

Attentional bias toward substance cues in Methamphetamine-Addicted patients

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ABSTRACT

Background & objectives: Attentional bias is a type of cognitive disorder, which involves a different part of human life. Substance abuse causes attention-related disorders by a reward system disturbing in the brain which causes attentional bias of substance-addicted patients toward substance-related visual cues (SRC). **Methods:** In this study, 15 Methamphetamine-addicted patients (MAP) participated as an experimental group and 15 normal people (without dependence on any stimulants) participated as a control group. A visual probe task was used to measure the attentional bias of participants toward Methamphetamine-related (MR) images and neutral images (NI). Ten pairs of MR images and NI were shown for all participants in ten trials. In every trial, after disappearing of each pair of images, a visual probe task was shown instead of the place of one of two images and participants were asked to press a button which depicts the place of the visual probe. The time duration for participants to press the correct button after appearing visual probe was considered as reaction time (RT) of participants. **Results:** Independent Samples T-test was used to determine the difference average RTs toward MR images between control and experimental group. The calculated P-value was 0.001 which was lesser than α (0.05). So the hypothesis which illustrates that average RTs of two groups are not equivalent was accepted in β (0.95) confidence level. **Interpretation & conclusions:** RT toward special visual stimuli can be considered as a criterion of attentional bias. The average RTs of experimental group participants toward MR images was lesser than average RTs of control group participants. It shows that the MAP is more sensitive to Methamphetamine-related visual stimuli so they have an attentional bias toward them.

Keywords: component; Attentional bias; Cognitive disorder; Methamphetamine; Substance abuse; Visual probe task.

Introduction

The brain is an organ that is responsible for many biological processes. The function of the brain provides cognitive functions such as learning and attention. Brain functions damaging can be happened by traumatic injuries, mental disorders such as ADHD, and also, an addiction to psychological stimulants or substances^[1]. Substance addiction is a Chronic psychological illness which makes severe problems in different life aspects of human and it's also a general health problem that involves society with a lot of problems^[2].

Substance abusing alters brain functioning by disturbing neurotransmission steps between brain neurons^[3].

Substance abuse involves several brain circuits that constitute cognitive control system, memory and learning system, motivation system, and reward system. Each of these circuits has a certain region in the brain.

The mammalian Reward system is composed of several layers of neurons and certain psychological circumstances define the functioning of them. These neural structures motivate a large number of our activation such as eating food, drinking water, and sex^[4-6].

Reward system Creates assorted habits and they can be good or not. The function results of the reward system are not advantageous always. There are two types of rewards: negative rewards and positive rewards. Negative rewards consist of negative feelings such as suffering and pain and positive rewards consist of positive feelings such as enjoyment and gladness^[6,7]. In the early stages, the use of substance makes the user feel joy, and the use of a substance is considered a positive reward by the

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reward system. Substance addict faces powerful unpleasant feelings, which are called 'Negative Rewards', during abstinence of substance-using. Negative rewards stimulate substance addicts toward repetitive substance-using to escape from undesirable feelings. Substance using causes disappearing of unpleasant feelings, so substance-using is considered as 'positive reward' in this situation^[8,9].

A neurotransmitter, which is called dopamine, plays a crucial role in addiction. Activation of Dopamine neurons in the striatum is associated with positive and negative feelings^[10,11]. As a result, dopamine-releasing has a close relationship with positive and negative rewards^[12] and it's related to the motivation of humans^[13].

Studies demonstrate that the use of stimulants augments extracellular dopamine in the striatum^[14, 15] and alters the sensitivity of D1 receptors (a type of dopamine receptors)^[16]. These processes establish dangerous behaviors in substance-addicted patients such as drug-seeking behaviors^[17]. Substance addiction disturbs essential cognitive functions of the human brain such as learning, memory, and also attention^[14].

Attention plays a crucial role in different dimensions of human life. Attention enables us to focus on a particular certain issue while we are exposed to several issues at the same time^[15].

Formerly, there were no shreds of evidence about the physical foundation of human attention and attention-related brain regions. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have developed to find that what regions of the human brain provide different aspects of attention^[16]. Some studies based on PET have done to realize which neural pathways activate when attention is paid to certain issues such as shape and color^[17].

In one study on selective and divided attention, activation of brain regions was evaluated by showing participants colorful graphic shapes as visual stimuli. The results of this study illustrated that when participants pay attention to the color of visual stimuli, certain brain regions activate and they are the same when participants pay attention to the shape of stimuli^[16].

Visual cues can activate the reward system and involve attention toward the issue of cues that is called attentional bias. Depending on the type of cues, a reward system can make different consequences. For example, when someone copes with food cues, reward system activating involves attention to eat food^[18]. Attentional bias toward SRC is associated with the conditioned state formed by using of drugs^[19].

