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### Article

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**Acute psychotropic, autonomic, and endocrine effects of 5,6-methylenedioxy-2-aminoindane (MDAI) compared to 3,4-methylenedioxymethamphetamine (MDMA) in human volunteers: a self-administration study.**

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## Supporting Information – Drug Testing and Analysis

**Table S1.** Mean  $\pm$  SEM values for the acute effects of MDMA and MDAI

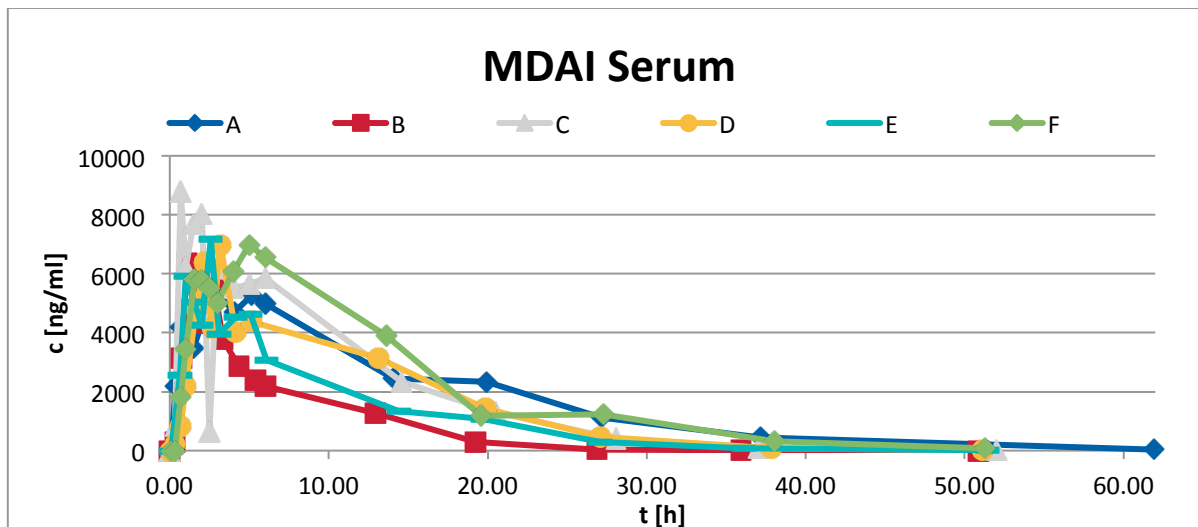
			MDMA 75mg <sup>a</sup>	MDMA 125mg <sup>b</sup>	MDAI 3.0 mg/kg
<b>Vital signs</b>					
	Systolic blood pressure (mm Hg)	E <sub>max</sub>	145.0 $\pm$ 2.5	154.9 $\pm$ 3.4	150.0 $\pm$ 6.1
	Diastolic blood pressure (mm Hg)	E <sub>max</sub>	83.8 $\pm$ 1.5	94.8 $\pm$ 2.8	94.0 $\pm$ 2.1
	Mean arterial blood pressure (mm Hg)	E <sub>max</sub>	103.1 $\pm$ 1.6	114.5 $\pm$ 2.0	112.0 $\pm$ 3.0
	Heart rate (beats/min)	E <sub>max</sub>	83.5 $\pm$ 3.1	93.5 $\pm$ 4.3	72.5 $\pm$ 4.5
	Body temperature (°C)	$\Delta$ E <sub>max</sub>	0.35 $\pm$ 0.06	0.83 $\pm$ 0.11	0.27 $\pm$ 0.14
<b>Subjective effects</b>					
Visual Analog Scale (VAS, %max)					
	Any drug effect	$\Delta$ E <sub>max</sub>	57.5 $\pm$ 5.5	78.2 $\pm$ 7.4	80.0 $\pm$ 12.5
	Good drug effect	$\Delta$ E <sub>max</sub>	58.6 $\pm$ 5.5	77.3 $\pm$ 7.5	79.7 $\pm$ 12.5
	Bad drug effect	$\Delta$ E <sub>max</sub>	21.2 $\pm$ 5.2	20.1 $\pm$ 6.3	13.8 $\pm$ 7.1
	Drug high	$\Delta$ E <sub>max</sub>	56.3 $\pm$ 5.8	75.9 $\pm$ 7.7	68.8 $\pm$ 15.0
	Drug liking	$\Delta$ E <sub>max</sub>	57.2 $\pm$ 6.1	80.7 $\pm$ 6.9	82.7 $\pm$ 8.1
	Stimulated	$\Delta$ E <sub>max</sub>	56.3 $\pm$ 5.8	76.4 $\pm$ 8.2	68.0 $\pm$ 14.9
	Happy	$\Delta$ E <sub>max</sub>	20.0 $\pm$ 3.0	35.1 $\pm$ 4.6	37.8 $\pm$ 7.1
	Open	$\Delta$ E <sub>max</sub>	20.9 $\pm$ 2.9	32.3 $\pm$ 4.5	35.0 $\pm$ 7.1
	Trust	$\Delta$ E <sub>max</sub>	16.8 $\pm$ 3.0	32.6 $\pm$ 5.3	25.3 $\pm$ 8.7
	Close to others	$\Delta$ E <sub>max</sub>	15.9 $\pm$ 3.0	30.3 $\pm$ 5.0	25.8 $\pm$ 8.9
Adjective mood rating scale (AMRS score)					
	General activity	$\Delta$ E <sub>max</sub>	1.3 $\pm$ 0.6	1.2 $\pm$ 1.1	-0.2 $\pm$ 1.8
