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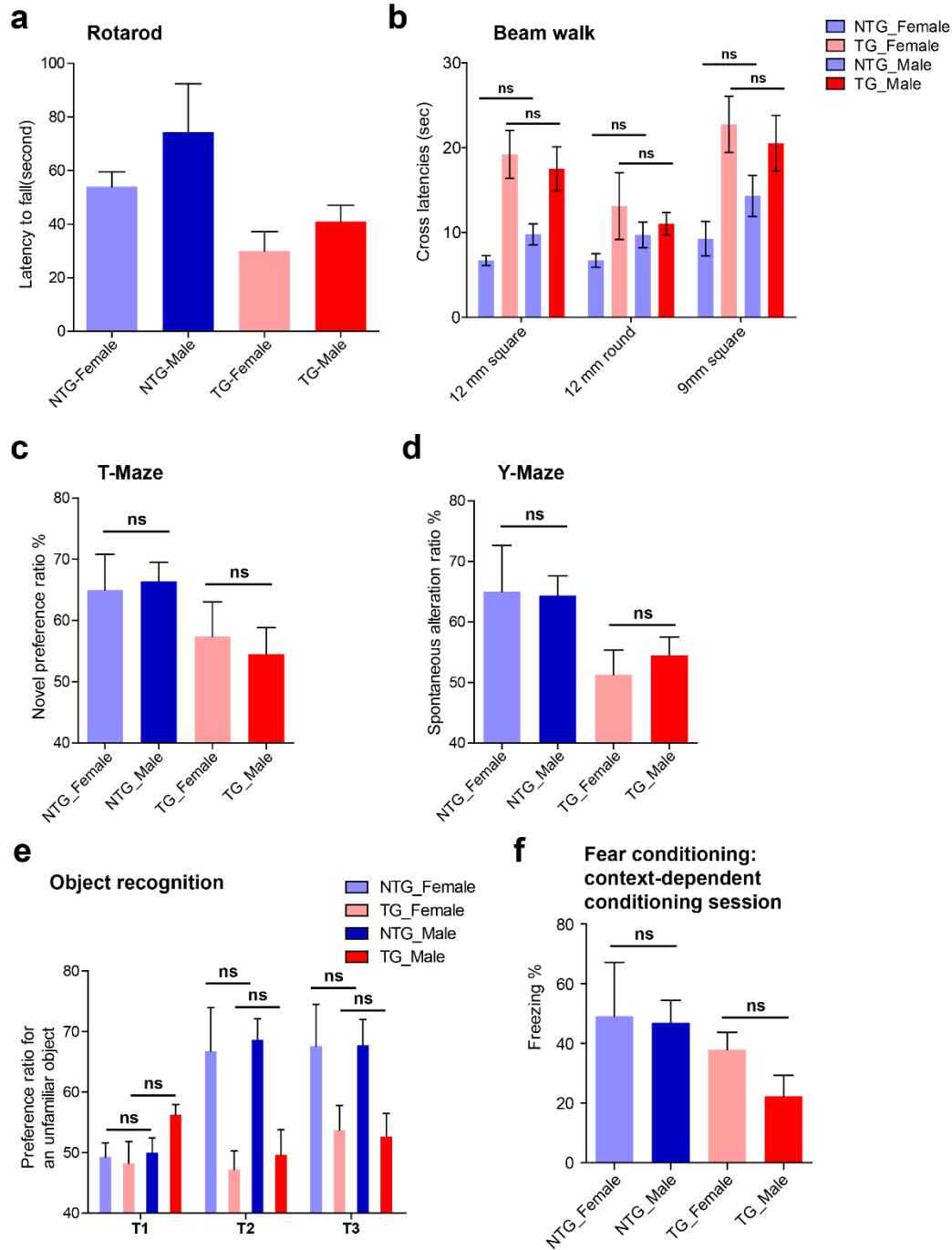
Supplemental Information

