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Psychophysiological and self-reported responses in individuals with methamphetamine use disorder exposed to emotional video stimuli

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ABSTRACT

Individuals with methamphetamine use disorder (MUD) exhibit irritability and compulsive emotional responses, yet the relevant study is scarce. The characteristic of their positive and negative emotional responses can provide effective targets for the clinical intervention. In this study, we compared the emotional responses of 60 participants with MUD and 30 healthy participants to visual stimuli. They watched four types of video to elicit anger, fear, amusement, and joy emotional responses. The self-report of emotional responses (i.e., arousal, valence, and proximity), skin conductance level, and startle response were measured. Comparing to the healthy controls, the methamphetamine group's subjective arousal level of fear is significantly lower ($t = 3.763$, $p < .01$); the skin conductance level of joy is significantly higher ($t = 2.086$, $p < .05$), and the level of anger is marginal significantly higher ($t = 1.984$, $p = .05$); the startle response level of anger ($t = 2.069$, $p < .05$) and joy ($t = 2.406$, $p < .05$) is significantly higher. The methamphetamine group exhibited an enhanced emotion response to anger and a decreased response to joy which may indicate the emotion dysregulation problem caused by drug. These results provide effective targets for clinical intervention in treating patients of MUD with emotion dysregulation problems.

1. Introduction

Emotion dysregulation is a common problem of methamphetamine users after withdrawal (Okita et al., 2016). Long-term abuse of methamphetamine causes a decreased activity in the anterior cingulate and orbital frontal cortex, as well as an increased reactivity in the amygdala (Payer et al., 2011; Uhlmann et al., 2016). The dynamic relationship between the anterior cingulate, orbital frontal cortex, and amygdala is the key mechanism in emotional experience regulation (Hariri et al., 2003), therefore the dysfunction of these regions may indicate that the dysfunctional emotional experience is the main problem in MUD (Parrott et al., 2011; Wardle and Wit, 2012; Carrico et al., 2013).

The emotional dysregulation in MUD manifest as subjective negative emotion and dysfunctional emotion reactivity. Research shows that depression and anxiety are the two most prominent negative emotions in methamphetamine users (London et al., 2004), and they also demonstrate abnormal reactions to positive and negative emotion stimuli. Studies show that subjects with methamphetamine use disorder (MUD) showed a decreased reactivity to positive emotion stimuli (May et al., 2013; Carrico et al., 2013; Wardle and Wit, 2012). However, findings of the reactivity to negative emotion stimuli were inconclusive. Some studies showed an increased reactivity to negative emotion stimuli (Cohen et al., 2003; London et al., 2004), yet in some studies, no significant difference was found between the subjects with MUD and normal controls (Payer et al., 2008; Kim et al., 2011a). The inconsistent results may be attributed to different research paradigms. Some studies applied a cognitive research paradigm which emphasizes emotion recognition, such as affective pictures matching, Payer et al., 2008; Kim et al., 2011b), and facial expression recognition (Kim et al., 2011a), whereas some studies focused on the emotional experiences (London et al., 2004). The neural mechanisms of emotion recognition are different from emotional experience. Emotion recognition involves a neural circuit that mainly related to cognition process, including the inferior frontal gyrus, fusiform gyrus, ventrolateral prefrontal cortex, dorsolateral prefrontal cortex, and amygdala (Payer et al., 2008; Kim et al., 2011b), while emotional experience involves a neural circuit of the brain regions that mainly associated to emotional regulation,

Abbreviations: MUD, methamphetamine use disorder; EMG, Eye-blink Electromyography

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including the anterior cingulate, orbital frontal cortex, insular cortex, and amygdala (Davidson et al., 2000; London et al., 2004; Kose et al., 2015).

Emotional experience can be measured using subjective self-report as well as physiological measurement. For physiological measurement, skin conductance level is commonly used to record the emotion response, especially the level of arousal. Skin conductance level increases with a more stressful and excited state and decreases with a more relaxed state (Ohme et al., 2009). Startle response measures the valence of emotion. Research shows that positive emotional experiences inhibit the startle response, and negative emotional experiences potentiate the startle response (Grillon et al., 1996; Bradley et al., 2006). Psychophysiological data reflect the changes of autonomic nervous system that closely related to the emotion experience with or with no consciousness, whereas subjective data provide information that related to emotion recognition. Therefore, the combination of self-report, skin conductance, and startle reflect can provide both subjective and objective measurements for evaluating the arousal and valence of emotion, as well as emotional experience and recognition.

