

experiences have been funding cuts and lack of incentives. Some examples will be presented.

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## Symposium: making medicines out of illicit drugs – ECNP symposium hosted by EPA

### JS07

#### Can ecstasy treat the agony of PTSD?

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**Introduction** Two serotonin reuptake inhibitors (SSRIs) have received FDA indication for treatment of PTSD, however the effectiveness of pharmacotherapy for PTSD is limited. Psychotherapy, including several well established evidence based methods, is the mainstay of PTSD treatment. Despite advances in this area, a significant percentage of PTSD patients are refractory to existing treatments. Recent research has explored the possibility that certain drugs could increase the effectiveness of psychotherapy when administered intermittently in conjunction with psychotherapy sessions. The most robust published. Results to date using this approach have been in early clinical trials of  $\pm$  3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy. These studies primarily involved civilians with treatment-resistant, crime-related PTSD. A more recent phase 2 trial, completed in 2015 yielded equally promising. Results in a cohort of military veterans, police officers and firefighters, mostly veterans from the wars in Iraq and Afghanistan.

**Methodology** In these double blind controlled trials subjects with PTSD refractory to prior treatment are randomized to an active dose of MDMA or an active or inactive placebo administered to each individual on only two or three occasions during eight-hour psychotherapy sessions one month apart, in conjunction with preparatory and follow-up psychotherapy sessions. Outcome measures are repeated one or two months after the second MDMA-assisted session before the blind is broken. Subjects who were randomized to full dose MDMA are then eligible for one additional, open label, MDMA-assisted session. Those randomized to placebo or a lower dose of MDMA are eligible for three open-label full dose sessions. Outcome measures are repeated two months following the third MDMA-assisted session. The primary outcome measure is the Clinician Administered PTSD Scale (CAPS). Additional measures include the Beck Depression Inventory-II (BDI-II), Global Assessment of Functioning (GAF), Pittsburgh Sleep Quality Index (PSQI) and Posttraumatic Growth Inventory (PTGI).

**Results** In the original study comparing MDMA with inactive placebo along with the same psychotherapy PTSD was resolved in 83% of the MDMA group vs. 25% of the placebo group receiving the same therapy. Improvement was maintained for at least 74% of subjects at long-term follow-up a mean of 45 months later. In a more recent, unpublished, study both the high dose and the medium dose of MDMA showed large effect sizes in reducing CAPS scores, and improvements in secondary measures: and BDI-II, PSQI, GAF and PTGI.

**Conclusion** Evidence in phase II trials suggest that MDMA-assisted psychotherapy is effective in treating PTSD in both civilians and veterans who have not responded to established treatments. Phase III trials are necessary to definitively establish safety and efficacy of MDMA-assisted psychotherapy for PTSD.

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### JS08

#### Treatment of heroin dependence with ibogaine

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**Background** The use of the hallucinogen ibogaine as an anti-addiction agent has been described in several case reports, dating back to the eighties. The anti-addiction properties of ibogaine have been confirmed in a large body of animal work. Ibogaine has been shown to be effective in reducing withdrawal severity and substance use for a variety of substances, including cocaine and opiates. Animal studies also show some potentially dangerous adverse reactions, including cerebellar toxicity and potential cardiac effects. While pharmacological treatment options for opiate and cocaine dependence are still limited, ibogaine assisted treatment might be a promising new option. Therefore more systematic studies on its toxicity and efficacy are warranted. In our studies we address these two research questions: is ibogaine treatment for opiate dependence safe and effective for treating opiate withdrawal and relapse prevention? A secondary objective is to explore the pharmacokinetic properties of ibogaine.

**Methods** Animal work: first we performed a systematic review and meta-analysis of animal studies on ibogaine. Thirty studies were included in the systematic review, of which 27 could be analyzed in meta-analysis. Human studies: fifteen opiate dependent patients will be treated with ibogaine (10 mg/kg), on top of treatment as usual. Ibogaine toxicity will be assessed through close monitoring with electrocardiography, with QTc prolongation as main outcome measure, repeated assessments of ataxia using the (SARA) and observation of psychotic symptoms by using the Delirium Observations Scale (DOS). Ibogaine efficacy will be measured, using repeated evaluations of opiate withdrawal severity (Subjective Opiate Withdrawal Scale: SOWS; Objective Opiate Withdrawal Scale: OOWS), craving intensity (using a Visual Analogue Scale) and substance use, with a six-month follow-up. Clinical observations in ibogaine treated individuals will be compared with a cohort of opiate dependent patients treated with a rapid detoxification procedure. Both acute and long-term effects will be linked with serum ibogaine and noribogaine levels.

**Results** Animal work: overall, ibogaine reduced drug self-administration, particularly during the first 24 hours after administration. Ibogaine had no effect on drug-induced conditioned place preference. Ibogaine administration resulted in motor impairment in the first 24 hours after supplementation, and cerebral cell loss even weeks after administration. Data on ibogaine effect on cardiac rhythm as well as on its neuropharmacological working mechanisms are limited. Human studies: human data are still being collected. Treatment of the first patients confirmed strong effects of ibogaine on heart rhythm (QTc prolongation) and ataxia, while the opiate withdrawal symptoms were relatively mild. The first observations on the clinical effect of ibogaine on craving and substance use will also be shared.

**Conclusions** Based on our meta-analysis of animal data, there is strong evidence that ibogaine is effective in reducing drug self-administration in animals. This warrants further studies into the clinical efficacy of ibogaine in substance dependent patients in reducing craving and substance use. Our first clinical experiences in