

Fig. S1. Time course for *Npc1^{m1N}* model on different backgrounds. (A) Time course of composite phenotype scores for BALB/cNctr-*Npc1^{m1N}*/J mice (Jackson Laboratory Stock No. 003092) evaluated in laboratory A by one individual. (B) Time course of composite phenotype scores for C57Bl/6:SV129:BALB/c-*Npc1^{m1N}* evaluated in laboratory B by two individuals. (C) Time course of composite phenotype scores for C57Bl/6:BALBc-*Npc1^{m1N}* mice evaluated in laboratory B by two individuals (previously published data with modifications to graph layout as permitted by the open access Creative Common CC BY license (Cawley et al., 2020)). Even with different mixed backgrounds, *Npc1^{m1N}* mice exhibit very similar phenotype scores as disease progresses. All values represent mean±s.e.m. for biological replicates.

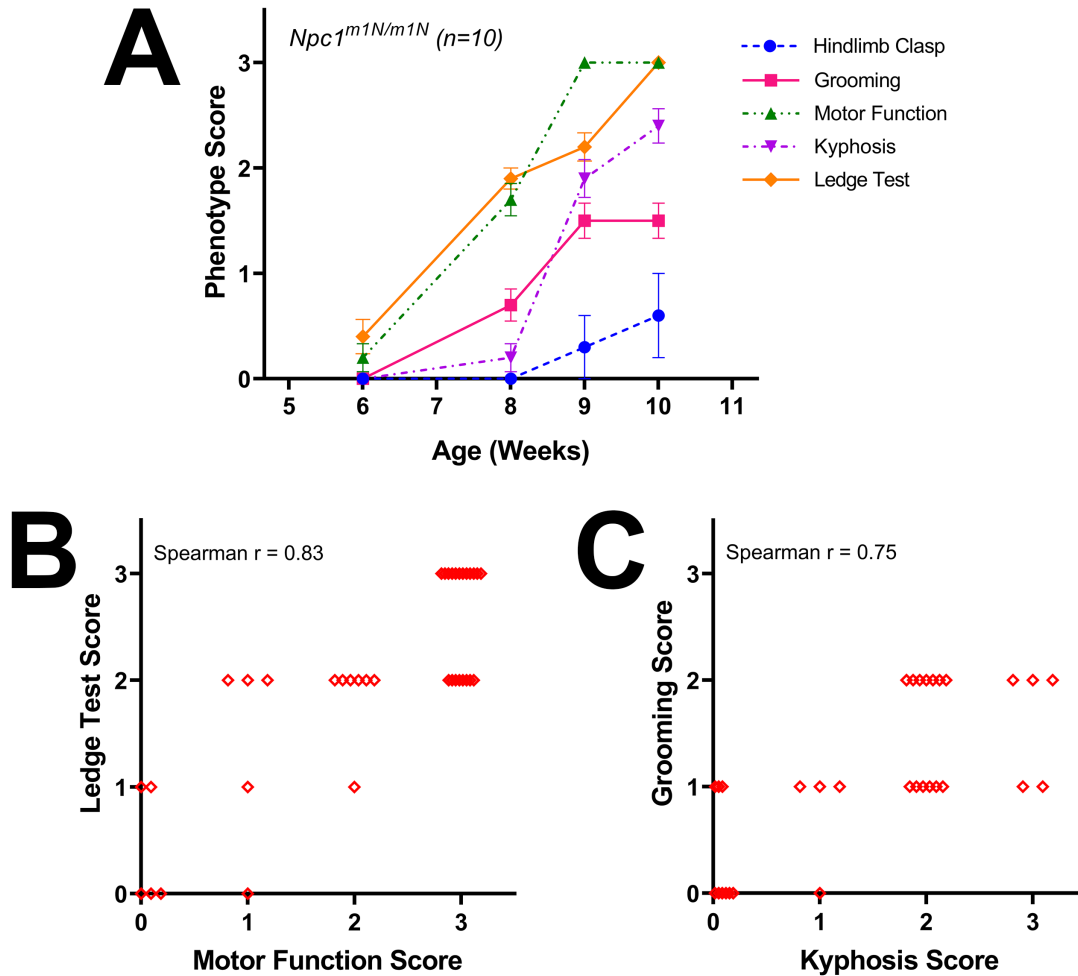


Fig. S2. Individual parameters over time and correlation between parameters. (A) Using the *Npc1^{m1N/m1N}* mice depicted in Supplemental Fig. 1A as an example, the time course for each phenotype parameter is presented (n = 10). (B, C) Although some parameters seem to overlap, analysis of correlation suggest incomplete agreement for ledge test and motor function (B; Spearman's coefficient $r = 0.83$) as well as grooming and kyphosis (C; Spearman's coefficient $r = 0.75$). Values in (A) represent mean \pm s.e.m. for biological replicates. Values in (B, C) represent biological replicates over time (scores for mice depicted in (A) at 6, 8, 9, and 10 weeks of age).

Table S1. Reliability Coefficient Guidelines (Landis & Koch, 1977)

| kappa | Interpretation |
|-------------|-------------------------------------|
| 0.00 | Completely Random Agreement |
| 0.01 – 0.20 | Slight agreement |
| 0.21 – 0.40 | Fair agreement |
| 0.41 – 0.60 | Moderate agreement |
| 0.61 – 0.80 | Substantial agreement |
| 0.81 – 1.00 | Almost perfect to perfect agreement |

Table S2. Krippendorff's alpha for ratings analyzed as nominal and ordinal categories

| Parameter | Sample size | Krippendorff's alpha | |
|------------------|----------------------|----------------------|---------------|
| | | nominal | ordinal |
| Hindlimb clasp | 14 raters, 5 videos | 0.808 | 0.907 |
| Bootstrap 95% CI | | 0.319 – 1.000 | 0.508 – 1.000 |
| Grooming | 14 raters, 7 images | 0.692 | 0.859 |
| Bootstrap 95% CI | | 0.410 – 0.864 | 0.567 – 0.958 |
| Motor function | 14 raters, 5 videos | 0.750 | 0.906 |
| Bootstrap 95% CI | | 0.295 – 0.950 | 0.399 – 0.998 |
| Kyphosis | 14 raters, 5 videos | 0.788 | 0.923 |
| Bootstrap 95% CI | | 0.337 – 1.000 | 0.337 – 1.000 |
| Ledge test | 17 raters, 12 videos | 0.733 | 0.899 |
| Bootstrap 95% CI | | 0.549 – 0.860 | 0.767 – 0.951 |

Bootstrap confidence intervals computed using n = 1000 replications.

References

- CAWLEY, N. X., LYONS, A. T., ABEBE, D., WASSIF, C. A. & PORTER, F. D. 2020.
Evaluation of the Potential Role of Proprotein Convertase Subtilisin/Kexin
Type 9 (PCSK9) in Niemann-Pick Disease, Type C1. *Int J Mol Sci*, 21.