinical Interview for DSM (SCID) (78) but were currently drug abstinent for a minimum of 3 weeks. All MA subjects were interviewed using the Methamphetamine Experience Questionnaire (MEQ), which is an interview based on the Cocaine Experience Questionnaire (79,80). The MEQ is designed to assess the lifetime frequency of psychotic episodes associated with MA use and conditions in which psychotic episodes occur, as well as the persistence of these symptoms. In this study, the MEQ was administered in conjunction with the SCID to determine the presence or absence of MA-induced paranoia. Nineteen of the MA subjects reported lifetime psychotic symptoms associated with MA abuse and 11 reported no psychosis (Table 1).

Procedure

Stroop Stimuli—A computerized single-trial version of the Stroop color-word task was administered to all subjects in the scanner. Three colors were employed in this experiment: red, green, and blue. The conflict stimuli (i.e., incongruent trials [I]) were created by printing each of the three color names in the two other ink colors. The nonconflict stimuli (i.e., congruent stimuli [C]) were created by printing each of the three color names in its own color. Stimuli were back-projected on a screen that could be viewed by the subjects through a mirror on the head coil.

Task Procedure—Subjects were instructed to respond to the color ink of colored words that were either congruent or incongruent by depressing a button on a response device attached to their dominant hand. Each button was mapped to a specific color (red button, green button, or blue button). Stimuli were presented for 1500 milliseconds with a fixed intertrial interval of 2500 milliseconds. Both speed and accuracy of responses were emphasized. To increase the level of conflict elicited by incongruent trials as well as maintain error rates, 70% of trials were nonconflict trials (i.e., C) and 30% of the trials were conflict trials (i.e., I). A commission error was defined as an incorrect button press. The task included a total of 6 runs of 62 trials each. All subjects completed two blocks of task practice trials outside the scanner before the functional magnetic resonance imaging session.

Behavioral Analysis

The numerical algorithm quantile maximum probability estimator (54) was used to estimate the ex-Gaussian parameters. RT variability was estimated within each word type (I and C) for all subjects. We defined intraindividual RT variability as the variability of Gaussian

component (σ) and the exponential component (τ) as expressed by the following equation: IIV = σ + τ.

To ascertain whether any potential differences in IIV were explained by an increase in the number of excessively long RTs, we also examined tau separately.

Analysis of variance (ANOVA) procedures for repeated measures were used to analyze the data in a 2 × 2 mixed ANOVA with group as a between-subjects factor (MA vs. control subjects) and word type (I vs. C) as within-subject variables, as well any possible group × word type interaction on Stroop percent correct, errors, correct RT, and RT variability measures. Incorrect responses were not included within the analysis of variance for RT. As we wished to examine the effects of combined tau and IIV (I plus C) in addition to the relative effects across conditions (I and C), independent samples *t* tests between groups (MA, control) also compared combined IIV and combined tau separately. One-way ANOVA with psychosis status (methamphetamine-dependent subjects who had experienced MA-induced psychosis [MAP+]; methamphetamine-dependent subjects who had not experienced MA-induced psychosis [MAP−]; and control subjects) as a between-subjects factor examined combined IIV and tau separately. As group differences in trial-to-trial adjustments were observed between MA and control subjects in our previous study (81), we also examined whether MAP+ and MAP− subjects would differ in RT adjustments across trial sequences (Supplement 1).

Imaging Procedure and Analysis

Functional magnetic resonance imaging data were collected on a 3T Siemens Trio Total Imaging Matrix MRI System (Erlangen, Germany) (see Supplement 1 for scanning parameters and image preprocessing details). Analyses were performed using a general linear model as implemented in SPM5 (www.fil.ion.ucl.ac.uk/SPM5). In a first-level analysis, individual subject general linear models were fitted to each subject's functional data. The statistical models included regressors coding for seven covariates: congruent trials preceded by other congruent OR incongruent trials (cC and iC, respectively), incongruent trials preceded by other incongruent OR congruent trials (iI and cI, respectively), errors, posterrors, and nonresponses. The coding of trial-to-trial regressors allowed us to examine both within-trial effects (e.g., I − C), as well as trial-to-trial adjustments (e.g., iI − cI). Parameter estimates obtained from this first-level analysis were used to compute maps of the contrasts of interest for effects of RT conflict (I − C).

