A Volumetric Analysis of the Adult Zebra Finch Brain after Ecstasy Exposure

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Introduction

The use of the recreational drug 3,4-methylenedioxymethamphetamine (MDMA, or more commonly, Ecstasy) has increased worldwide in recent years. Previous human studies have shown that some MDMA users experience long lasting confusion, depression and impairment in learning and memory [1,2]. The aim of this study is to investigate possible MDMA-induced neurodegeneration in the neuronal network of the zebra finch, a model pertinent to the study of high order cognitive processes. To assess morphological changes in neuroanatomy, magnetic resonance microscopy (MRM) was performed at 11.75 T.

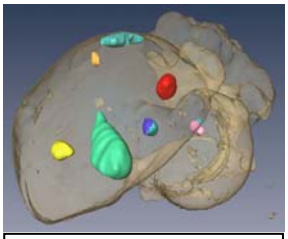

Fig 1. 3D volume rendering of song nuclei.

Experimental

Eighteen adult male zebra finches were used in this study (9 MDMA treated + 9 age-matched controls). MDMA (or saline vehicle) was administered (10 mg/kg, i.p.) with single, double or triple treatments. Six hours following the final administration, brains were excised and fixed in paraformaldehyde. All MR data were acquired using an 11.75-T vertical magnet equipped with a Bruker Avance Console and Micro2.5 gradients. Using a 10-mm birdcage coil, three-dimensional gradient-recalled echo (GRE) scans (TE/TR=15/200 ms) were acquired at an isotropic resolution of 40 µm. After scanning, Luxol Fast Blue (LFB) staining was performed on 18-µm thick brain sections to evaluate myelin content in the song nuclei.

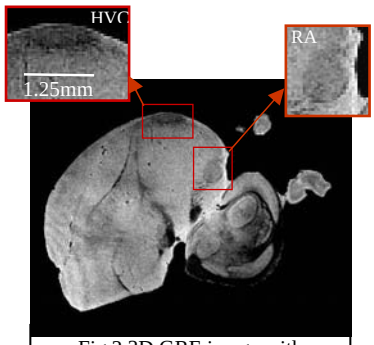

Fig 2.3D GRE image with isotropic resolution 40µm, showing the HVC.

Results and Discussion

In this study, we were able to identify and segment numerous structures (including song nuclei) in the excised zebra finch brain without the use of exogenous contrast enhancement. Volumetric data demonstrated certain trends. Comparison between MDMA and saline-treated animals displayed an overall decrease in the sizes of the telencephalon and most song nuclei, including the robust nucleus of the arcopallium (RA) and the medial nucleus of the dorsolateral thalamus (DLM). The HVC (formerly called the high vocal center), however, showed the opposite trend, namely an increase in volume, when comparing the treatment groups with their corresponding controls. In addition, the volume of the HVC may increase with the number of MDMA treatments. In a preliminary study, we showed that a single administration of MDMA induced a significant decrease of song production in adult male zebra finches. Previous studies also have shown that the amount of produced song depends on the volume of song nuclei [3,4]; therefore, decreases in the RA and DLM may be consistent with reduced song production. Histological sections displayed demyelination with increased number of MDMA treatments. This demyelination may impact our ability to quantify volumetric changes in certain song nuclei, particularly the HVC.

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