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Original Article

The effects of methadone maintenance treatment on heroin addicts with response inhibition function impairments: Evidence from event-related potentials

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ABSTRACT

Response inhibition has been a core issue in addictive behavior. Many previous studies have found that response inhibition abilities are damaged in those with drug dependence. However, whether heroin addicts who are treated with methadone maintenance have an abnormal response inhibition ability is not clear. In order to investigate the response inhibition functions in heroin addicts who were treated with methadone maintenance, electroencephalography (EEG) was used to examine 14 heroin addicts treated with methadone maintenance (HDM), 17 heroin addicts (HD), and 18 healthy controls (HC) in an equiprobability Go\NoGo task. The reaction times (RTs) for the Go stimuli in the HD group were slower than those in the HDM and HC groups. Event-related potential (ERP) measurements showed that NoGo stimuli elicited larger N2 amplitudes than Go stimuli in the HDM and HC groups. However, for the HD group, the N2 amplitudes were similar for the two conditions. In addition, the HDM and HD groups were associated with longer P3 latencies. Our results demonstrated that methadone maintenance treatment might ease the deficits in response inhibition that result from long-term drug abuse. However, compared to normal people, HDM patients have serious problems evaluating and inhibiting inappropriate behaviors.

1. Introduction

To date, there have been many theories of addiction that assume that executive function plays an important role in generating drug dependence and addictive behavior [1–2], and that response inhibition is the core of executive function [3]. Response inhibition refers to the conscious inhibition of a response that is unrelated to the current task and that is automatically activated [4]. Response inhibition, which is a

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core component of executive function, plays an important role in the inhibition of an inappropriate response in an individual in order to adapt to survive. Response inhibition is a prerequisite for appropriate behavior, and response inhibition damage or abnormalities will lead to inappropriate or illegal behavior [5]. Some researchers have found that response inhibition and addictive behaviors are highly correlated, which means that individuals with weaker response inhibition are more prone to addictive behavior. Thus, individuals with high impulsivity and low response inhibition are more likely to use and be dependent on drugs [6]. Therefore, response inhibition is a core issue in addictive behavior.

Heroin addiction is a type of addictive behavior, and the study of heroin addicts' response inhibition abilities have found that long-term heroin use can damage brain structures, resulting in damage to the response inhibition ability. At the behavioral level, there have been many studies that have used Stroop, Go/NoGo, and Stop Signal tests to examine the response inhibition of heroin addicts by using their reaction time (RT) and percentage correct as indexes, and these studies have found that heroin addicts have much longer RTs and less accuracy in response inhibition tasks [7–8]. Neuroimaging studies that examine brain function at the structural level have further confirmed that the structure that is associated with executive control in the brains of heroin addicts is damaged. Fu et al [9] have used event-related potential (ERP) technology to determine the obstacles that heroin addicts face during the conflict-monitoring stage. Yang et al [10] have used functional magnetic resonance imaging technology and have found that heroin addicts have some deficits in response inhibition, even after the drug is withdrawn. These studies have used different methods and techniques to confirm that the inhibition of heroin addicts' control function is due to varying extents of defects or damage and that these defects or damage to the function are the main reason that leads to their drug addiction or relapse.

Methadone maintenance treatment is one of the main alternative therapies used to treat patients with opiate addiction worldwide, and more and more heroin addicts are participating in methadone maintenance treatment in China. Some researchers found that methadone maintenance treatment can significantly reduce the patient's withdrawal symptoms, but there are no significant improvements in the abnormalities in the neural mechanisms that are associated with heroin dependence. Long-term heroin consumption causes adaptive changes in brain systems that may persist for a long time [11]. The research of Verdejo et al [12] has discovered that methadone itself produces significant cognitive impairments and increases the already present cognitive impairments in addicts who take it. Some researchers have found that rehabilitation can effectively improve the cognitive function damage that is caused by buprenorphine, placebo, and methadone [13]. The effects of methadone maintenance treatment on the heroin addicts' neural mechanisms underlying response inhibition need further discussion. In China, a large number of people take part in methadone maintenance treatment. However, relapse and furtive inhalation phenomenon often occur. Thus, an investigation of the effects of methadone maintenance treatment on heroin addicts' response inhibition has important practical significance.

Most previous studies on response inhibition have examined ERPs with a high time resolution, and they have displayed the time course of the information processing and provided electrophysiological indicators of cognitive function. Most of these studies have used classical paradigms, such as Go/NoGo, Stop Signal, oddball, and some others, that have been adapted for these studies. Because the stop signal and stimulation that evoke electroencephalography (EEG) components in the Stop Signal paradigm can generate some interferences, and in the oddball paradigm there are some novel stimulus effects on brain electrical components other than the stimulation-evoked EEG components, this study adopted the Go/NoGo paradigm. The classic Go/NoGo paradigm asks participants to react to the high probability of a Go stimulus and to inhibit the NoGo stimulation with a small probability. Stimulus probability may affect the amplitude of EEG components, and the low probability usually produces a larger component of P3 [14]. In order to eliminate the probability of interference in the experiment, this study employed the equiprobability Go/NoGo paradigm.

The Go/NoGo task induced two ERP components that reflect response inhibition processing under NoGo conditions [15]. The first ERP component is the NoGo-N2, which is the largest negative component that appears in the frontal scalp when the stimulus is presented for 200 milliseconds. Compared to the Go condition, the NoGo condition results in N2 with a more negative amplitude. This phenomenon is called the NoGo-N2 effect, and N2d (the amplitude of NoGo-N2 with the amplitude of Go-N2 subtracted) indicates this effect [16–17]. It has been argued that the NoGo-N2 effect reflects response inhibition, which is a top-down mechanism that suppresses the incorrect tendency to respond and operates at a processing stage prior to motor execution [18]. A study by Yin and Liu [19] has found that the relationship between response inhibition and the effect of NoGo-N2 is that NoGo-N2 reflects the process of response inhibition. The second ERP component is NoGo-P3, which is the largest positive component that appears in the central area when the stimulus is presented for 300–500 milliseconds, and Go-P3 reaches the maximum in the parietal position [20]. NoGo-P3 has a larger positive amplitude than Go-P3 does at the central scalp—this phenomenon is called the NoGo-P3 effect. NoGo-P3 is the electrophysiological reflection of response inhibition. A previous study has found that a reduction in NoGo-P3 that may be related to alterations in successful inhibition is the dominant reaction [21], and it has no connection with the process of response inhibition.

Consequently, the participants in the present study were heroin addicts who participated in methadone maintenance treatment, and we employed the equiprobability Go/NoGo paradigm; we used ERP technology to investigate the neural mechanisms of response inhibition in the heroin addicts who participated in methadone maintenance.

2. Methods

2.1. *Participants*

Fourteen heroin addicts (9 males and 5 females) receiving methadone maintenance treatment (HDM) were selected