	General Inactivity	$\Delta$ E <sub>max</sub>	1.80 $\pm$ 0.84	4.88 $\pm$ 0.93	5.00 $\pm$ 1.90
	Well-being	$\Delta$ E <sub>max</sub>	3.3 $\pm$ 0.9	5.6 $\pm$ 1.3	4.3 $\pm$ 1.6
	Emotional excitation	$\Delta$ E <sub>max</sub>	2.1 $\pm$ 0.6	3.7 $\pm$ 1.5	2.8 $\pm$ 1.1
	Concentration	$\Delta$ E <sub>max</sub>	0.1 $\pm$ 0.4	-0.4 $\pm$ 0.6	-0.7 $\pm$ 1.3
	Extraversion	$\Delta$ E <sub>max</sub>	1.4 $\pm$ 0.5	2.5 $\pm$ 0.7	3.7 $\pm$ 1.3
	Introversion	$\Delta$ E <sub>max</sub>	0.2 $\pm$ 0.3	2.1 $\pm$ 0.5	0.8 $\pm$ 0.5
	Self-confidence	$\Delta$ E <sub>max</sub>	1.1 $\pm$ 0.4	2.9 $\pm$ 0.7	1.5 $\pm$ 0.7
	Heightened mood	$\Delta$ E <sub>max</sub>	2.4 $\pm$ 0.6	3.3 $\pm$ 0.6	3.3 $\pm$ 0.9
	Anger	$\Delta$ E <sub>max</sub>	0.1 $\pm$ 0.2	0.3 $\pm$ 0.4	0.0 $\pm$ 0.0
	Dreaminess	$\Delta$ E <sub>max</sub>	1.5 $\pm$ 0.4	3.6 $\pm$ 1.0	3.5 $\pm$ 1.3
Altered State of Consciousness (5D-ASC score)					
	3D-ASC total score	% score	6.39 $\pm$ 1.25	17.0 $\pm$ 4.2	10.8 $\pm$ 3.5
	Oceanic Boundlessness	% score	10.35 $\pm$ 2.1	26.0 $\pm$ 5.6	18.5 $\pm$ 5.5
	Anxious Ego-Dissolution	% score	3.2 $\pm$ 0.78	10.05 $\pm$ 4.3	3.9 $\pm$ 1.7
	Visionary restructuralization	% score	4.15 $\pm$ 1.08	11.67 $\pm$ 4.2	7.2 $\pm$ 3.0
	Experience of Unity	% score	6.61 $\pm$ 2.03	30.4 $\pm$ 7.9	15.8 $\pm$ 6.3
	Spiritual Experience	% score	1.84 $\pm$ 1.17	6.11 $\pm$ 2.67	7.9 $\pm$ 5.2
	Blissful State	% score	21.12 $\pm$ 4.1	37.6 $\pm$ 9.6	29.5 $\pm$ 7.7
	Insightfulness	% score	4.02 $\pm$ 1.53	4.96 $\pm$ 2.72	8.2 $\pm$ 5.6
	Disembodiment	% score	5.99 $\pm$ 2.01	13.5 $\pm$ 6.4	6.8 $\pm$ 3.5
	Impaired Control and Cognition	% score	7.37 $\pm$ 1.71	15.2 $\pm$ 5.0	7.8 $\pm$ 3.6
	Anxiety	% score	0.61 $\pm$ 0.31	5.79 $\pm$ 4.29	0.4 $\pm$ 0.3
	Complex Imagery	% score	3.46 $\pm$ 1.14	3.89 $\pm$ 2.18	8.0 $\pm$ 4.6
	Elementary Imagery	% score	1.22 $\pm$ 0.71	12.0 $\pm$ 7.4	0.2 $\pm$ 0.1
	Audio-Visual Synsthesiae	% score	0.69 $\pm$ 0.54	4.60 $\pm$ 3.04	2.6 $\pm$ 1.6
	Changed Meaning of Percepts	% score	9.77 $\pm$ 3.46	24.6 $\pm$ 7.3	16.3 $\pm$ 6.7
<b>Hormones</b>					
	Cortisol (nmol/l)	E <sub>max</sub>	648 $\pm$ 43	770 $\pm$ 45	1015 $\pm$ 65
	Prolactin (mU/l)	E <sub>max</sub>	356 $\pm$ .47	874 $\pm$ 125	1498 $\pm$ 415