Several limitations exist in the previous studies. First, most of the previous studies used self-report (Okita et al., 2016) and brain imaging techniques (e.g., fMRI, MRI, PET; Sekine et al., 2006; Kim et al., 2011a; Payer et al., 2012) to investigate the neural mechanism of the emotional process in MUD. There is a lack of physiological measurements, such as skin conductance and startle reflex for measuring the emotional reactivity. Second, the emotion stimuli using emotional pictures (Kim et al., 2011b; Wardle and Wit, 2012) and emotional faces (Payer et al., 2011) lacked the self-report on the valence and arousal of emotions, therefore the validity of emotional induction was limited. Third, the emotions were only divided into positive and negative category with no further distinction (Parrott et al., 2011; Wardle and Wit, 2012). Given these limitations, this study combined the skin conductance and startle reflex to investigate the emotional responsivity in MUD. The study utilized emotional videos to induce response after the self-report of emotional valence and arousal was filled out, and the researchers further distinguished emotions by selecting two positive emotions (joy and amusement) and two negative emotions (anger and fear). The two positive and negative emotions were selected for comparing the approach motives. Previous studies show that the approach motive was found in joy (Roseman, 2008) but not in amusement; the approach motive was also found in anger emotion while the avoidance motive was found in fear.

The aim of the study is to investigate the responses of people with MUD to positive and negative emotional stimuli through the measurements of self-report, skin conductance, and startle reflex. We hypothesized that comparing to normal controls, 1) people with MUD have a higher reactivity to negative emotion stimuli; 2) people with MUD have a lower reactivity to positive emotion stimuli; 3) People with MUD have a higher approaching motive to anger comparing to fear; 4) people with MUD have a higher approaching motive to joy comparing to amusement.

2. Material and methods

2.1. Participants

Sixty methamphetamine users (30 male, 30 female) aged 18–53 years participated in the study as the experimental group. They were patients from the Beijing Tian-Tang-He Compulsory Drug Rehabilitation Center and Beijing Xin-He Compulsory Drug Rehabilitation Center. Three psychologists interviewed the participants to collect the demographic and clinical information. Thirty healthy participants (17 male, 13 female) aged 23–45 years were recruited in control group. The study was carried out in accordance with the Declaration of Helsinki. All the participants obtained an informed content to participate the study. The study was approved by the ethics committee of the Institute of Psychology, Chinese Academy of Sciences.

Inclusion criteria for the experimental group: (1) a drug withdrawal period from 3 to 6 months before the date of screening; (2) aged 18–55 years; (3) a history of methamphetamine use corresponding to the diagnosis of stimulant addiction disorder in the Chinese version of Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5). For the control group, all subjects reported having no history or current use of illegal drugs.

Exclusion criteria: (1) a history of using other kind of drugs (e.g., heroin, cocaine); (2) illiteracy; (3) a history of brain damage or a coma over 30 min; (4) a history or family history of psychotic illness; (5) hearing problems; (6) a vision or corrected visual acuity less than 1.0.

2.2. Materials

Four neutral videos and eight emotional videos were utilized as emotional stimuli and neural stimulus for the startle reflex testing. Most of these videos were selected from a standardized database of 16 emotional film clips (Liu et al., 2017). Thirty participants watched these film clips and their emotional responses was tested using EEG and self-report. These film clips evoked similar discrete emotions with an accuracy of 86.43% for three positive emotions (joy, amusement, tenderness) and an accuracy of 65.09% for four negative emotions (anger, disgust, fear, sadness). In this study, the neutral videos include four technical introduction video segments (60–90 s per one), such as an introduction video of "How to install Windows 8". The eight emotional videos (60–90 s per one) were categorized into four kinds (i.e., anger, fear, amusement, joy) of emotional stimuli to induce the corresponding emotion. Two angry videos contained the segments of a kindergarten child being abused and the Nanjing Massacre. Two fearful videos were excerpted from the classic horror film Interception. Two amusing videos were selected from popular funny videos on internet. Two joyful videos included a scene of two lovers and a happy scene of a father and his son playing together. Videos were played on a 17 in. computer monitor.

The researchers used Biopac 16 Physiological multichannel instrument (BIOPAC MP150, sampling rate 400 KHZ) to collect subjects' skin conductance level. The unit of skin conductance level is microsiemens/cm.

