INTRODUCTION

A synthetic drug, methamphetamine has a high potential for abuse and dependence. It is illegally produced and sold in a pill form, capsules, powder and chunks. Methamphetamine was developed from its parent drug amphetamine and was originally used in nasal decongestants, bronchial inhalers, and in the treatment of narcolepsy and obesity (Ando et al. 1993; Fry 1998; Anglin et al. 2000). In the 1970s, methamphetamine became a Schedule II drug - a drug with little medical use and a high potential for abuse. The drug is referred to by many names including "meth," and "speed" (Beebe and Walley 1995). Pure methamphetamine hydrochloride, the smokeable form of the drug, is called "L.A." or, because of its clear and chunky crystals which resemble frozen water, "ice," or "crystal" (Cho 1990; Mack 1990).

Methamphetamine hydrochloride is easily produced using ephedrine, hydroiodic acid, or pseudoephedrine (Frank 1983; Windahl et al. 1995; Rothman et al. 2003). It can be smoked, taken intranasally (snorted), injected intravenously, or ingested orally (Derlet and Heischober 1990; Dixon 1989). The practice of "eating" methamphetamine by putting it on paper or food and chewing it also has been reported. The drug alters mood in different ways, depending on how it is taken. Immediately after smoking or intravenous injection, the user experiences an intense "rush" or "flash" that lasts only a few minutes and is described as extremely pleasurable. Smoking or injecting produces effects fastest, within five to ten seconds. Snorting or ingesting orally produces euphoria - a high but not an intense rush. Snorting produces effects within three to five minutes, and ingesting orally produces effects within 15 to 20 minutes. In all forms, the drug stimulates the central nervous system, with effects lasting from four to 24 hours. Methamphetamine use can not only modify behavior in an acute state, but after taking it for a long time, the drug literally changes the brain in fundamental and long-lasting ways. It kills by causing heart

failure (myocardial infarction) (Kaiho and Ishiyama 1989; Hong et al. 1991), brain damage, and stroke and it induces extreme, acute psychiatric and psychological symptoms (Sato et al. 1983; Fujimori et al. 1989) that may lead to suicide or murder (Bailey and Shaw 1989). Symptoms of prolonged methamphetamine abuse can resemble those of schizophrenia (Robinson and Becker 1986; Kalivas and Stewart 1991) and are characterized by anger, panic, paranoia, auditory and visual hallucinations, repetitive behavior patterns, and delusions of parasites or insects on the skin. The person may exhibit anxiousness; nervousness; incessant talking; extreme moodiness and irritability; purposeless, repetitious behavior, such as picking at skin or pulling out hair; sleep disturbances; false sense of confidence and power; aggressive or violent behavior; disinterest in previously enjoyed activities; and severe depression. All addictive drugs have two things in common: they produce an initial pleasurable effect, followed by a rebound unpleasant effect. Methamphetamine, through its stimulant effects, produces a positive feeling, but later leaves a person feeling depressed. This is because long term use of methamphetamine suppresses the normal production of dopamine. The user physically demands more of the drug to return to normal. This pleasure/tension cycle leads to loss of control over the drug and addiction.

Methamphetamine is a serious problem of drug abuse in Thailand because illicit methamphetamine tablets are sold in many places of Thailand by very low price. This tablet called YABA in Thai contains about 20-30 mg methamphetamine and since it is this substance that make user get addiction.

In this study, methamphetamine's effects on central nervous system, EEG, locomotor activity, and stereotyped behavior were measured and analyzed in order to reflect changes of dopamine pathways. Dopamine pathway consists of four pathways; (1) hypothalamopituitary pathway that dopamine neuron in hypothalamus is projected to pituitary involved in release of prolactin; (2) nigrostriatal pathway that dopamine neuron in substantia nigra is projected to striatum (caudate-putamen) involved in movement (Robbins and Everitt 1992); (3) mesolimbic pathway that dopamine neuron in ventral tegmental area (VTA) is projected to striatum (nuclear accumben) involved in emotion and locomotor activity; and (4) mesocortical pathway that dopamine neuron in ventral tegmental area (VTA) is

projected to prefrontal cortex involved in cognition and attention. When methamphetamine causes an increase in dopamine release from dopamine pathway, dopamine binds to dopamine receptor and eventually affects the neurons in cerebral cortex. Then, EEG that records potential summation or subtract on dendrite of neuron in cerebral cortex would be changed. When methamphetamine increased a dopamine level in the mesolimbic pathway that stimulates locomotion center, locomotor activity would increase (Kelly and Iversen 1976; Sessions et al. 1980; Kehne et al. 1981; Swerdlow et al. 1986). And when methamphetamine increased a dopamine level in the nigrostriatal pathway (Creese and Iversen 1974; Kelly et al. 1975; Kelly 1977), the signal from this pathway would inhibit movement via pyramidal tract. When this pathway does not worked well, it can not control movements and would produce stereotyped behavior.

Methamphetamine has a structure that is exactly same as amphetamine except for the addition of an extra methyl group on the branched chain. The methamphetamine's effects on central nervous system are greater than amphetamine. Melega et al. (1995) have shown that dose-dependent increases in amphetamine and methamphetamine plasma levels resulted in proportional increases in striatum levels that were equivalent for both drugs; elimination rates also were similar and were characterized by a first-order decay process. Most of the results indicate that amphetamine and methamphetamine pharmacokinetics and their subsequent dopamine responses in the striatum are equivalent.

In this study, it was tested if the effects of methamphetamine on EEG pattern, locomotor activity, and stereotyped behavior would be similar to amphetamine. The purpose of experiments was to study the effects of methamphetamine on EEG, locomotor activity and stereotyped behavior in rat. EEG power spectrum is a quantitative tool to define changes in the brain. By using the superior power and flexibility of the computer to store and to analyze the EEG, an invention was of fundamental importance: the so-called analog-digital converter. Essentially, it is an electronic device that takes a continuously variable wave and transforms it to a power of frequency band. EEG has proceeds in real time. To assist in the estimation of EEG spectral content (one of the most difficult tasks by visual inspection), EEG data are entered into a computer and spectral content is rigorously determined by the use of techniques of mathematical signal

analysis (typically by the FFT or Fast Fourier Transform algorithm). EEG technology is more practical and affordable than other neuro imaging technologies, including magnetic resonance imaging (MRI), positron emission tomography (PET), or single photon emission computed tomography (SPECT) and it can be realistically implemented into a variety of treatment settings. As for the application of this study to human beings, quantitative electroencephalography (EEG) may be a sensitive and specific screening test to identify those substance abuse patients with the highest risk of relapse. If it is confirmed that EEG is sensitive for detecting changes of neural activity created by methamphetamine, it would be used to detect the abuse patients.