Whole-Brain Analysis

Only correct responses were included in the reported contrasts. To examine how changes in IIV between conditions related to conflict-related brain activity (I − C) for control and MA groups separately, we employed I − C IIV as a regressor. We also conducted between-group analyses (control vs. MA) on these regression maps to investigate any potential group differences between groups in variability-associated brain activity. All between-group contrasts were thresholded at the voxel level with $p < .01$ and clusters were considered significant if they survived cluster-level family-wise error correction of $p < .05$. Due to the relatively small number of subjects in the MA group ($n = 11$), we did not conduct these

regressions separately for the MAP+ and MAP− groups. Instead, we conducted exploratory analyses within regions of interest (ROI) plotting the betas from the I − C contrast maps generated from our previously published study (81) against combined IIV in the control, MAP+, and MAP− groups separately.

Region of Interest Analyses

As the PFC has consistently emerged as a region of interest with regard to elevated RT variability, as well as an area of between-group difference in our previous study of RT variability in schizophrenia (41), we opted to examine prefrontal ROIs derived from our previous article based on the same data set as used here (81), namely bilateral Brodmann area (BA) 10. Within these two ROIs, we examined withingroup (control, MAP+, MAP−) relationships between IIV and betas derived from the conflict contrast maps using Spearman's rho.

Conjunction Analyses

To assess any potential shared regions of IIV-related activity between the MA and control groups, we conducted a conjunction analysis based on the global null (82) thresholded at a more conservative voxel level at $p = .001$ and cluster corrected as described above.

RESULTS

Behavioral Data

Reaction Time Analyses—Analyses revealed main effects of Stroop word type ($F_{1,55} = 140.93$, $p < .0001$) but no group by word type interaction ($p = .56$). No group differences were observed on within-trial Stroop conflict effects ($F < 1$) (81). When examining combined IIV and tau, independent samples t tests revealed no significant between-group (MA and control) differences (IIV: $t_{55} = -1.51$, $p = .14$; tau $t_{55} = -1.32$, $p = .19$), suggesting that the MA group as a whole did not differ significantly from control subjects in terms of RT variability (Table 2 and Figure 1).

We also examined differences between the MAP+ and MAP− subjects in IIV and tau (Table 3 and Figure 2). Results revealed a significant main effect of group (MAP+, MAP−, control) in IIV only ($F_{2,54} = 3.74$, $p = .03$; tau $p = .15$). Post hoc comparison (least significant difference) revealed that MAP+ subjects displayed increased IIV combined across I and C conditions compared with both MAP− subjects ($p = .02$) and control subjects ($p = .03$). Due to a lack of significant group difference in tau, the rest of our analyses focused on IIV only. An analysis of trial-to-trial RT adjustments between the MAP+ and MAP− subjects also failed to reach significance ($p = .15$).

Error Analyses—Analyses revealed a main effect of word type ($F_{1,55} = 34.78$, $p = .0001$) with both groups making significantly more errors in the incongruent condition (5%) than in the congruent condition (2%). There were no group differences in incongruent ($p = .54$) or congruent errors ($p = .43$).

Correlations between IIV and Clinical Measures

Given the patterns with IIV and presence of MA-induced paranoia, we ran statistical correlations with the frequency of MA-induced paranoid episodes and IIV in the 19 MAP+ subjects. Despite the differences in IIV patterns between the MAP+ and MAP− subjects, the correlations between IIV and frequency of MA paranoia failed to reach significance. There were no significant correlation patterns that emerged between RT IIV and drug use patterns (years use, time abstinent, or age of first MA use) among the MA subjects.

