

Metabolic Characteristics of Primary Neuron Cultures from BACHD Rats Compared to Induced Lesion Models

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Background

The BACHD rat is by now a well-characterized animal model of Huntington's disease (HD), presenting several disease relevant symptoms and pathologies. The BACHD rat represents one of the few animal models that overexpresses the full length human mutant huntingtin (mHTT) and is thus of great value for HD research. The aim of this study was to compare the metabolic properties of primary striatal, hypothalamic and cortical neurons of BACHD rats with the L-glutamate or MPP+ induced rat striatal lesion models to establish BACHD primary cells as valuable *in vitro* HD model.



Materials and Methods

Hemizygous BACHD and wildtype rat pups were dissected at embryonic day 19 and primary neurons of the striatum, hypothalamus and cortex were cultivated. Cells were analyzed after 1, 7 and 14 days *in vitro* (DIV). For the lesion models, primary striatal embryonic day 19 wildtype rat neurons were cultivated for 15 days and lesioned with L-glutamate or MPP+ for 24 hours. All samples were analyzed with the LDH- and MTT-assay.

Results

Our data show that primary neurons (PNs) of embryonic BACHD rats have a significantly decreased metabolic activity in the striatum and hypothalamus (Fig. 1, 2). These results are comparable with data obtained by L-glutamate or MPP+ lesions in primary striatal neurons of wildtype rats (Fig. 3). Our most recent method development shows that polyQ HTT can be quantified by sandwich immunosorbent assay with a high specificity (Fig. 4).

