INTEGRATIVE CHARACTERIZATION OF A RODENT ALZHEIMER’S DISEASE MODEL

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BACKGROUND

→ Alzheimer’s Disease (AD) is a severe neurodegenerative disorder with progressive loss of memory and cognitive functions.
→ To investigate Alzheimer-related pathophysiology, several transgenic mouse and rat lines have been established in recent years.
→ Despite their general applicability in basic and applied research, quantitative tools to monitor pathophysiology as well as associated rewiring of metabolic pathways on a systemic level are lacking.

AIM

→ Use an integrative approach – behavioral tests, immunofluorescence and untargeted nuclear magnetic resonance (NMR)-based metabolic phenotyping to get a better understanding of (patho-) physiological alterations in complex biological networks involved in AD.

MATERIALS AND METHODS

→ Tg4-42 and Wild-type mice of different ages were tested in the Morris water maze test to receive read-outs of the disease related to spatial learning and memory.
→ Neuroinflammation and plaque load were analyzed by immunofluorescent labeling with GFAP, Iba-1 and Aβ1-42 antibodies, respectively.
→ Untargeted NMR spectroscopy to monitor perturbations in a large pool of metabolites

RESULTS

→ Behavioral test

<table>
<thead>
<tr>
<th>Group</th>
<th>PT - Time spent in NE quadrant</th>
<th>PT - Latency to first visit target zone</th>
<th>PT - Swim length</th>
</tr>
</thead>
<tbody>
<tr>
<td>3Mo ntg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3Mo Tg4-42+/+</td>
<td></td>
<td></td>
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<tr>
<td>6Mo ntg</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>6Mo Tg4-42+/+</td>
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<tr>
<td>9Mo ntg</td>
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<tr>
<td>9Mo Tg4-42+/+</td>
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→ NMR-based metabolic phenotyping

CONCLUSION

→ The combination of different methods is important to link biomarkers in the brain and the associated dysregulation of metabolic pathways with changes in neuropathology and behavior.

This integrative approach (behavioral studies, immunofluorescence, NMR-based metabolic phenotyping) not only contributes to the understanding of this devastating neurodegenerative disease and the related pathophysiological processes on a systemic level, but sets the base for a wide range of biomedical applications. It can be easily extended to other tissues, matrices, or disease models and translated across species.

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