Imaging Analyses

Whole-brain regression analyses within the control and MA groups separately revealed a relationship between IIV and activity in the MA group in a broad network of brain regions, including those involved in cognitive control such as bilateral prefrontal and left parietal cortices (Figure 3; Table 4). Greater variability was associated with increased activity in similar regions in control subjects, although these clusters did not reach significance. Between-group comparisons of these regression maps revealed greater activity in the MA over control group in three regions, including the left precentral gyrus (Table 4). Conjunction analysis examining any potential shared IIV-related activity between the MA and control groups revealed one significant region in the left inferior frontal gyrus (BA 45) and insula extending laterally into BA 46.

ROI Analysis

To further probe any potential between-group differences in the relationship between brain activity and IIV, we examined bilateral prefrontal ROIs as outlined above. Conflict-related activity in right and left BA10 correlated positively with IIV in control subjects (r_{27} = .40, p = .04; r_{27} = .42, p = .03, respectively). Conflict-related activity in the right (r_{19} = .49, p = .03) but not left (p = .33) BA 10 correlated positively with IIV in the MAP+ group. There were no significant correlations between brain activity in either BA 10 region and IIV in the MAP− group (p > .50) for both correlations.

DISCUSSION

The current study examined the dynamics of cognitive control instability in MA abusers using a RT distributional analysis. The findings revealed an increase in RT variability in those MA subjects with psychosis compared with both MA abusers without psychosis and control subjects. Contrary to our hypothesis, we did not find a significant increase in the degree of unusually long RT (i.e., tau) in the MA abusers compared with control subjects. Our results from whole-brain activation analyses revealed that in participants with MA dependence increased IIV was associated with more activity in cognitive control regions, including bilateral PFC, as well as the right parietal lobe. Activity in the control group in these regions did not reach significance. However, conjunction analysis revealed an area of common activation in both groups in the left prefrontal cortex. Significantly greater activity associated with increased IIV in the MA group compared with control group was evident in a number of regions including the left precentral gyrus. When we examined the relationship between brain activity and IIV separately in those MA abusers who had experienced MA psychosis and those who had not, different patterns were observed. MA abusers who had

experienced MA-induced psychosis, like control subjects, displayed a significant correlation between IIV and conflict-related activity in lateral PFC, whereas MA abusers who had never experienced MA-induced psychosis did not. Unlike control subjects, however, the relationship between IIV and brain activity in the MAP+ group was not distributed bilaterally but limited to the right PFC only.

Increased IIV has previously been associated with inefficiency in response preparation and selection (72,83), topdown self-regulation (84,85), and problems with arousal (50). Although our analysis revealed no behavioral differences in IIV between the MA and control groups, differences emerged when participants with MA dependence were classified as those who had experienced (MAP+) and had not experienced MA-induced psychosis (MAP−); MAP+ experienced elevated IIV compared with MAP− and control subjects. This suggests that in this subgroup of MA users there is an overarching problem with cognitive control in terms of attention control, response preparation, and/or response selection. This difference cannot be explained by a preponderance of unusually long RT, representing mind-wandering episodes, as we did not find any significant differences specifically in tau. This is in agreement with previous studies that have also found a relationship between increased RT variability and psychosis (19,41,63,64,75,76).

We then sought to examine the patterns of conflict-related functional brain activity associated with IIV in the MA and control groups. Previous research in healthy control subjects has linked activity in cognitive control regions with increased RT variability (44,74). Although we did not find any behavioral difference in IIV between the overall MA group and control subjects, the MA group displayed an increase in IIV-related brain activity compared with control subjects in regions associated with cognitive control. Conjunction analyses revealed one common region of IIV-related activity within left prefrontal cortex in both the MA and control groups. Left lateral PFC has been associated with storing task goals and rules, maintaining task set, and re-establishing top-down attention processes or preparing response rules (86-92). Previous research (74) found that in healthy control subjects, increased RT variability was associated with increased activity in cognitive control regions, whereas subjects with lower IIV displayed great activity in regions associated with motor preparation and execution. The authors posited that a more successful performance strategy, indicated by lower levels of RT variability, was reflected in a more automatic response tendency rather than overreliance on higher order cognitive control regions. In other words, poor performance was linked to overthinking one’s performance. In the current study, the MA-dependent group displayed increased IIV-related activity in cognitive control regions despite comparable behavioral measures of IIV. It may be that MA-dependent participants engaged cognitive control to a greater degree than the control group to achieve a similar behavioral result.