According to recent studies, a visual probe task is a validated method to measure attentional bias induced mental disorders. In this task, two images are shown on the screen with a certain distance beside each other for some time. After the disappearance of the images, a visual probe (for example a dot or x letter) will be shown. In this stage participants should press the left or right button on the keyboard, depending on the place of the visual probe. The output of this task is RT of participants that are considered as the time elapsed pressing button by a participant after showing a visual probe. Images, which are used in Attentional bias evaluation of addiction disorders, are of two

types: NI, which is not substance-related images, and substance-related images^[20].

Recently a large number of studies have been done to evaluate attentional bias toward SRC and results of them illustrate that substance-abusing disturbs attention cognitive function.

The study of Franken et al. was on the selective cognitive processing of Heroin addicted patients. Stroop task was used to evaluate attentional bias of participants. Results illustrated that addicted patients had significant attentional bias facing Heroin-related visual cues^[21].

In the study of Ehrman et al., attentional smokers were investigated. The Dot-probe task with using of cigarette-related and neutral images was employed for participants' attentional bias evaluation (fig.1). Smokers reacted faster than non-smokers in pressing the correct key. In the end, smokers showed considerable attentional bias toward cigarette-related visual cues^[22].

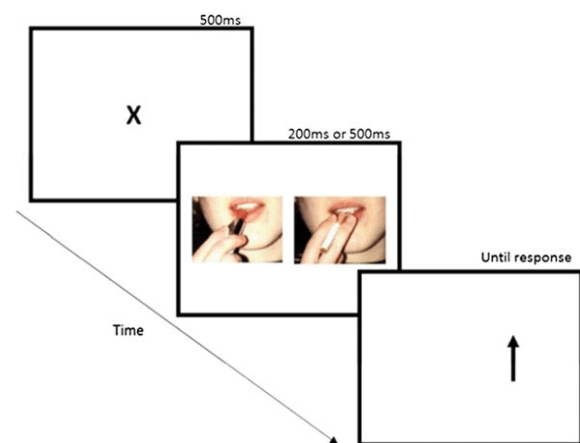


Figure 1. Dot-probe task for attentional bias evaluation toward cigarette-related visual stimuli^[22].

In the study of Hester et al., the attentional bias of cocaine-addicted patients was evaluated. The results of this study demonstrate that cocaine-addicted patients had a serious problem with controlling their attention when they face cocaine-related pictures^[23].

Field et al. studied on attentional bias toward cannabis-related cues inducing cocaine addiction. The findings illustrated that cocaine-addicted patients reacted faster toward cocaine-related visual cues. Consequently, cocaine-addicted patients have an attentional bias toward the cues of this substance. Also, the results of this study corresponded with the results of the studies on tobacco smokers and heavy drinkers^[24].

Frankland et al. studied on attentional bias toward SRC in opioid-dependent patients. Patients were in the period of abstinence with using methadone. According to the results of this study, opioid-dependent patients showed an attentional bias toward opioid-related visual stimuli^[20].

In the study of Field et al., the selective attention of alcohol-addicted patients was evaluated in their abstinence period. A visual probe task was used to evaluate reaction times of participants toward alcohol-related visual cues. Alcohol-addicted

patients showed bigger attentional bias toward alcohol-related visual stimuli^[25].

The other important point is that the attention of substance-addicted patients will be biased toward drugs even in the period of abstinence. Also, attentional bias can be considered as an index to forecast relapsing in a period of substance addiction treatment^[26].

As a result, attentional bias toward SRC can afford us information to find how substance-abusing divert attention as a fundamental cognitive function of the brain.

According to the studies on attentional bias toward SRC, no study has done on the attentional bias of Methamphetamine-addicted patients toward MR images. Attentional bias evaluation of MAP can provide us information about the craving size of MAP when they face SRC. Craving the size of MAP can help us to find out how likely MDP is to relapse and use substances.

In this study, we want to evaluate the attentional bias of MAP to find out the effect of Methamphetamine abusing human attention.

In material and methods, we speak about the Statistical community of this research and the method of attentional bias evaluation. In results, we speak about outputs of evaluation and depict them with charts and tables. In the discussion, we debate about deduction through the results.

Material and Methods

In this study 15 males, Methamphetamine addicted aged from 25 to 30 participated as an experimental group. They were screened among addicted patients who were under care in the " Banyan Javan" addiction treatment center located in Isfahan province in Iran. They met the criteria of Diagnosis and Statistics of Mental Disorder 5th edition (DSM-V) for methamphetamine dependence. Also, 15 normal men without dependence on any psychostimulants participated as a control group.

