2nd International Conference on HIV/AIDS, STDs & STIs October 27-29, 2014
Las Vegas, USA

Alteration of choline acetyltransferase activity in piglet brain after EncephaloMyoCarditis Virus (EMCV) infection.

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The work is supported by Austrian “Fonds der Wissenschaftlichen Forschung”. FWF Project No. 15371 to Prof. H. Baran, PhD

Introduction

- **EMCV (Encephalo-Myo-Carditis-Virus) infection in piglets mainly affects heart tissue and leads to CNS alterations (Noack and Liebermann, 1992), however no reliable data are available.**

- **Clinically, EMCV causes a sudden death syndrome in piglets due to acute myocarditis, however the mechanism(s) has not been elaborated yet.**

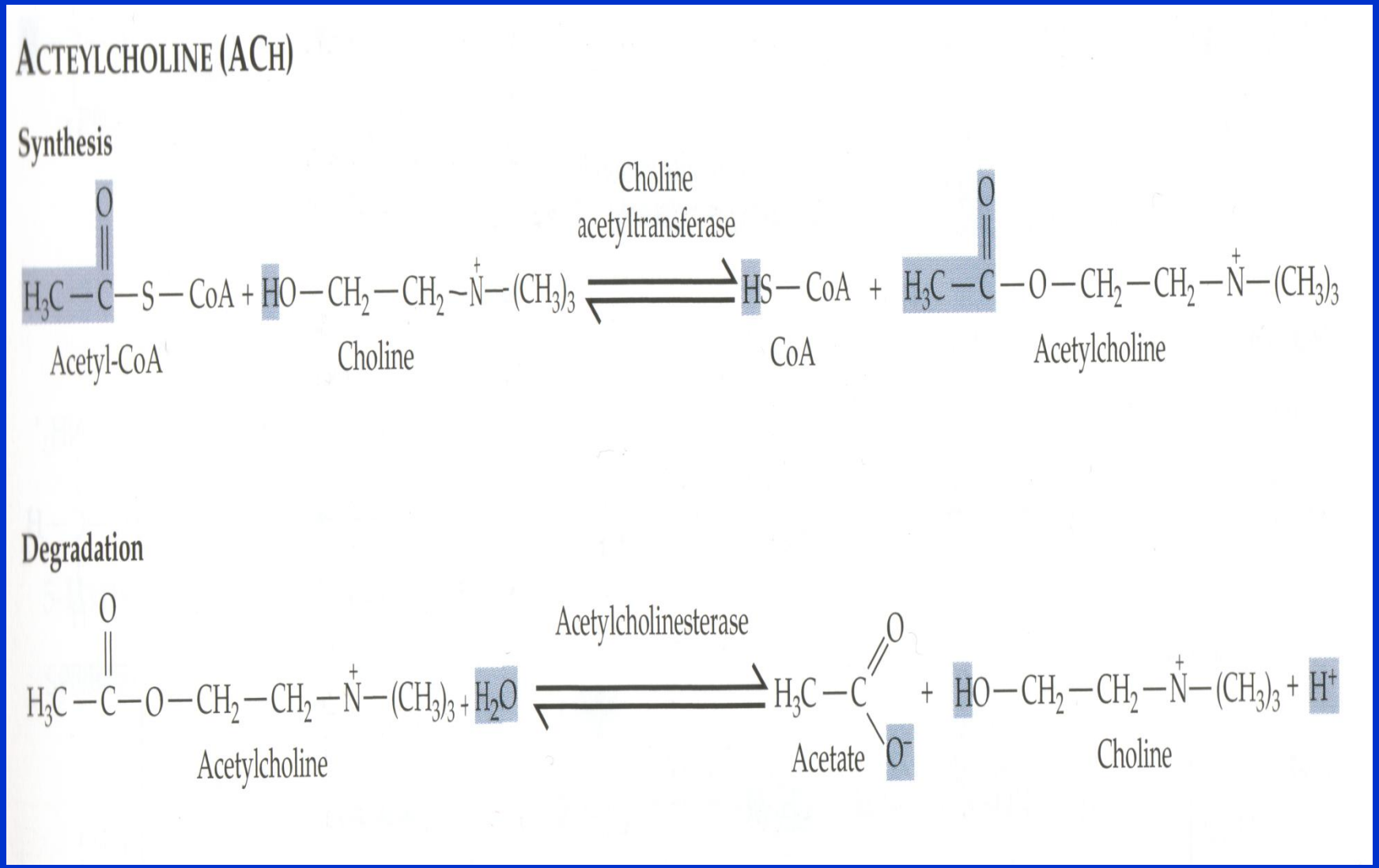
- **In hippocampal cell culture EMCV leads to neurodegeneration (Weiping Su, 1999).**