As the presence of a history of MA-induced psychosis resulted in significantly elevated rates of IIV, we next chose to examine whether conflict-related brain activity was differentially related to IIV in MAP+ and MAP− groups. To this end, we examined activity in bilateral PFC (BA 10) in each group separately and found that only the MAP+ group displayed a relationship between IIV and brain activity, whereby those individuals with greater IIV were also those individuals that activated PFC more. However, although control subjects showed

a relationship between conflict-related activity in bilateral PFC and IIV, the MAP+ group displayed that relationship in the right hemisphere only. The different patterns of lateralized activity between the MAP+ group and control subjects may suggest the employment of different strategies. The right lateral PFC has been associated with vigilance, alerting, and arousal processes (93-101). As the MAP+ group displayed a relationship between increased activity in right PFC and IIV in this task, it is possible that a history of psychosis may be related to hypervigilant behavior, causing an increased level of concentration on cognitive tasks. Although somewhat speculative, published data from our lab are consistent with this model in that MAP+ subjects exhibit hyperalerting on tasks of attentional orienting (102,103). Collectively, these findings between drug-induced paranoia and cognitive function could suggest greater vigilance and focused attention in those MA subjects with a history of druginduced psychosis. As we would not predict to see increased vigilance in the MAP− group, this might explain the lack of PFC activation across either hemisphere. It is also possible that the relatively small number of subjects in this group (n = 11) did not allow us to detect this relationship.

Limitations

Potential limitations of this study include the use of subjects in our MA group that were recruited from treatment facilities rather than from a generalized community sample. Thus, our MA group may not be representative of the MA-dependent population at large. With regard to sample size, our MAdependent group without a history of drug-induced psychosis was relatively small (n = 11), which somewhat limited our ability to examine brain activity specifically related to this group. However, we conducted hypothesis-based regionspecific analyses to probe brain activity in MAP+ and MAP− groups. Nonetheless, it is possible that our relatively small sample size limited our ability to detect potential relationships between behavioral and clinical variables. It is also possible that the MAP+ group had preexisting psychosis before drug use; however, careful screening for preexisting psychosis was conducted using two structured interviews (i.e., SCID and MEQ) to distinguish between drug-induced psychosis and psychosis unrelated to drug use.

Conclusion

The results of the present study inform our understanding of the nature of impaired cognitive control by showing elevated IIV during Stroop task performance in a subset of MAdependent individuals with a history of MA-induced psychosis. Our findings suggest that cognitive control tasks that measure within-subject RT variability and recruit prefrontal regions can be powerful tools to detect meaningful relationships with substance-induced psychiatric symptoms. Future research in substance dependence should consider the inclusion of RT variability measures in addition to simple RT and measures of performance accuracy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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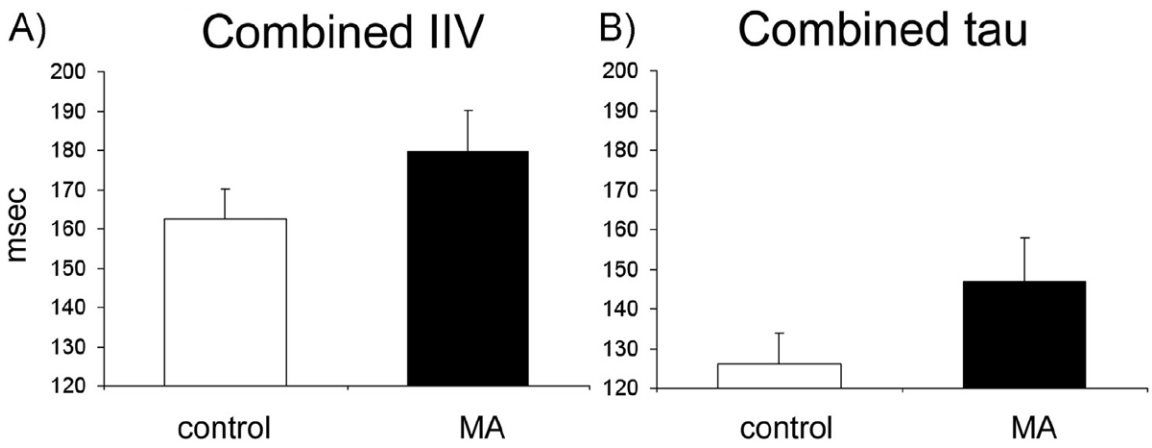