Quantification of polyQ HTT

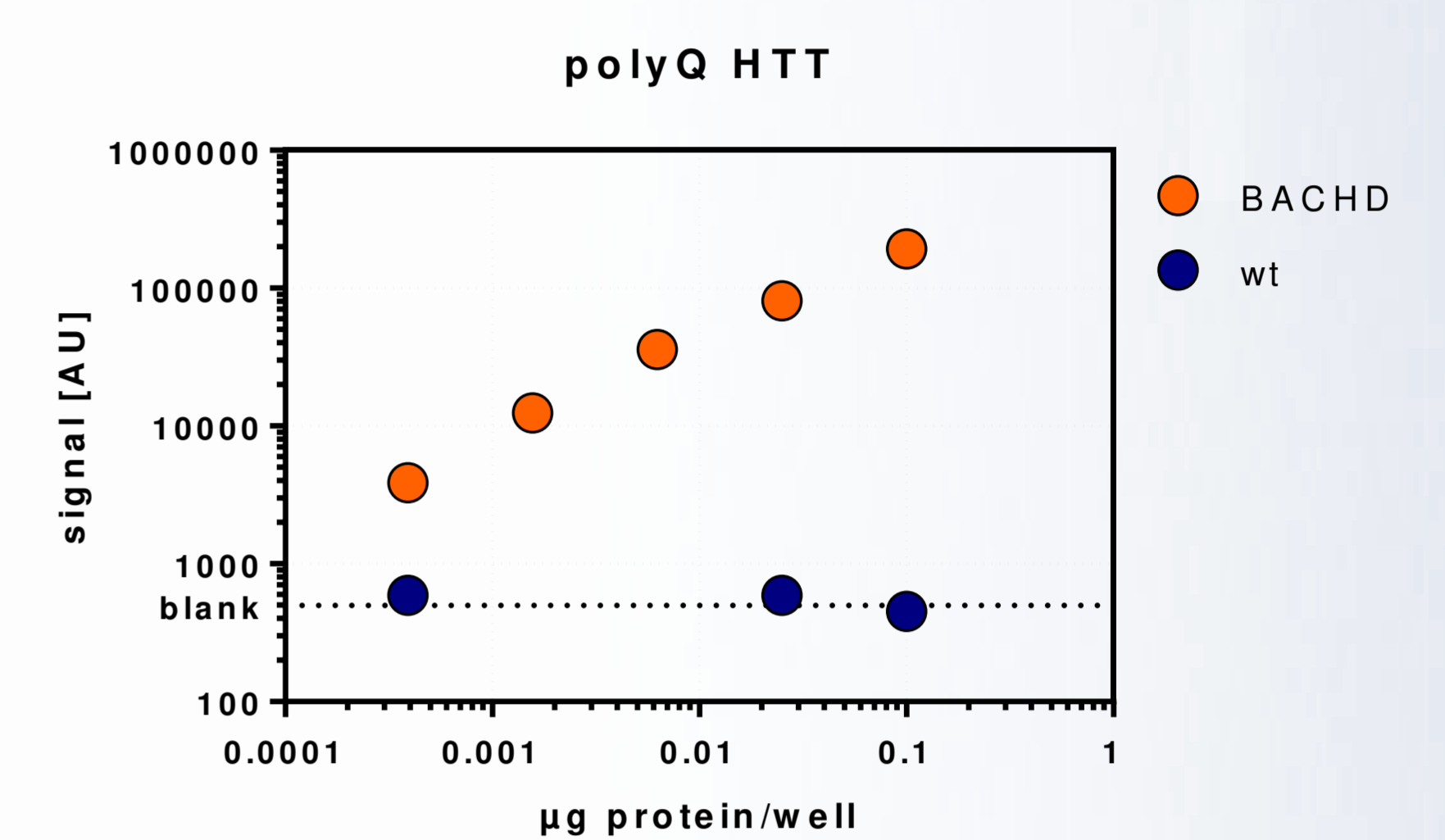
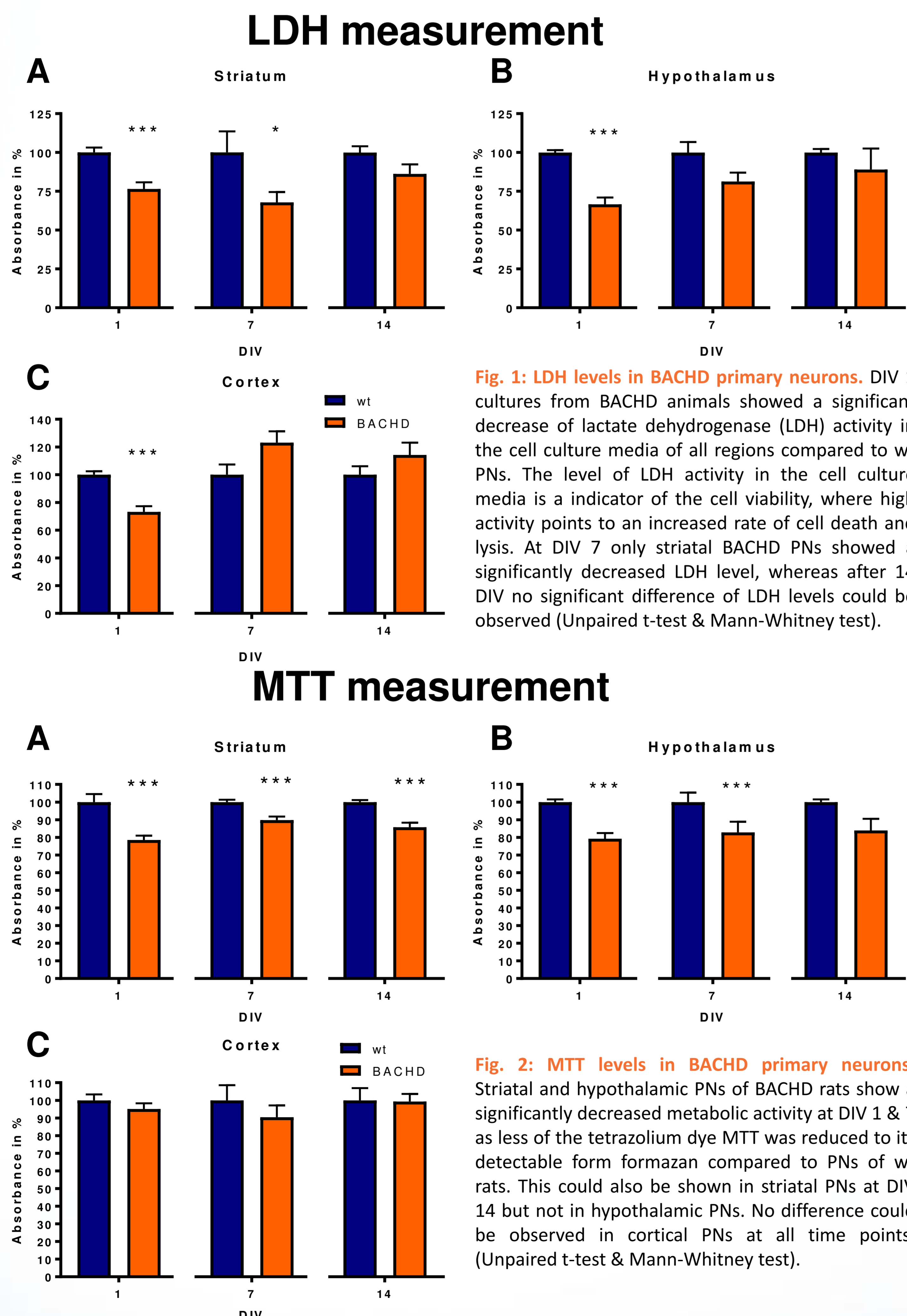
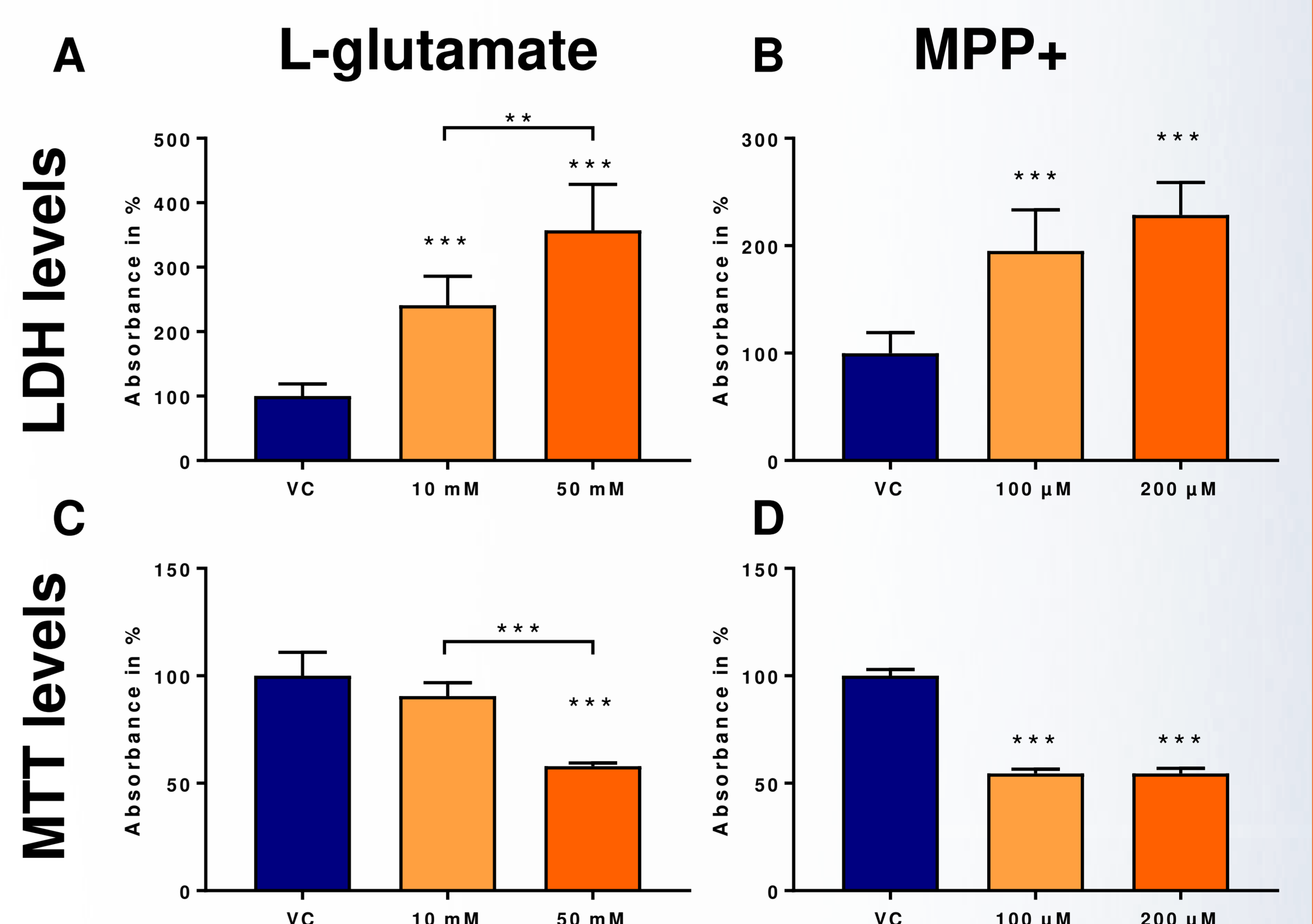


Fig. 4: Quantification of polyQ HTT by sandwich immunosorbent assay using the MesoScale Discovery platform. Whole brain lysate of a 6 months old hemizygous rat and a non-transgenic littermate were used in a dilution series of 1:10, 1:40, 1:160, 1:640 and 1:2560.

Primary Neuron System of BACHD Rats



Lesion Models of Wildtype Striatal Neurons



Summary and Conclusion

We conclude that the BACHD rat model is a valuable tool for the *in vitro* evaluation of HD-related metabolic properties. Future experiments can further be analyzed by polyQ HTT immunosorbent assay.

We look forward to support your research