A53T-mutated Human alpha-Synuclein is Involved in Blood Glucose Regulation of Western Type Diet-fed Parkinson's Disease Mice

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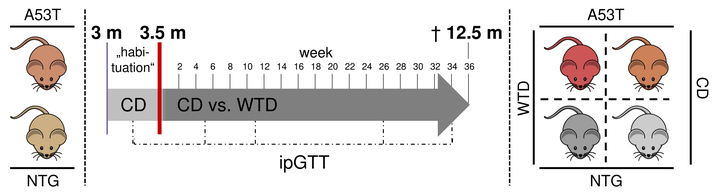
BACKGROUND

Besides genetic modifications, diabetes and obesity have been suggested to be a risk factor for the development and progression of Parkinson's Disease (PD). To better understand the impact of diabetes and obesity caused by diet and PD, we focused on investigating the effects of a Western type diet (WTD) that contains high fat and sucrose, as well as supplemented cholesterol on a PD animal model, the A53T mouse.

MATERIALS and METHODS

Transgenic mice overexpressing human A53T mutated alpha-Synuclein (A53T) and non-transgenic littermates (NTG) received a control diet (CD) for 2 weeks, starting at 3 months of age. Afterwards animals were fed a WTD or control diet (CD) until the end of their life. To monitor the animals' response to the diet, the food intake, and body weight were evaluated weekly. Additionally, glucose metabolism was investigated using the intraperitoneal glucose tolerance test (ipGTT) after 5, 11, 26, and 34 weeks on the diet.



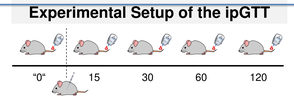


Figure 1. Performance of the ipGTT. Mice were fasted over night before basal blood glucose levels ("0") were measured from venous blood. Afterwards a single dose of a 20 % glucose solution was applied intraperitoneally before additional blood glucose concentration measurements 15, 30, 60, and 120 minutes post injection.

SUMMARY and CONCLUSION

In summary, our findings add evidence indicating an impact of A53T-mutated human alpha-Synuclein on glucose regulation. Further research on this topic might pave the road for new therapeutic approaches in the field of PD.

For more information about the model please visit: www.qpsneuro.com
or send us an e-mail: office-austria@qps.com

RESULTS

Both, NTG and A53T mice on WTD had a higher caloric intake which resulted in an elevated weight gain compared to CD-fed control animals of both genotypes (Figure 2). Intriguingly, fasting blood glucose levels were increased only in NTG mice already as early as 5 and 26 weeks on the WTD (Figure 3). Injecting a glucose solution intraperitoneally led to higher blood glucose levels in WTD-fed A53T and NTG mice 5 and 11 weeks after starting the dietary intervention. However, after 26 weeks, only NTG mice demonstrated elevated glucose levels. After 34 weeks on the diet, none of the groups demonstrated elevated glucose levels in the ipGTT (Figure 4).

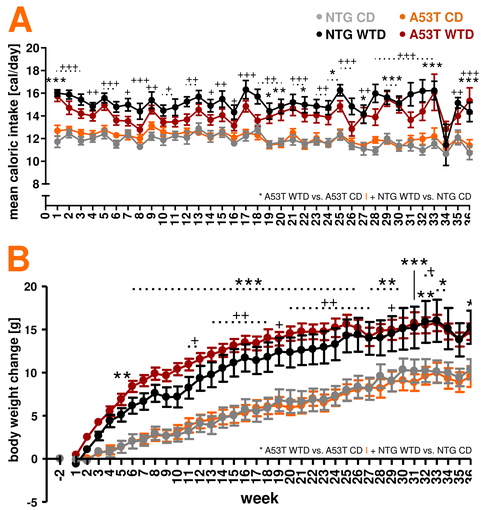
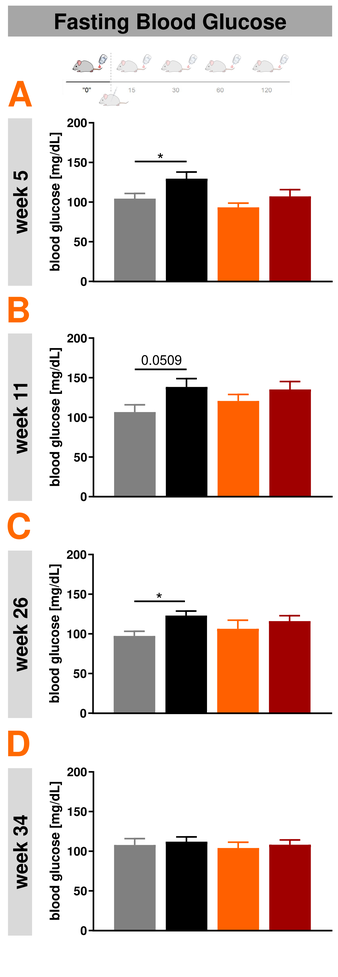


