

Thesis Title	Alteration of Plasma Biogenic Amines and Hormones in Heroin- and Amphetamine-Addicted Subjects
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Abstract

Heroin and amphetamine are well-known as drugs of abuse. The reinforcing effects of both drugs appear to be crucial factors for addiction in humans. From a previous study, it was suggested that the positive reinforcement in drugs of abuse comes from the alterations of the norepinephrine in the locus coeruleus, and also involves the mesolimbic and mesocortical dopaminergic system. To determine the neurochemical changes in plasma caused by heroin or amphetamine in heroin- and amphetamine-addicted subjects, neurochemical data in both subject groups was obtained by using the ion-pairing high-performance liquid chromatographic method coupled with electrochemical detection.

During the withdrawal period, heroin addicts showed a variety of withdrawal signs, including pupil size dilatation, temperature decrease and increased pulse rates.

In order to determine the effects of heroin or amphetamine on biogenic amines, blood from each subject was taken and protein was extracted by perchloric acid. During the addiction period, heroin caused an increase in 5-HT levels ($p < 0.05$), whereas, it decreased 5-HIAA, the major metabolite of 5-HT. Amphetamine caused a

DA, but its metabolite, DOPAC, did not change. DA turnover in heroin addicts decreased during this period and did not return to normal levels even after one year. However, it increased 5-HT and 5-HIAA levels in plasma, with a significant change being shown only in 5-HIAA. This study found that 5-HT turnover was decreased in both heroin and amphetamine addicts.

A short withdrawal period (24-36 hr and 36-72 hr after either heroin and amphetamine were withdrawn) caused a significant decrease in DA levels ($p < 0.05$) and an increase in DOPAC levels ($p < 0.001$) returning to normal levels after 72 hr following drug withdrawal. DA turnover in amphetamine addicts markedly increased during this period and returned to normal levels after 72 hr following drug withdrawal. 5-HT levels during a short withdrawal period (24-36 hr in the case of amphetamine addicts and 36-72 hr in the case of heroin addicts) were high and maintained their high levels from the addiction period, but 5-HIAA in both addiction types did not change during this time.

A long withdrawal period of both heroin and amphetamine caused a significant decrease in DA levels ($p < 0.05$), with for heroin, DA levels returning to normal levels over one year later. However, DA levels in amphetamine subjects had a tendency to revert to normal levels after withdrawal from the drug for two months. In heroin subjects 5-HT levels decreased, whereas 5-HIAA levels increased significantly, but this change in 5-HT and 5-HIAA levels was not found in amphetamine subjects.

The study of hormonal changes in this study found that during the addiction period, prolactin increased and testosterone decreased in both heroin- and amphetamine-addicted subjects. These hormonal changes in heroin addicts reverted to normal levels after six months following drug withdrawal. Cortisol levels during the addiction period increased in heroin addicts and returned to normal one year after drug withdrawal, however, they were decreased in amphetamine addicts.

The present results suggest that the changes in plasma obtained from heroin and amphetamine addicts during the addiction and withdrawal periods are mediated by dopamine. The fall in DA output is the correlate of the aversive subjective symptomatology in withdrawal. Therefore, measuring DA output might be a model for studying drug potential effectiveness in treating psychological dependence.