The researchers utilized a 9-point Likert scale for subjective report of emotional experience. Participants rated their emotional valence and arousal level to each video immediately after watching it.

2.3. Procedure

First, the researchers helped the subject to affix physiological sensors and electrodes and wear a SONY (MDE-Z7) headphone for measuring skin conductance and startle reflex. The subject sat for 1 min to collect the physiological baseline data. Five white noises (i.e., sound probe) were played randomly within 2 min before the videos for subjects to adapt to the startle test. Then four kinds of emotional videos and neutral videos were played at a counterbalanced sequence. There was a 1-minute interval between the two videos of same emotion and a 3-minute between the videos of different emotions. Four white noises (100 dB, 50 ms per one) were inserted in each video at a random time interval to evoke startle reflex response.

For startle data recording, the raw and integrated Eye-blink Electromyographic (EMG) data of the orbicularis oculi were collected using two mini-electrodes placed directly below the left eye (Larson et al., 2005). The startle response elicited by a 50-ms burst of 100 dB white noise was measured digitally as EMG activity of the left orbicularis oculi muscle. EMG activity (μv) was automatically recorded after each white noise. EMG signals pass through bandpass filters were set at 10 and 500 Hz, and then were amplified to 40,000 times. The signals were then rectified, integrated, and stored at 1000 Hz. EMG activity was recorded similarly on the left corrugator supercilii and the

Table 1
Demographic information of the participants.

	Experimental group $n = 60(SD)$	Control group $n = 30(SD)$	p
Age (year)	30.17 (7.09)	33.00 (6.05)	.06
Education level (year)	9.175 (3.04)	12.1 (2.28)	.00**
Abstinent period (month)	4.85 (1.12)	–	–
Total time of drug use (month)	33.12 (24.99)	–	–
Total amount of drug used within one year (gram)	79.548 (121.51)	–	–

** $p < .01$.

zygomaticus major and stored at 1 ms. The startle reflex's EMG and skin conductance level were recorded during the whole experimental process.

3. Data analysis

The maximal peak value of the startle reflex EMG was obtained from 150 ms after the end of the sound. The effective numerical range of the maximum peak latency is 20-120 ms (Larson et al., 2005). Skin conductance level was obtained using the average response value during the video playing period. A data point is excluded as outlier if it beyond 3 standard deviations from the mean. The Statistical Product and Service Solutions (SPSS) 17.0 was utilized for data analysis. The comparison of demographic information, skin conductance, and startle response were analyzed using independent sample *t*-test. The subjective report of emotions was analyzed using 2×2 analysis of repeated measurement between groups.

4. Results

The demographic information of the participants is shown in Table 1. A significant difference was found on the educational level between the two groups ($p < .01$).

4.1. Startle responses

We subtracted the subjects' startle response value of neutral emotion from each of other emotion state. The results showed that the value of startle response of anger ($t = 2.069$, $p < .05$) and joy ($t = 2.406$, $p < .05$) is significant higher in the methamphetamine group comparing to the health control (Fig. 1).

4.2. Skin conductance level

We subtracted the subjects' skin conductance level of the calm state from each of other emotion response state. As shown in Fig. 2, comparing to the healthy control, the skin conductance level of anger ($t = 1.984$, $p = .05$) and joy ($t = 2.086$, $p < .05$) is significantly higher in the methamphetamine group. No significant difference was found in the skin conductance level of fear and amusement between the two groups.

4.3. Subjective emotional experiences

We compared the valence and arousal of four emotions between the two groups. Analysis of variance of repeated measure indicates an interactive effect between the valence and arousal of fear emotion, as well as between the two groups. The arousal of fear emotion response group is significantly higher ($t = 3.763$, $p < .01$; Fig. 3) in the methamphetamine group.

No significant difference was found between male and female participants within group in all outcomes.

5. Discussion

Individuals with MUD exhibit abnormal responses to emotion stimuli. The study found that, comparing to the normal controls, the methamphetamine group showed a higher level of response to anger across both objective measures (i.e., startle response and skin conductance). They also demonstrated a lower level of response to joy (Fig. 1). Long-term use of drugs causes the change in the nervous system associated with abnormal emotional processing (Moratalla et al., 2015; Perry et al., 2011). Previous studies show that people with drug abuse problems have a lower arousal to happy stimuli than healthy controls, yet they have a higher arousal to unhappy stimuli (Aguilar et al., 2005) which is consistent with this study.

