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Research report

# Immediate and persisting effect of toluene chronic exposure on hippocampal cell loss in adolescent and adult rats

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ABSTRACT

Abuse of toluene-containing volatile inhalants has become widespread among adolescents. Besides, because toluene is usually used as an industrial solvent in manufacturing of chemical pharmaceuticals and multiple commonly used household and commercial products, it has high potential for abuse for adults also. Long-term exposure to toluene vapor has a severe impact on the central nervous system, resulting in numerous neurological, neurobiological and behavioral impairments. Recently in the hippocampus some molecular and biochemical changes as a result of toluene chronic exposure were described. Such data point out the involvement of this area in the toluene addiction. However it remains uncertain whether toluene provokes structural alterations in the hippocampus. In this study we exposed male Wistar rats to 2000 ppm inhaled toluene for 40 days in rats at ages P 28–32 (adolescents) and P 70–75 (adults). The immediate and delayed effects of toluene chronic exposure (immediately after the end of toluene chronic inhalation and 90-day after the end of toluene chronic inhalation, correspondingly) on pyramidal cell loss in adolescent and adult rats was investigated. The results reveal that (i) chronic exposure to 2000 ppm of toluene chronic exposure alters the structure of hippocampus in adolescent and adult rats provoking both, immediate and delayed effects; (ii) the character of structural alterations depends upon the postnatal age of testing of the animals.



## 1. Introduction

Abuse of toluene-containing volatile inhalants has become widespread among adolescents, young people and children. Besides, because toluene is usually used as an industrial solvent in manufacturing of chemical pharmaceuticals and multiple commonly used household and commercial products, such as gasoline, glue, rubber cement or paints, it has the highest potential for abuse for adult workers also [1–3]. Experimental and clinical data demonstrate that long-term exposure to toluene vapor has a severe impact on central nervous system of children, adolescents and adults, resulting to numerous, sometimes long-lasting neurological, neurobiological and behavioral impairments as well as diffuse changes in white matter [4–8].

It is clear that toluene share common cellular mechanisms and has similar actions to other drugs of abuse, namely, it activates the mesolimbic dopaminergic reward system—the major substrate of addiction [9–12]. But, compared with other abusive substances, relatively few experiments have been done exploring the alterations provoked by toluene at different levels of the organism of different age. Thus, while some studies have assessed outcomes of chronic misuse of toluene-containing substances in adults, there are few data on its effects in younger animals [5,12,13]. Besides the biggest part of investigations concerning toluene's addictive nature has focused on its immediate effect, while persisting effect (months or years after withdrawal) is not well known.

The importance of learning and memory in addiction is an area of increased interest. More and more studies indicate that presentation of addictive drugs to abusers is associated with the activation of brain regions that are involved both, in addictive and learning processes [14,20,15,16]. Based on these data, it was suggested that addiction and learning and memory can shares the nervous substrates. As potential substrates for both processes mesocorticolimbic system—including the hippocampus, have been identified.

Hippocampus, along with amygdala, is considered to be critical for cue-elicited drug-seeking taking [17,18,19]. Thus, recently it was shown that hippocampal pathways are highly implicated in drug-seeking that is elicited by contextual stimuli [15,20,21]; the hippocampus participates in strengthening connections in the areas that are involved in addiction, suggesting that drug-induced

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