Acetylcholine

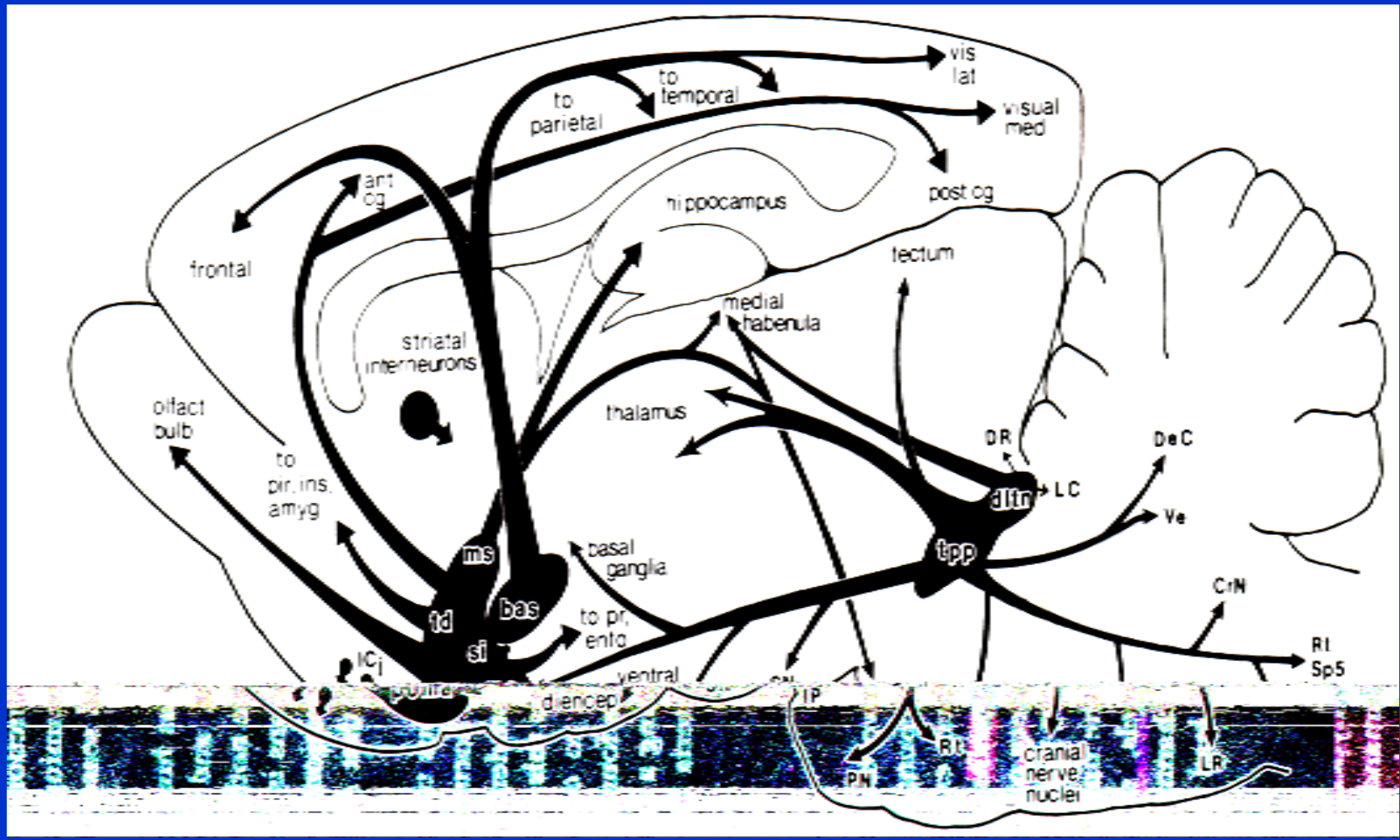
- **excitatory neurotransmitter**
- **a well known endogenous agonist of the nicotinic and muscarinic cholinergic receptors,**
- **is synthesised in cholinergic neurons**
- **is involved in neurodegenerative disorders (as Alzheimers's)**

Alteration of choline acetyltransferase activity in piglet brain after EMCV infection

Synthesis and degradation of Acetylcholine



Cholinergic neurons in the rat brain



si *substancia innominata* ms *medial septal nucleus* bas *nucleus basalis* poma *magnucellular preoptic field*
tpp pedunculopotin nuclei dltn *laterodorsal tegmental nuclei* ICj *islands of Calleja*

Aim of the study

To estimate whether EMC-Virus infection induces molecular changes of the marker of cholinergic neurons,

Choline acetyltransferase (ChAT) was selected and activity of enzyme was investigated in the CNS in piglets at 4 days after EMC-Virus infection.

