MDMA can increase cortisol levels by 800% in dance clubbers

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Wolff et al. (2012) described some very interesting new data on genetic polymorphism related to the neurohormonal effects of recreational ecstasy/MDMA. They collected biological samples from volunteers before and after dance clubbing, with MDMA presence indicted via urine analysis. They found that levels of cortisol were 110% higher in MDMA users post-clubbing, compared with dance clubbers who had not taken MDMA. They claimed that their study was 'The first *in the field* replication' of previous laboratory study findings on MDMA and cortisol release (Wolff et al., 2012, p. 425). However, we have undertaken two previous studies of cortisol levels in dance clubbers, with MDMA also biochemically confirmed, with saliva analyses (Parrott et al., 2007, 2008). However, we reported far larger increases in cortisol, with peak group mean increases of 800% in MDMA-users monitored in the dance club.

Wolff et al. (2012) collected samples pre-clubbing and post-clubbing; but they did not collect samples from clubbers during the period of peak MDMA activity. Their post-clubbing samples showed that cortisol values were 110% higher in those who had previously taken MDMA, in comparison with non-users. This increase was broadly similar to the post-clubbing values found in our studies. In Parrott et al. (2007) we reported a 130% cortisol increase 24 hours post-MDMA, while in Parrott et al. (2008) we found a 70% increase 48 hours post-MDMA. Crucially in both studies we collected saliva samples from the dance clubbers while they were actively partying. In Parrott et al. (2008), we found that cortisol values were 800% higher at 2.5 hours post-MDMA, when compared with pre-drug baseline (0.3 μg dl^{-1} at baseline, 2.2 μg dl^{-1} after 2.5 hours, $p < 0.001$). In another study of ecstasy/MDMA users at a house party (Parrott et al., 2007), cortisol values again peaked at 800% higher than baseline, at 4 hours post-MDMA (0.3 μg dl^{-1} at baseline, 2.3 μg dl^{-1} after 4.0 hours, $p < 0.001$). In both studies, we assessed the same individuals attending the same dance club/party venue on other weekends, when they had not taken MDMA or any other stimulant drugs. Under these abstinence conditions, the cortisol values did not change significantly from baseline.

Wolff et al. (2012) discussed the practical implications of their cortisol changes, and noted that: 'Chronic excessive use of MDMA may be contributing to the dysfunction of the HPA axis' (see also Gerra et al., 2003; Harris et al., 2002). They further noted the role of cortisol in sleep and circadian rhythm, psychobiological functions known to be adversely affected in abstinent ecstasy/MDMA users (McCann et al., 2009). Cortisol is involved in a wide array of psychobiological functions (Herbert et al., 2007), including memory (Backhouse et al., 2006; Wolf et al., 2005), higher cognitive processing (McMorris et al., 2006), impulsivity (Fishbein et al., 1989), neuronal damage (Herbert et al., 2007), and hippocampal activity (Nagaraja et al., 2007). These same functions have been shown to be adversely affected in abstinent ecstasy/MDMA users, with deficits in memory (Montgomery et al., 2010), higher cognition (Fox et al., 2002), impulsivity (Butler and Montgomery, 2004), neuronal damage (Reneman et al., 2006), and hippocampal changes (Jacobsen et al., 2004; Den Hollander et al., 2011). The acute and chronic changes in hypothalamic–pituitary–adrenal (HPA) axis activity may, therefore, be involved in many of the diverse biological effects of recreational ecstasy; the putative role(s) of cortisol for these neuropsychobiological effects is debated more fully in Parrott (2009).

In summary, we agree with Wolff et al. (2012) about the importance of cortisol for understanding the neuropsychobiology of MDMA. However, the acute cortisol release following recreational MDMA can be far stronger than they suggest. The neurohormonal findings from our applied studies emphasize the insights to be gained from real-world research; hence, it is crucially important to biologically monitor dance clubbers in the situations where they are actually using these illicit substances (Morefield et al., 2009; Parrott and Lasky, 1998; Parrott et al., 2007, 2008; Wolff et al., 2006, 2012). The cortisol changes indicate the profound energetic stress being caused by this powerful methamphetamine derivative, especially when it is taken in stimulating dance club or party environments (Darvesh and Gudelsky, 2005; Parrott, 2004, 2006). These periods of HPA axis overactivity, may have adverse implications not just during the acute drug phase, but also for the longer-term neurobiological/neurotoxic effects of MDMA (Den Hollander et al., 2011; Erritzoe et al., 2011; Kish et al., 2010).

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