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EDITORIAL

# Pharmacoterrorism: the potential role of psychoactive drugs in the Paris and Tunisian attacks

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*In memoriam: the victims of the Paris attacks of November 13th 2015*

On the evening of November 13th 2015, a series of coordinated terrorist attacks, consisting of mass shootings, suicide bombings, and hostage taking, occurred in Paris, France (Hirsch et al. 2015). The attacks were the deadliest attacks in France since World War II and the deadliest attacks in the European Union since the Madrid train bombings in 2004 (Lynch 2015). The Islamic State of Iraq and the Levant (ISIL) claimed responsibility for the attacks (CNN 2015), and French President François Hollande said the attack was an act of war by ISIL (Reuters 2015).

Beginning at 21:20 Central European Time, there were three suicide bombings outside the Stade de France in Saint-Denis, along with another suicide bombing and a series of mass shootings at four locations in Paris (Reuters 2015). The attackers killed 130 people (Paris attacks death toll rises to 130 2015), including 89 at the Bataclan theatre, where they took hostages before engaging in a 3-hour standoff with police. Three hundred sixty-eight people were injured, including more than 80 seriously injured. Seven of the attackers also died, and the French authorities continue the search for accomplices.

Eyewitnesses have described how some of the Bataclan killers were "zombie like" during the siege ('Zombie-like' 2015). Syringes thought to have been used by the gang before the Paris attacks were found inside hotel rooms. The French police are investigating whether the ISIL gang launched their killing spree under the influence of a psychoactive drug, dubbed a "terror potion" by some commentators, which could explain the extreme barbarity of the ISIL operatives (Liban 2015). The "terror potion" may be Captagon counterfeit tablets (CCT). Production of CCT has been increasing in recent years, particularly in areas such as Syria where ISIL are active. According to the World Customs Organization (WCO), the amount of Captagon seized has increased from 4 t in 2012 to more than 11 t of Captagon in 2013 (World Customs Organization 2013).

Captagon is the brand name for fenethylline [7-(2-a-methylphenyl-aminoethyl)-theophylline]. Fenethylline was first synthesized by the German company Degussa AG in 1961 and manufactured until the 1980s. It is a chemical linkage of N-alkylated amphetamine and theophylline and behaves as a prodrug to both drugs. One of the main advantages of fenethylline over amphetamine is that it does not increase blood pressure to the same extent as amphetamine, so it can be used by patients suffering from cardiovascular conditions. Fenethylline is usually taken orally but it can be dissolved into a liquid and injected, which is the route it has been suggested the Paris bombers used. Amphetamines are dopamine transporter blockers and also release dopamine through their effects on the dopamine vesicle transporter vesicular monoamine transporter (VMAT) 2 and by reversing the direction of the transport of dopamine from the extracellular space (Torres & Ruoho 2014). The pharmacological effects of amphetamines are primarily attributed to their effects on central

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catecholamine neurotransmission, particularly through the increase in levels of dopamine and norepinephrine (Wallace 2012; Karoum et al. 1994). Fenethylline was primarily used as a treatment for attention deficit hyperactivity disorder but became illegal in most countries in 1986 after being listed by the World Health Organization for international scheduling under the Convention on Psychotropic Substances (Kristen et al. 1986). It was considered too addictive and too dangerous given the potential for severe behavioural side effects, including increased aggressiveness and delusional symptoms.

Seifeddine Rezgui, the terrorist who shot and killed 38 people at a beach in Tunisia in the summer of 2015, took CCT before carrying out his shootings. According to testimony during the shooting, he was smiling and laughing whilst he committed the massacre (Panenka et al. 2013).

Whilst many factors, most notably ideological indoctrination, underlie terrorist actions such as those committed in Paris and Tunisia, several lines of evidence suggest that the constituents of CCT could facilitate the extreme violence seen during these attacks. It should be noted that Captagon counterfeit tablets have also been shown to contain other psychoactive substances. For example, a gas chromatograph mass spectrometry analysis of CCT has identified the presence of amphetamine and theophylline (the derivatives of fenethylline) as well as other psychoactive compounds, including caffeine, procaine, a local anaesthetic that may explain the painkiller effect attributed to CCT, and ephedrine, a sympathomimetic that may increase the stimulant effect of CCT (Grant et al. 2012).

Amphetamine use has been associated with impulsive, aggressive, antisocial, and, in cases, homicidal behaviour in some studies (Qu'est-ce que le captagon, la drogue des djihadistes 2015; Alabdalla 2005; Sekine et al. 2006; Scott et al. 2007; Freese et al. 2002), especially when used in higher dosages and with longer use (Anglin et al. 2000). A study of 1016 amphetamine users reported high levels of psychiatric symptoms, particularly depression and attempted suicide, but also anxiety and psychotic symptoms (Lineberry & Bostwick 2006). The users also reported high levels of problems controlling anger and violent behaviour, with a correspondingly high frequency of assault and weapon charges (Zweben et al. 2004). Amphetamine consumers also self-report alexithymia (Payer et al. 2011) and have been found to show reduced ventral inferior frontal gyrus activity, which could indicate lower emotional regulation, and, in turn, may contribute to heightened aggression (Payer et al. 2011). Amphetamine use has also been found to increase emotional empathy for positive emotions and to reduce the recognition of negative emotions as indexed using sad faces (Schmid et al. 2014; Hysek et al. 2012). However, moral judgement was not found to be altered in amphetamine consumers (Schmid et al. 2014). Psychosis linked to amphetamine use may also lead to hostility and aggression (Panenka et al. 2013). Between 26 and 46 % of subjects with amphetamine dependence has been estimated to develop amphetamine-associated psychosis (Grant et al. 2012).

From a historical point of view, it should be underscored that the use of amphetamines in war is not new. Both the Allies and Nazis used amphetamines for enhancement purposes during World War II (Defalque & Wright 2011; Rasmussen 2011). At the time, increased aggressive behaviour and increased confidence were described in fighters taking these drugs (Defalque & Wright 2011; Rasmussen 2011).

Clearly, CCT use is not responsible for the recent terrorist attacks. However, CCT appears to be increasingly used by the organizations behind recent terror attacks to facilitate fighting and seems to have been used by the terrorists prior to the Paris and Tunisian attacks. This has implications for security services and others responding to a terrorist attack as, for example, negotiations with hostage takers may be complicated by the effects of CCT use on empathy and the possibility of psychotic symptoms.

The use of CCT by Islamic terrorists is a new chapter in the misuse of psychoactive drugs. Given the potential effects of CCT and that CCT use amongst Islamic fighters looks set to increase; research into the behavioural and neurobiological consequences of CCT use is needed.

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