Material and Methods

- Piglets at an age of 8 weeks were used.
- Infected with 8 ml suspension 10^7/ml of EMC-virus - strain B279/95; nasal and oral, each 4 ml (5 controls & 7 EMCV).
- 4 days after EMCV infection animals were sacrificed and brain regions were prepared immediately.
- ChAT activity was determined by radioenzymatic method.

Dissected regions:

1 – Frontal Cortex

2 - Parietal Cortex

3 - Temporal Cortex

4 - Hippocampus

5 - Caudate Nucleus

6 - Putamen

7 - Globus Pallidus

8 - Thalamus

9 - Hypothalamus

10 - Substantia Nigra

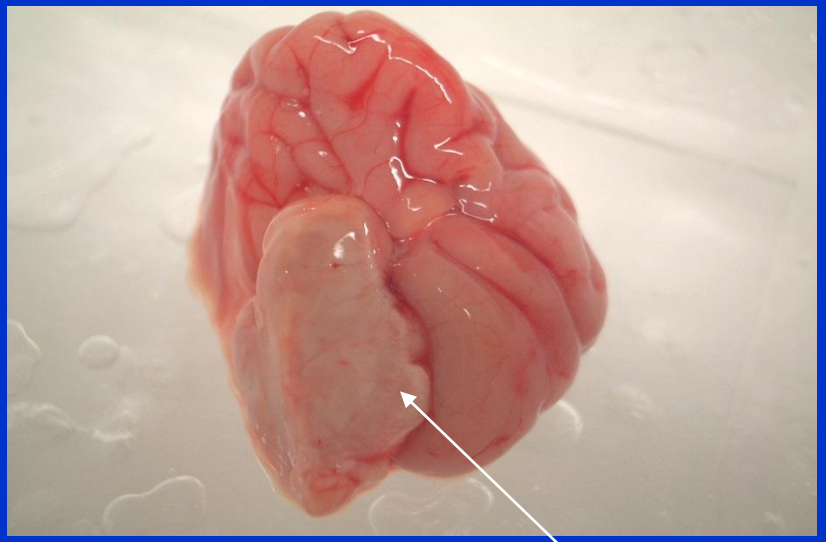
11 - Cerebellum

12 - Bulbus olfactorius

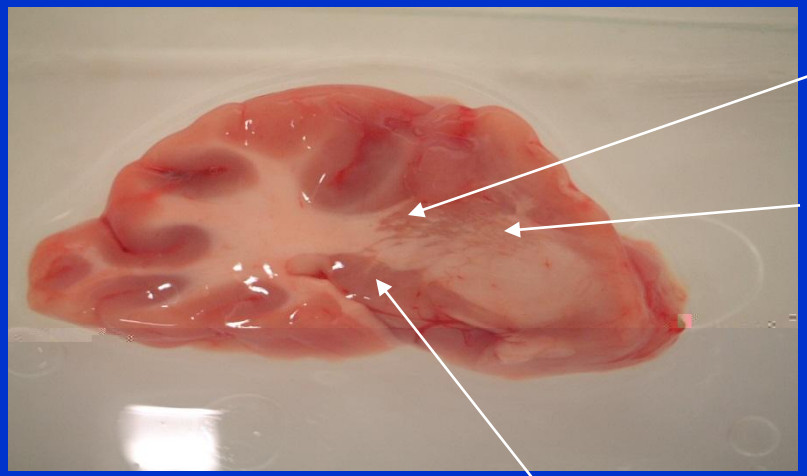
13 - Midbrain

14 - Pons

15 - Medulla



Substantia Nigra

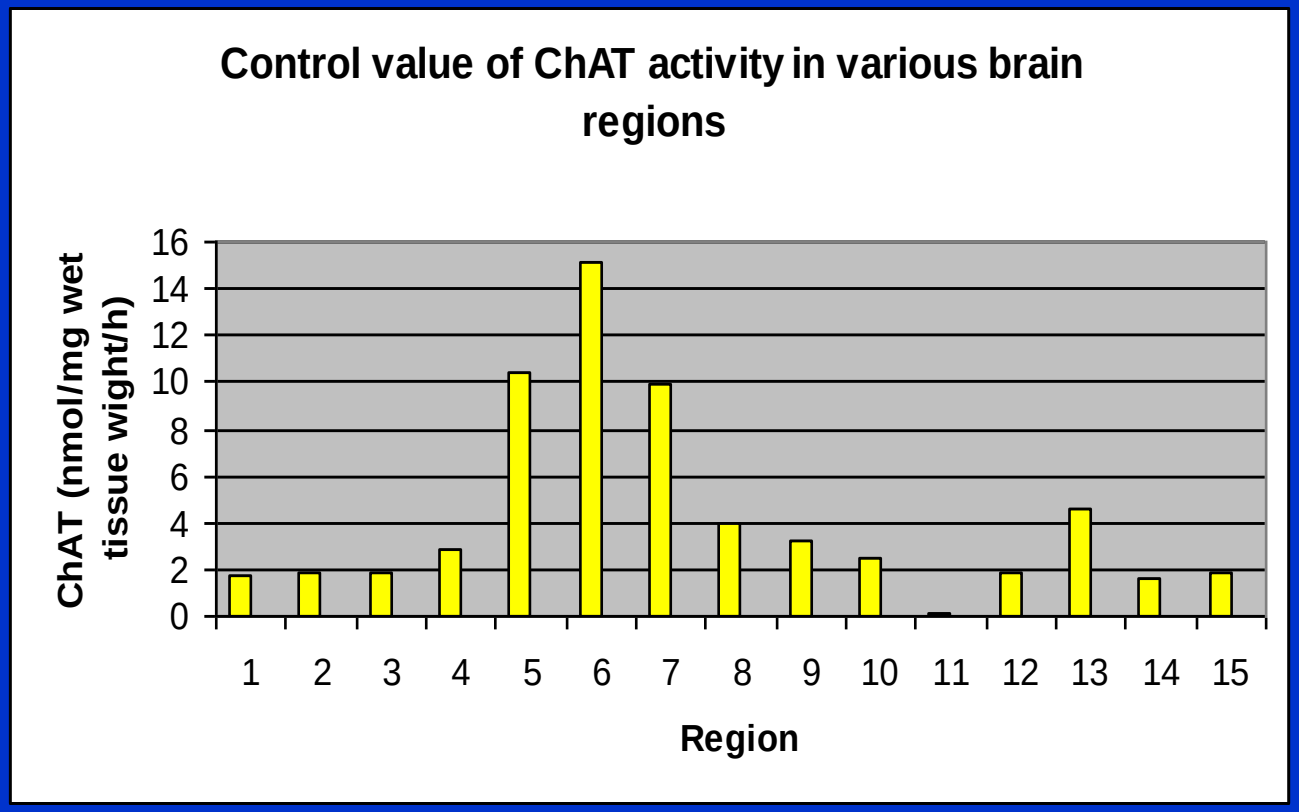


Putamen

Globus Pallidus

Caudatus Nucleus

Choline acetyltransferase (ChAT) in control pig brain



Regions:

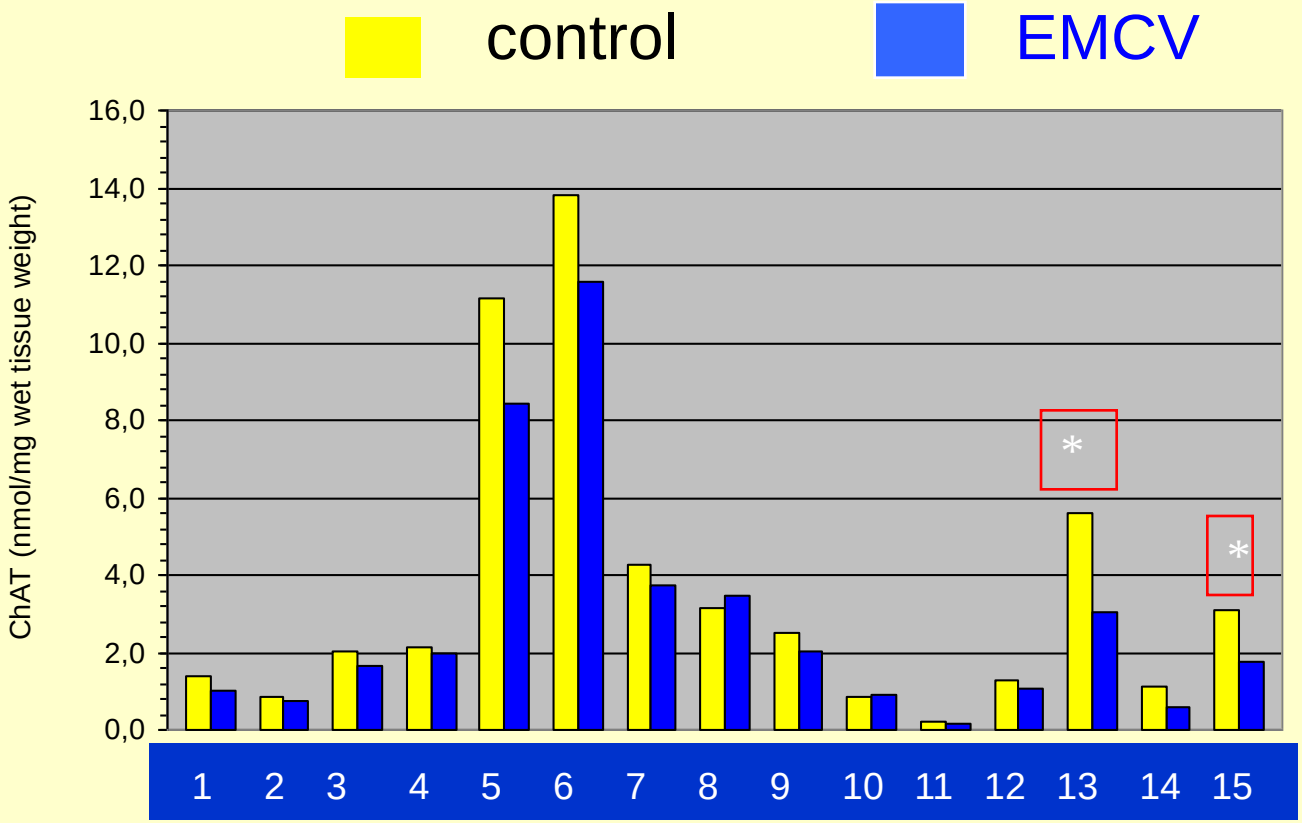
1 – Frontal cortex
2 - Parietal cortex
3 - Temporal cortex
4 - Hippocampus
5 - Caudate nucleus
6 - Putamen
7 - Globus pallidus
8 - Thalamus
9 - Hypothalamus
10 - Substantia nigra
11 - Cerebellum
12 - Bulbus olfactorius
13 - Midbrain
14 - Pons
15 - Medulla

Comparison between ChAT activity in the rat and pig brains:

	ChAT (nmol/mg wet tissue weight/h)	
	Rat	Pig
Frontal Cortex:	16,32	1,72
Temporal Cortex:	15,86	1,82
Hippocampus:	17,10	2,13
Caudate Nucleus :	26,46	10,45

Kinetic analysis of ChAT in the hippocampus revealed a value of K_m = 0,023 mM for Acetyl-CoA and a V_{max} =2,22 (nmol/mg wet tissue weight/h).

Choline acetyltransferase (ChAT) activity in the pig brain 4 days after infection



Regions:

1 – Frontal cortex
2 - Parietal cortex
3 - Temporal cortex
4 - Hippocampus
5 - Caudate nucleus
6 - Putamen
7 - Globus pallidus
8 - Thalamus
9 - Hypothalamus
10 - Substantia nigra
11 - Cerebellum
12 - Bulbus olfactorius
13 - Midbrain
14 - Pons
15 - Medulla

Observation

ChAT in control pig brain

- **Within investigated brain regions the highest activity of ChAT was seen in the putamen and the caudate nucleus and the lowest ChAT activity was found in the cerebellum.**
- **Enzymatic analyses of ChAT show K_m value of 0.02 mM for Acetyl-CoA, which is comparable to other species including human.**

Observation

ChAT at 4 days after EMCV infection

- **reduced activity was measured in the midbrain (54 % of control) and in the medulla (56 % of control).**
- **in putamen and caudate nucleus ChAT activity was moderately lowered.**

In most other regions a tendency of enzyme activity reduction was found.

Conclusion

- **EMCV infection in piglets causes a significant reduction of ChAT activity in the midbrain and in the medulla 4 days after inoculation.**
- **Reduction of ChAT activity would suggest an affection of the cholinergic system.**
- ***ChAT reduction may progress very likely with time and intensity of the disease.***
- ***Reduction of ChAT is an indicator for an neurodegenerative process.***

Remark

EMCV infection in piglets leads not only to ChAT activity reduction in the midbrain and in the medulla ……..but also to:

……significant alterations of kynurenic acid metabolism ! ***…….visit …….***

Poster:

Halina Baran et al., KYNURENIC ACID METABOLISM in PIGLETS after ENCEPHALO-MYOCARDITIS-VIRUS (EMCV) INFECTION

Thank You for Your attention!