All the participants were right-handed and none of them has vision-related disorders.

Addicted patients were screened between all addicted patients visiting the addiction center which is located in Esfahan province in Iran.

All participants gave written informed consent for participation in this study. Ethics commission in medical research of the Azad University of Najafabad has adopted this study (approval id: IR.IAU.NAJAFABAD.REC.1397.069).

We made software by *c#* programming language to evaluate the attentional bias of participants by visual probe task. 10 pairs of images were used in this task. 10 images were related to Methamphetamine. 10 images were NI, which consists of different subjects such as landscape images. Each pair of images, which consists of MR images and NI, were shown beside with equal size (1 cm × 1 cm) on-screen on both sides of the fixation sign (+) for 500 ms (Fig.2).



Figure 2. One of ten pairs of images shown for participants: (a) neutral image, (b) Methamphetamine-related image.

After the disappearing of two images, a visual probe ("x" letter) appeared at the place of one of two images, on the right or left side of the fixation sign (Fig.3). Participants had been asked to press "A" or "D" button on keyboard according to the situation of "x" letter as quickly as possible (if x letter appeared on the right side of fixation sign, the participant had to press "D" button and if it appeared on the left side of fixation sign, the participant had to press "A" button). It should be noted that in the visual probe task, two buttons that are located on the right and left of a certain button can be considered as buttons that show right and left directions.

The period lasted for participants to press the related button after appearing "x" letter conceived as RT. If participants had pressed the wrong button, the wrong answer would have considered in the result of that certain trial.

Statistical analysis

In this study, we have used the Independent Samples T-test to find out whether there is a significant difference between average RTs of control and experimental groups toward MR images.

Results

Average RTs toward MR images (453.8 ms) were further than average RTs toward NI (381.76 msec) in the control group (Fig. 4). According to the Difference between Average RTs toward MR images and average RTs toward NI, which was 72.04 ms, control group participants reacted slower when visual probe appears instead of MR images that depict that they did not pay attention to the SRC significantly.

Average RTs toward MR images (364.73) was less than average RTs toward NI (416.43 ms) in experimental group Difference between Average RTs toward MR images and average RTs toward NI was 51.70 ms which illustrates that experimental group participants' attention was trapped by MR images and it caused the faster reaction(Fig.5).



Figure 3. Visual probe appearing instead of one of two images

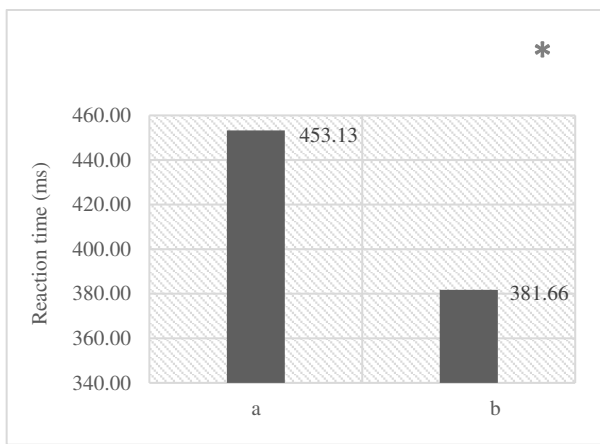


Figure 4. Comparison of average RTs in the control group: (a) Average RTs of participants when the visual probe appeared instead of MR images, (b) Average RTs of participants when visual probe appeared instead of NI.

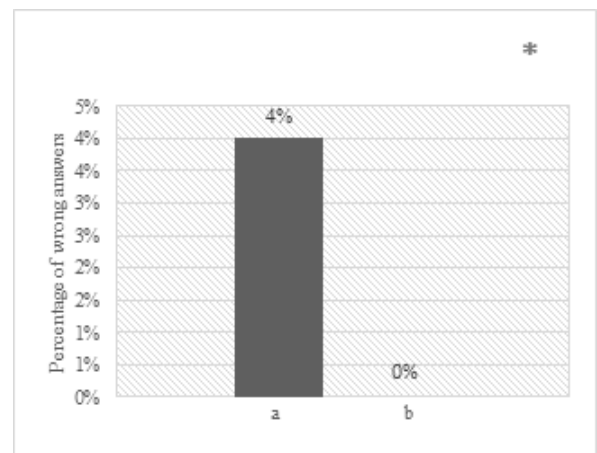


Figure 6. Comparison of percentage of wrong answers in experimental and control groups: (a) Percentage of wrong answers in the experimental group, (b) Percentage of wrong answers in the experimental group.