Motor-Coordination and Cognitive Dysfunction

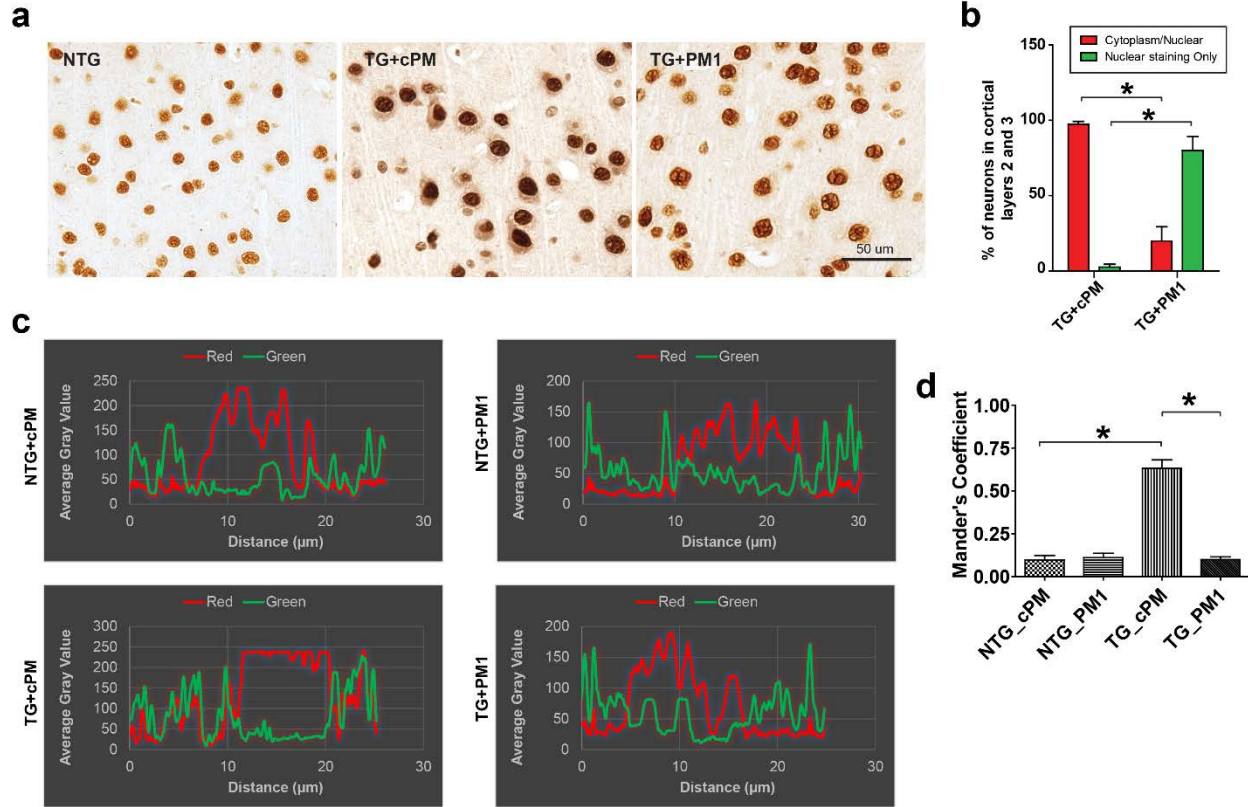
Caused by Mutant TDP-43 Could Be Reversed