The methamphetamine group reported a lower arousal level to fear emotion stimuli comparing with healthy controls. The lower emotional arousal of the methamphetamine group to fear emotion in self-report indicates a biased cognitive response to fear emotion. This may increase the difficulty for the people with drug addiction to avoid negative stimuli, which may later become a motivation of compulsive drug seeking behavior. The disability of recognizing, mastering, and regulating negative emotions can increase the risk of relapse.

The abnormal emotional responses in people with MUD reflect the emotion dysregulation. The overreaction of the methamphetamine group to anger emotion indicates the dysregulation of anger. Research found that methamphetamine dependents show irritability, hostile, and aggressive behavior after withdrawal (Payer et al., 2011), and it may be

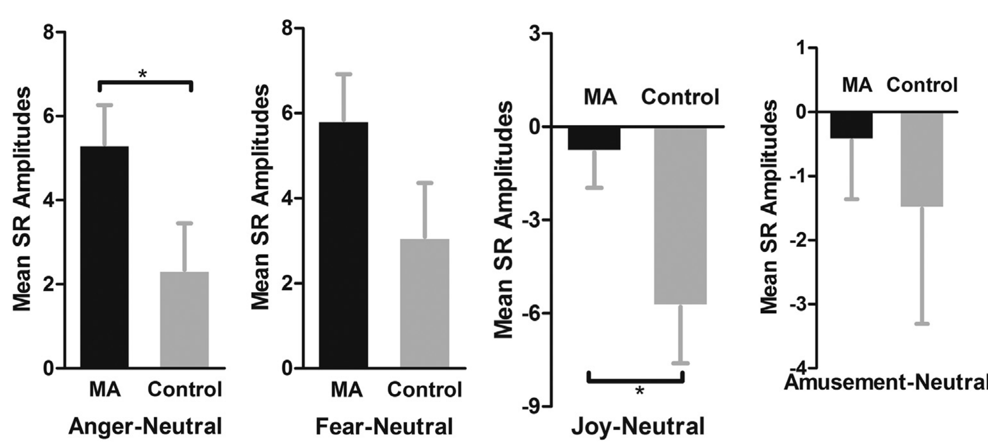

Fig. 1. The comparison between the two groups in startle responses.
Note. *: $p < .05$.

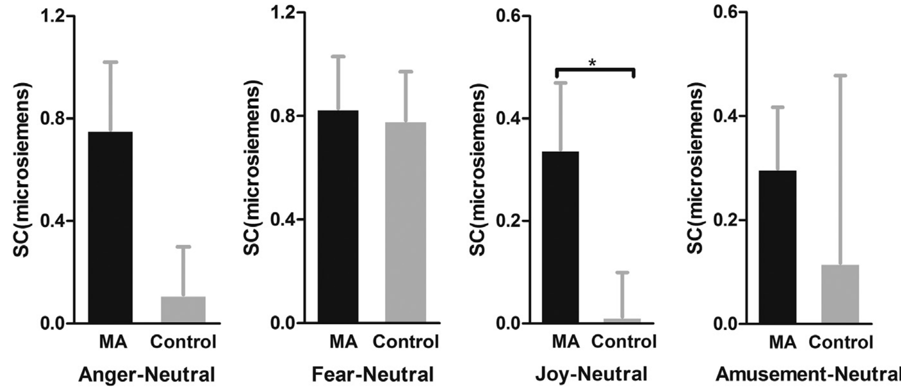

Fig. 2. The comparison between the two groups in skin conductance level.
Note. *: $p < .05$.