Figure 1.

Intraindividual reaction time variability (IIV) and tau during the Stroop task in methamphetamine (MA) and control groups. **(A)** Combined IIV (congruent + incongruent IIV) in the control and MA groups measured in milliseconds. There was no significant group difference in combined IIV between MA and control groups. **(B)** Combined tau (congruent + incongruent tau) in the control and MA groups measured in milliseconds. There was no significant group difference in combined tau between MA and control groups.

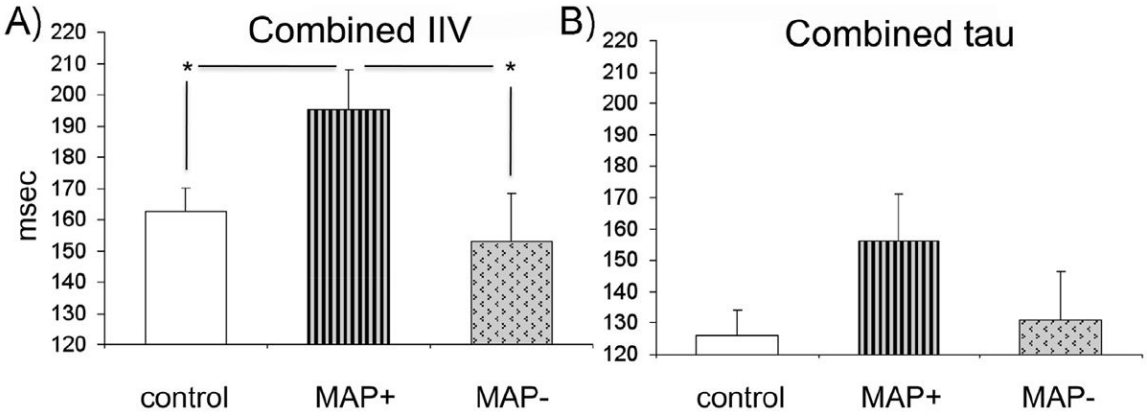

Figure 2.

Intraindividual reaction time variability (IIV) and tau among methamphetamine subjects with psychosis (MAP+) and methamphetamine subjects without psychosis (MAP−) compared with control subjects. **(A)** Combined IIV significantly differed between groups; the MAP+ subjects displayed significantly greater IIV than both MAP− and control subjects. *Significance at $p < .05$. **(B)** There was no significant between-group difference in combined tau.

