

UDK 616.8

ISSN 1331-5196

# Neurologia Croatica

SINCE 1953

## SAŽETCI ABSTRACTS

SUPPLEMENT

3. – 6. listopada 2018.

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Alzheimerovoj bolesti  
(CROCAD-18)  
s međunarodnim sudjelovanjem

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*Temeljna istraživanja i neuropatologija u AB / Basic research and neuropathology of AD*

## PROTOCOL FOR STEREOTAXIC DELIVERY OF TAU OLIGOMERS AND TAU FIBRILS INTO THE RAT ENTORHINAL CORTEX

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**Introduction:** The aim of this presentation is to describe stereotaxic surgery protocol for the delivery of different tau species into the rat entorhinal cortex. The surgical procedure has been optimized to result in minimal damage to brain parenchyma and to provide reproducible results. Several technical requirements had to be fulfilled before and during the procedure so that the target structure is attained with maximal precision.

**Methodology:** The study includes 3-4 months old male Wistar rats (n = 108) divided into three groups. Rats from the first experimental group will be stereotaxically injected with tau oligomers into the entorhinal cortex, the second group will be injected with tau fibrils and the third, control group, with phosphate-buffered saline. Animals will be tested and analyzed at 3 days, 3 months, 6 months and 12 months post-injection. Stereotaxic coordinates for entorhinal cortex are determined from the 2004 stereotaxic rat brain atlas of Paxinos and Watson, and optimized according to age and sex of the rats using cresyl violet stain.

**Results:** For calculating stereotaxic coordinates of the target structure it is important to take into account the organization of the cerebral vasculature of the animal and coordinates need to be validated relative to age, sex, and strain. For targeting the ventral entorhinal cortex of the rat it is necessary to use a 10° inclination of the microinjection unit in mediolateral direction. In addition, one must

be aware of the starting point of the descent of the cannula, as this may result in up to 1 mm difference in the final coordinates.

**Conclusions:** The aim of stereotaxic delivery of tau oligomers into the entorhinal cortex is to model spreading of Alzheimer's disease neurofibrillary changes with hope that these changes will mimic early events underlying human disease. By injecting a single dose of soluble oligomeric forms of human tau protein and tau fibrils into the entorhinal cortex we will try to answer whether trans-synaptic spread of protein aggregates is required for pathogenesis. Using this knowledge, we will be able to define possible new therapeutic targets and interventions aimed at blocking tau protein oligomerization, aggregation, and spread.

**Acknowledgments:** This work is financially supported by the Croatian Science Foundation (IP-2014-09-9730). The work of doctoral student Lea Langer Horvat has been fully supported by the "Young researchers' career development project - training of doctoral students" of the Croatian Science Foundation (DOK-2015-10-7200).

**Keywords:** stereotaxic surgery, tau protein, entorhinal cortex, trans-synaptic transfer