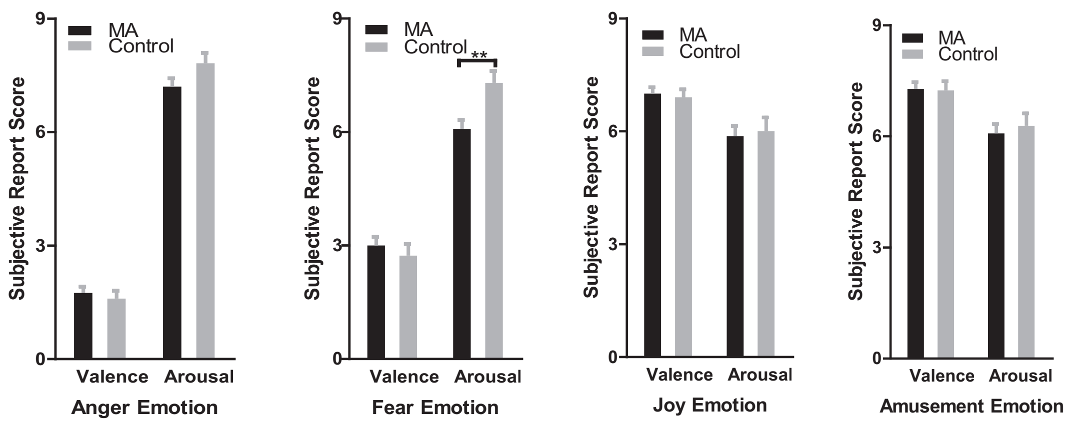

Fig. 3. The comparison between two groups in subjective emotional responses.
Note: $^{**}p < .01$.

associated with their overreaction to anger. The difficulty of emotion control in methamphetamine dependents is related to the impairment of medial prefrontal cortex, especially the abnormal regulation of orbital frontal and cingulate gyrus on amygdala. For example, brain imaging studies found that healthy subjects show an increased activity in orbital frontal lobe and cingulate gyrus when facing anger that may indicate the control on the over expression of anger emotion. However, the individuals who tend to use violence and aggressive behavior when feel angry show a decreased activity in orbital frontal lobe and cingulate gyrus (Davidson, 2000). These findings suggest the important role of anterior cingulate in the emotional regulation of anger.

The overreaction of methamphetamine dependents to anger stimuli is correlated with the functional and structural impairment in the orbital frontal cortex and anterior cingulate caused by drugs. First, lesion studies found that the patients with damaged orbital frontal lobe experience more anger emotion and less pleasant emotion comparing to healthy controls (Berlin, 2004). In terms of brain structure, evidence from PET study showed a low level of dopamine transporter at orbital frontal cortex in the subjects with a long-term drug abuse history (Sekine et al., 2003). In terms of brain function, studies of brain imaging found a lower activity in orbital frontal lobe in the inhibition task comparing to healthy controls (Paulus, 2002). These findings suggest that methamphetamine dependents suffer from the damage in orbital frontal lobe. Studies also found the severe degradation of grey matter in anterior cingulate which reflects the structural change of cingulate gyrus in MUD (Thompson et al., 2004). The PET study showed a decreased metabolism of glucose in anterior cingulate that is associated with the low activity of anterior cingulate (London et al., 2015). Comparing to healthy controls, methamphetamine dependents showed a decreased density of 5-HT transport in the anterior cingulate that may be related with emotional dysregulation disorder (Kish et al., 2009), and a lower level of *N*-acetyl aspartate in the anterior cingulate that is associated with the neuronal damage in this region (Salo et al., 2011). For methamphetamine dependents in their early withdrawal period (4–7 days), researchers found a decreased metabolism of glucose in anterior cingulate that indicate the low activity of anterior cingulate at the early withdrawal period. In summary, the research evidence above suggests the functional and structural damage caused by drugs on the orbital frontal cortex and anterior cingulate of methamphetamine dependents may provide the neural basis for their emotional dysregulation to anger emotion.

The study has several limitations. The education level, smoking amount between two groups were not sufficiently matched. Because the participants of the methamphetamine group were patients in compulsive drug rehabilitation centers and had no access to drugs, cigarette, or alcohol. All of the participants in the control group reported having no history or current use of illegal drugs. We did not have urine or blood test for recent drug use. In addition, we did not measure the cognitive ability of the methamphetamine group, such as attention, working memory, intelligence. The future study will improve the comparability between the groups, supplement necessary measurements (e.g., cognitive ability, empathy), as well as to investigate the specific emotional response of methamphetamine addicts to drug related cues.

In conclusion, the study utilized emotion videos to elicit emotional states and measured the emotion responses using both subjective and psychophysiological measurements. The results found that the methamphetamine dependent subjects have a higher response to negative emotion (i.e., anger) and a lower response to positive emotion (i.e., joy). These findings inform the development of clinical intervention for improving the emotional regulation function of people with methamphetamine dependent problems.

Author contributions statement

CG and XJ designed and implemented the experiment, analyzed the data. CG drafted the manuscript in Chinese, and XJ finalized the manuscript in English. YH and SN guided the study design and facilitated the experiment implementation.

Datasets are available on request

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

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Declarations of interest

None.

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