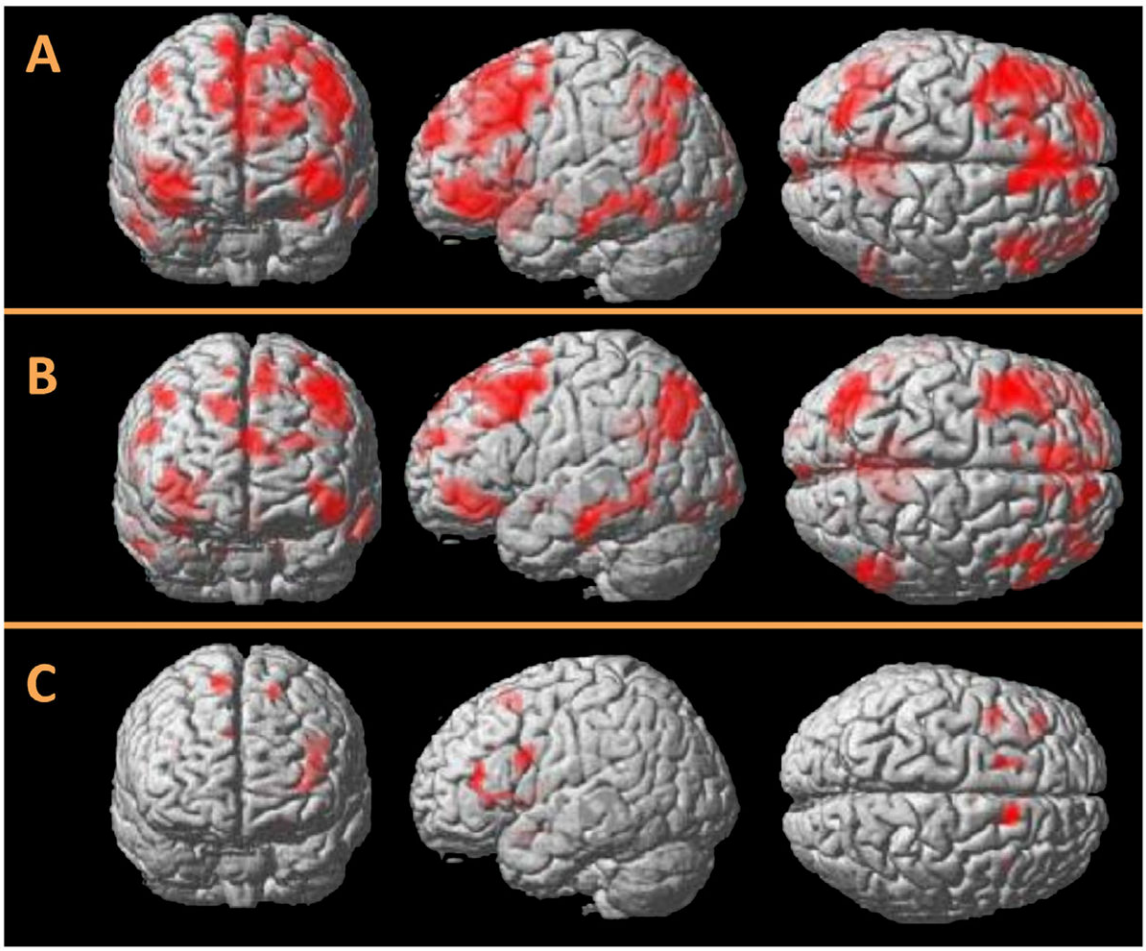

Figure 3.

Whole-brain regression maps displaying the relationship between conflict-related brain activity and intraindividual reaction time variability (IIV) in the Stroop paradigm. **(A)** Activity in the methamphetamine (MA) group (n = 30). Greater IIV was associated with more activity in cognitive control regions including bilateral frontal and parietal cortex. **(B)** Areas of greater activity in the MA group over control group (n = 27). Greater IIV-related activity was associated with more activity in MA users in left precentral gyrus, left middle and inferior temporal gyrus, and posterior cingulate cortex. **(C)** An area of common IIV-related activity in participants with MA dependence and control subjects was found in the left inferior frontal gyrus extending into insula and middle frontal gyrus (Brodmann area 46).