Values are mean  $\pm$  SEM of 30 subjects for MDMA 75 mg<sup>a</sup>, 16 subjects for MDMA 125 mg<sup>b</sup>, and 6 subjects for MDAI 3.0mg/kg. E<sub>max</sub> maximal effect;  $\Delta$ E<sub>max</sub>, maximal difference from baseline.

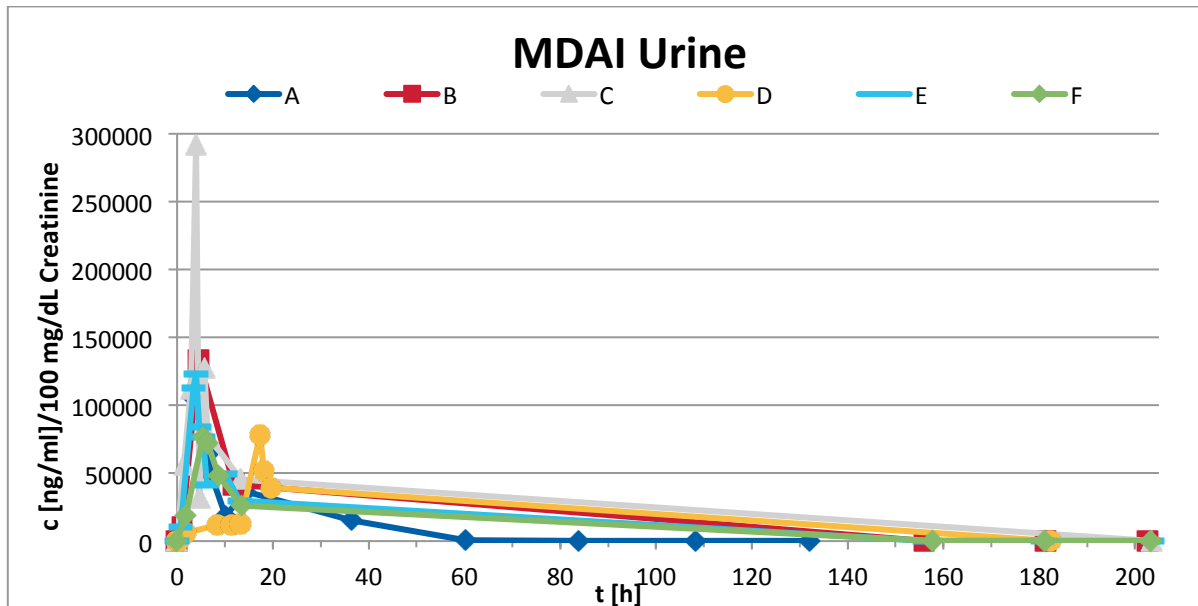
<sup>a</sup> Data from Schmid Y, Hysek CM, Simmler LD, Crockett MJ, Quednow BB, Liechti ME. Differential effects of MDMA and

methylphenidate on social cognition. *J Psychopharmacol.* 2014;28(9):847-856. doi:10.1177/0269881114542454.

<sup>b</sup> Data from Hysek CM, Simmler LD, Schillinger N, et al. Pharmacokinetic and pharmacodynamic effects of methylphenidate and MDMA administered alone or in combination. *Int J Neuropsychopharmacol.* 2014;17(3):371-381. doi:10.1017/S1461145713001132



**Figure S1.** Serum concentrations after a dose of 3.0 mg/kg body weight orally,  $c_{max}$  about 5000–9000 ng/ml;  $t_{max}$  about 1–3 hours after intake



**Figure S2.** Urine concentrations after a dose of 3.0 mg/kg body weight, normalized to 100 mg creatinine/dL, longest detection 9 days after intake ( $c = 2$  ng/mL) with highest MDAI urine concentration in participant A (poor metabolizer with CYP2D6).