Figure 2. Mean caloric intake and body weight gain during dietary intervention with CD and WTD. Caloric food intake (A) was evaluated by weekly weighing of provided and consumed food and subsequent data analysis. Body weight was recorded weekly (B) n: 9-12/group. Mean +/- SEM. */+p<0.05, **/++p<0.01, ***/+++p<0.001, two-way ANOVA followed by Bonferroni's *post hoc* test.



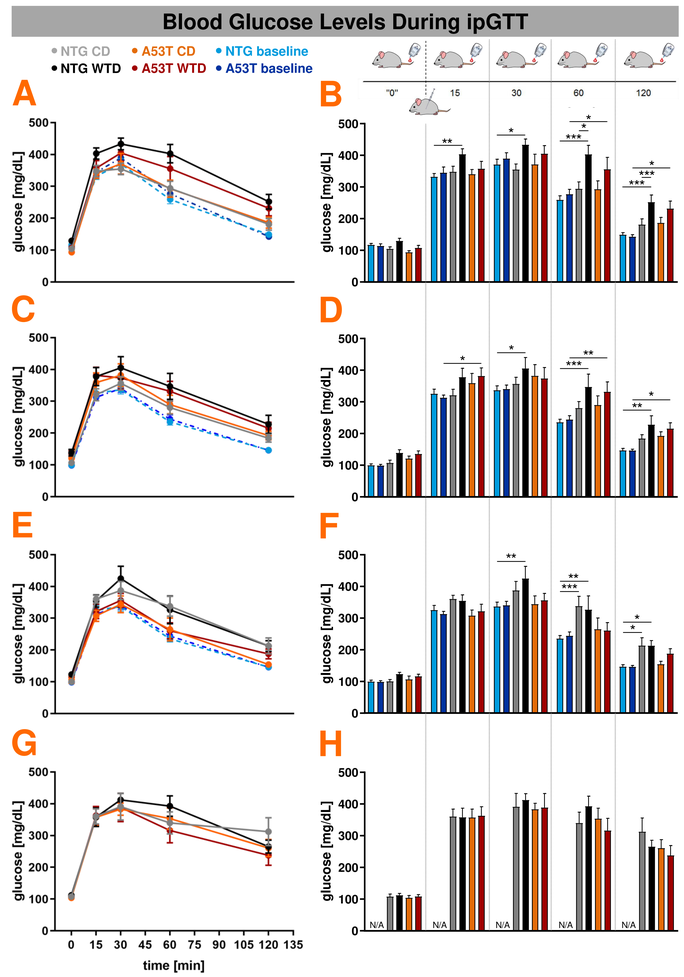


Figure 3. Fasting blood glucose levels in week 5, 11, 26, and 34. Before applying the glucose solution in the course of the ipGTT, blood glucose levels of fasted animals were evaluated in treatment week 5 (A), 11 (B), 26 (C), and 34 (D). n: 8-12/group. Mean +/- SEM. *p<0.05 two-way ANOVA followed by Bonferroni's *post hoc* test.

Figure 4. Blood glucose levels during experimental phase evaluated by ipGTTs. Animals' glucose metabolism was evaluated at baseline before starting the dietary intervention during habituation phase (light and dark blue bars) and in weeks 5 (A, B), 11 (C, D), 26 (E, F), and 34 (G, H). Blood glucose concentrations of each treatment group were compared to the respective glucose levels of the ipGTT performed at baseline during the habituation phase when all animals were fed with the CD. Note that animals tested at week 34 were not tested at baseline. n: 8-12/group. Mean +/- SEM. *p<0.05, **p<0.01, ***p<0.001 two-way ANOVA followed by Bonferroni's *post hoc* test. N/A: not available.