Table 1

Demographic and Clinical Characteristics of 30 Methamphetamine Abusers and 27 Control Subjects

	Methamphetamine Abusers (*n* =30)	Control Subjects (*n* = 27)
Demographic Variables		
Age, years, mean (SD)	35.5 (7.9)[a]	28.5 (7.2)
Range	21 to 48 years	20 to 47 years
Female subjects	15	11
Subject's education, years, mean (SEM)	12.5 (1.6)[a]	15.4 (1.2)
Parental education, years, mean (SEM)	13.1 (2.4)	14.7 (2.0)
NART	108.2 (4.8)[a]	111.9 (4.8)
Clinical Variables		
Methamphetamine use		–
Duration, years, mean (SD)	14.0 (6.4)	–
Range	4 to 28 years	
Months abstinent, mean (SD)	13.7 (15.4)	–
Range	2 to 60 months	
Age of first MA use, years, mean (SD)	17.7 (4.4)	–
Mean daily MA dosage (grams)	1.3 (.85)	–
History of cannabis abuse	24	–
Age of first cannabis use, years, mean	15.0 (3.8)	

NART, National Adult Reading Test; MA, methamphetamine.

[a]Significantly different from control group.

Table 2

Behavioral Results from 30 Methamphetamine Abusers and 27 Control Subjects

	Methamphetamine Abusers (*n* = 30)	Control Subjects (*n* = 27)
Stroop Effects, Median (SD)		
Congruent RT (msec)	642.8 (86.9)	617.2 (93.3)
Incongruent RT (msec)	786.5 (143.0)	742.9 (136.7)
Stroop conflict effect RT (msec)	143.7 (90.5)	125.7 (58.9)
Percent conflict errors	.05 (.04)	.06 (.06)
Percent nonconflict errors	.02 (.02)	.02 (.02)
Combined IIV (msec)	179.85 (56.74)	162.62 (39.23)
Combined Tau (msec)	146.97 (60.23)	126.10 (41.16)

IIV, intraindividual reaction time variability; RT, reaction time.

Table 3

Behavioral Results from 19 Methamphetamine Abusers with Psychosis (MAP+) and 11 Methamphetamine Abusers Without Psychosis (MAP−)

	MAP+ (*n* = 19)	**MAP− (*n* = 11)**
Stroop Effects, Median (SD)		
Congruent RT (msec)	664.87 (90.5)	604.77 (68.10)
Incongruent RT (msec)	818.93 (141.3)	730.54 (133.9)
Stroop conflict effect RT (msec)	154.06 (96.0)	119.6 (81.1)
Percent conflict errors	.05 (.04)	.05 (.05)
Percent nonconflict errors	.02 (.02)	.02 (.02)
Combined IIV	195.39 (55.03)	153.00 (51.32)[a]
Combined Tau	156.21 (64.60)	131.08 (50.65)

IIV, intraindividual reaction time variability; RT, reaction time.

[a]Significantly different from control group.

Table 4

Brain Regions with Significant Whole-Brain Differences Associated with Reaction Time Variability Conflict in 30 Methamphetamine Abusers in Regions Where MA Abusers Activated Significantly More Than 27 Control Subjects and in Regions Common to MA Abusers and Control Subjects

Region	Brodmann Area	Number Voxels	MNI Coordinates		
			x	y	z
MA Abusers					
Right inferior frontal gyrus	47	1884	44	26	−10
Right precuneus	31	1581	4	−56	32
Right lentiform nucleus		1308	10	−4	−2
Left inferior frontal gyrus	47	1805	−38	38	−2
Left middle frontal gyrus	9	5026	−44	14	40
Left angular gyrus/inferior parietal cortex	22	1417	−38	−60	16
MA > Control Subjects					
Left precentral gyrus	9	1549	−44	14	42
Left middle/inferior temporal gyrus	21	1673	−54	−24	−24
Posterior cingulate cortex	31	1640	0	−56	28
MA + Control Subject Conjunction Analysis					
Left inferior frontal gyrus/insula	45/46	175	−34	28	4

MA, methamphetamine; MNI, Montreal Neurological Institute.