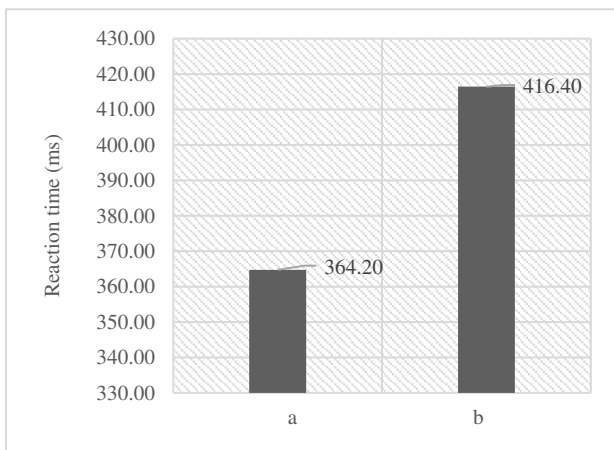


Figure 5. Comparison of average RTs in experimental group: (a) Average RTs of participants when the visual probe appeared instead of MR images, (b) Average RTs of participants when visual probe appeared instead of NI.

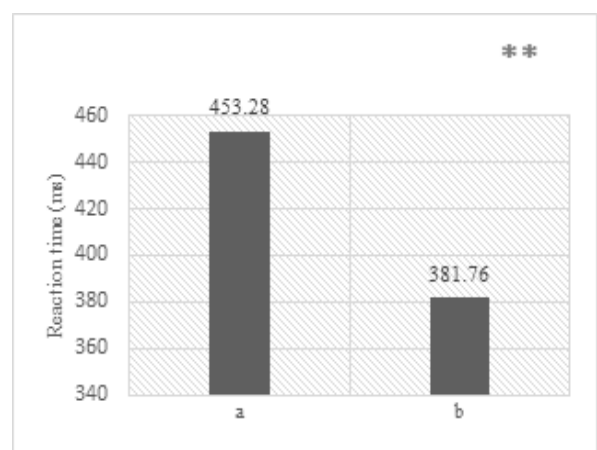


Figure 7. Comparison of average RTs in control group and experimental group (P-value = 0.001) : (a) Average RTs of the control group when visual probe appeared instead of MR images, (b) Average RTs of the experimental group when visual probe appeared instead of MR images.

Four percent of the Experimental group's trial results were wrong. Wrong answers happened when a visual probe appeared instead of an NI image but participants pressed the wrong button, which was related to the place of MR image.

Attentional bias toward SRC is the reason for the wrong answers. When the MR image and NI image appear on the screen, the patient pays attention to the MR images.

It causes pressing the wrong buttons by the patient after the disappearing of two images and appearing of a visual probe.

Also, there were not any wrong answers in the trial results of the control group (Fig. 6).

In this study, the null hypothesis was considered so that average RTs of both control and experimental groups were equal.

There is a significant difference between average RTs of experimental and control groups. The difference between average RTs of control and experimental groups toward MR images was 88.93 ms (Fig. 7).

Discussion

RTs of Participants can be considered as a criterion of attentional bias. For example, the Delay of participants, which happened when a visual probe appeared instead of a neutral image, shows the attentional bias of participants toward MR images.

Consequently, the analysis of RTs toward neutral and MR images illustrates the measure of attentional bias of participants of every group toward Methamphetamine-related visual cues. According to the results, which depict that Average RTs of participants toward MR images were further than average RT of participants toward NI in the control group, participants without Dependence to any drugs are not sensitive toward Methamphetamine-related visual cues.

However, in the experimental group, Average RTs of participants toward MR images were lesser than average RTs toward NI and average RTs of experimental group participants toward MR images were lesser than average RTs of control group participants. It illustrates that the MAP has a more attentional

bias toward substance-related visual cues (as predicted by hypothesis). Therefore the results of this study corresponded to the studies on affecting drug-abusing on attention in heroin, cannabis, and cocaine abusers^[21, 23, 24].

Also, the findings of this study are the same as the studies on attentional bias in smokers and alcohol-addicted patients^[22, 25].

Another important thing is that there were some wrong answers only in the results of the experimental group, which had occurred when the visual probe appeared instead of NI. Consequently, in these trials, the attention of some of the Methamphetamine-addicted participants distracted the substance-related images and they pressed the button that demonstrates the place of a substance-related image instead of pressing another button. This is another observation that shows that MAP has an attentional bias toward Methamphetamine-related visual cues.

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Table 1. Results of Independent Samples T-test

Variable	$\bar{X} \pm SD$		T-value	D.F	P-value	AD
Reaction time	<i>Control group</i>	<i>Experimental group</i>	3.78	28	0.001	645.33
	4246 ± 285.41	3600.93 ± 595.64				