Cortisol levels and MDMA-induced memory impairment

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Background

Ecstasy use is commonly linked with memory deficits in abstinent ecstasy users. Similar impairments are being found during ecstasy intoxication after single doses of MDMA [1]. The concordance of memory impairments during intoxication and abstinence suggests a similar neuropharmacological mechanism underlying acute and chronic memory impairments in ecstasy users. The mechanism underlying this impairment is to date not known.

Hypothesis

Cortisol might play an important role in this mechanism as cortisol, implicated in the regulation of memory performance [2], can be brought out of balance by stressors like MDMA [3].

Aim

To block the MDMA-induced acute memory defect by giving participants a cortisol synthesis inhibitor (Metyrapone®) together with a single dose of MDMA.

Methods

Subjects

- 17 Polydrug MDMA users
  - 6 ♀; 11 ♂
- Lifetime ecstasy use
  - 15 Ss ≤ 20 times
  - 2 Ss 85-120 times
- IQ_{verbal} [4]
  -110.29 ± 4.043 (range: 105-117)

Design

- Placebo-controlled, within subject
- 4 treatment conditions
  1. Placebo = Placebo (9.30AM) + Placebo (10.30AM)
  2. Metyrapone = Metyrapone (750mg) + Placebo
  3. MDMA = Placebo + MDMA (75mg)
  4. Metyrapone + MDMA

Test: 30- Word Learning Test (WLT)
-30 Dutch words; 3 learning trials
- Dependent Variables:
  -Immediate Recall (IR)
  -Delayed Recall (DR): after 30' delay

Cortisol assessments: Blood samples: 1h and 1.5h after respectively pretreatment & treatment

Time (AM)	9:00	9:30	9:35-10:25	10:25	10:30	10:35-11:55	11:55	12:00-13:15
Activity								

Figure 1. Schematic representation of a test day

Results

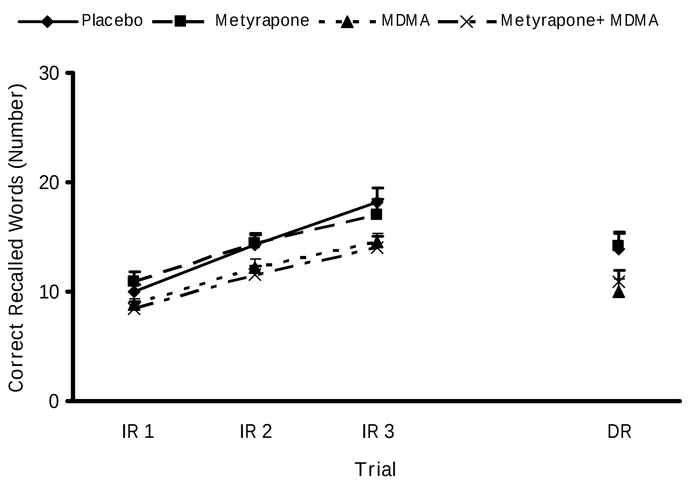

Figure 2. 30-WLT. After MDMA treatment, Ss recalled less words during immediate (7.7) and delayed (3.5) recall compared to placebo.

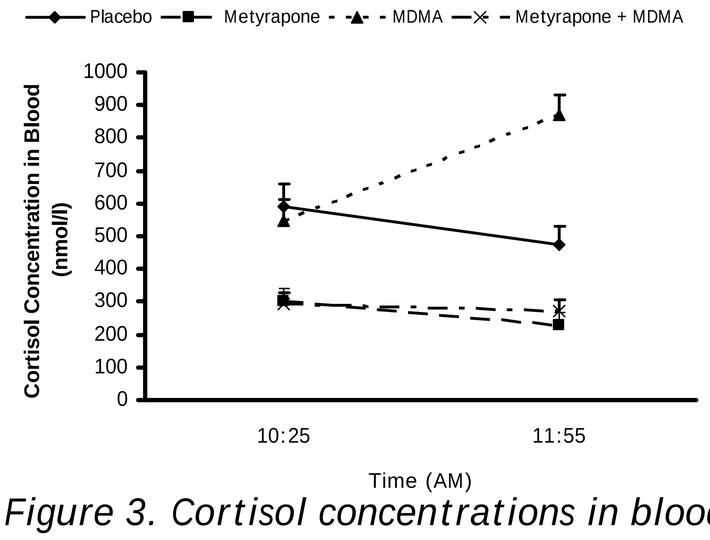

Figure 3. Cortisol concentrations in blood, (1h &) 1.5h after (pre)-treatment. Concentrations were significantly lower after Metyrapone treatment, and higher after MDMA treatment, compared to placebo. The MDMA-effect was absent when Ss were pretreated with Metyrapone.

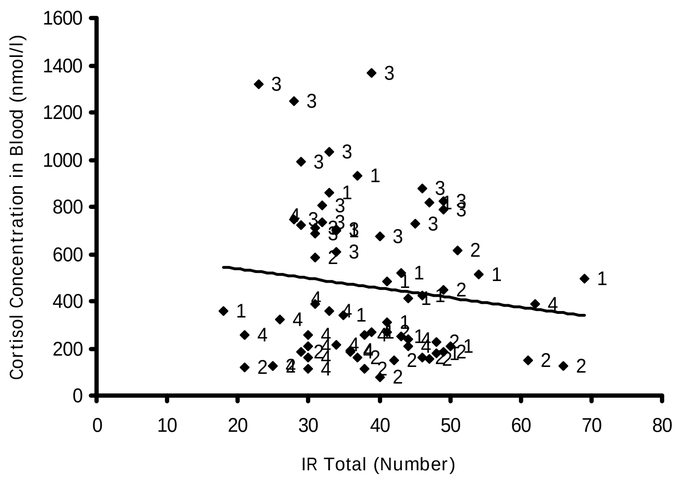

Figure 4. Absence of a significant correlation between total number of correct recalled words of the WLT and cortisol concentrations in blood (at the moment of WLT).

Conclusion

Main findings indicated that whereas pretreatment with Metyrapone blocked the expected MDMA-induced increase in cortisol levels in blood, it did not prevent the MDMA-induced memory deficit from happening. We therefore conclude that MDMA-induced increases in cortisol concentrations are not responsible for impairing memory performance while intoxicated with MDMA.

References

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[2] Erickson, K., Drevets, W., Schulkin, J., 2003 Glucocorticoid regulation of diverse cognitive functions in normal and pathological emotional states. Neuroscience and Biobehavioral Reviews 27, 233-246.
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