by Inhibiting Its Mitochondrial Localization

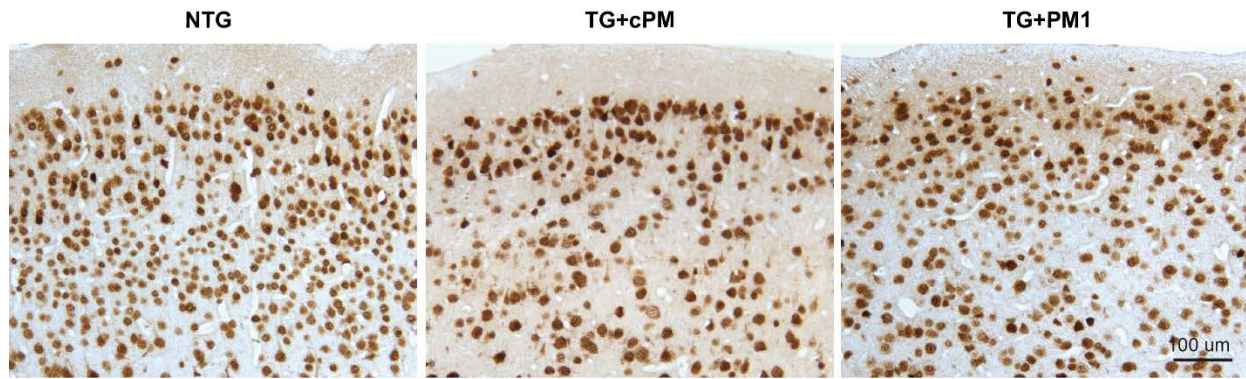
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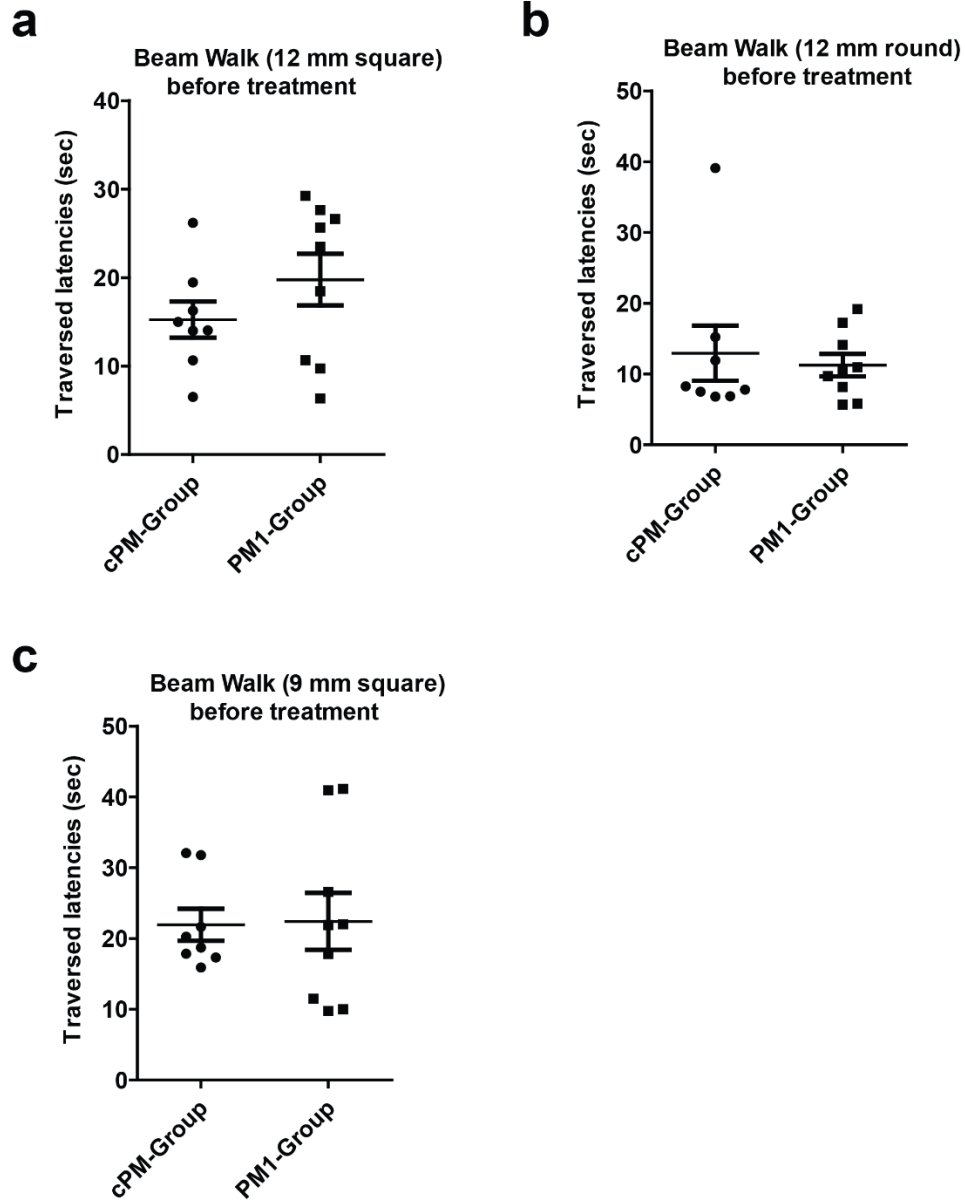
Supplemental Figure 1. Comparison of motor coordination and balance and cognitive performances between female and male NTG and TG mice (related to Figure 1). **(a, b)** Motor coordination and balance in female and male NTG and hemizygous TDP-43^{M337V} mice assessed by rotarod **(a)** and beam-walking tests **(b)**. **(c–f)** Cognitive performances of female and male NTG and hemizygous TDP-43^{M337V} mice evaluated by Y maze **(c)**, T maze **(d)**, novel object recognition **(e)** and fear conditioning tests **(e)**. All mice are at 8-9 month old. n= 11 for NTG (8 male/3 female) and 18 for TG (10 male/8 female). Data analyzed using two-way ANOVA followed by Bonferroni multiple comparisons. All data presented as means ± SEM; ns: non-significant.



Supplemental Figure 2. (a, b) Representative images (a) and quantification (b) of percentage of neurons with only nuclear TDP-43 staining or neurons with both nuclear and significant cytoplasmic TDP-43 in cortical layers II/III of 11 month old hemizygous TDP-43^{M337V} mice treated with cPM or PM1 (Related to Figure 3b). Neurons were stained by a pan-TDP-43 antibody. (c) Line scan analysis of TDP-43 and Tom20 by Image J RGB Profile Plot plugin, based on white solid lines shown in merged images of Figure 3b. The line-scan analysis was performed by Image J RGB Profile Plot plugin using lines with “2” width. (d) Quantification of degree of co-localization between cytoplasmic TDP-43 and Tom20 in cortical neurons from indicated mice by Manders's coefficient (% of both red and green signal co-localize; range from 0–1) that is independent of fluorescence intensity. A Mander's coefficient greater than 0.5 is considered significant co-localization (“0” means non-overlapping while “1” indicates complete overlapping). Data analyzed using two-way ANOVA followed by Bonferroni multiple comparisons. All data presented as means \pm SEM; * p <0.05.



Supplemental Figure 3. Representative images of immunohistochemistry on cortical layers I-V with a specific antibody against neuronal marker NeuN in 11 month old NTG and hemizygous TDP-43^{M337V} mice treated with 1.5 mg/kg/day cPM (control peptide for PM1) or PM1 continuously for 6 weeks by subcutaneous infusion. NTG: non-transgenic wild type mice; TG+cPM: hemizygous TDP-43^{M337V} mice treated with cPM; TG+PM1: hemizygous TDP-43^{M337V} mice treated with PM1.



Supplemental Figure 4. Motor coordination and balance of mice in two groups of hemizygous TDP-43^{M337V} mice assessed by the latency to traverse each beam.