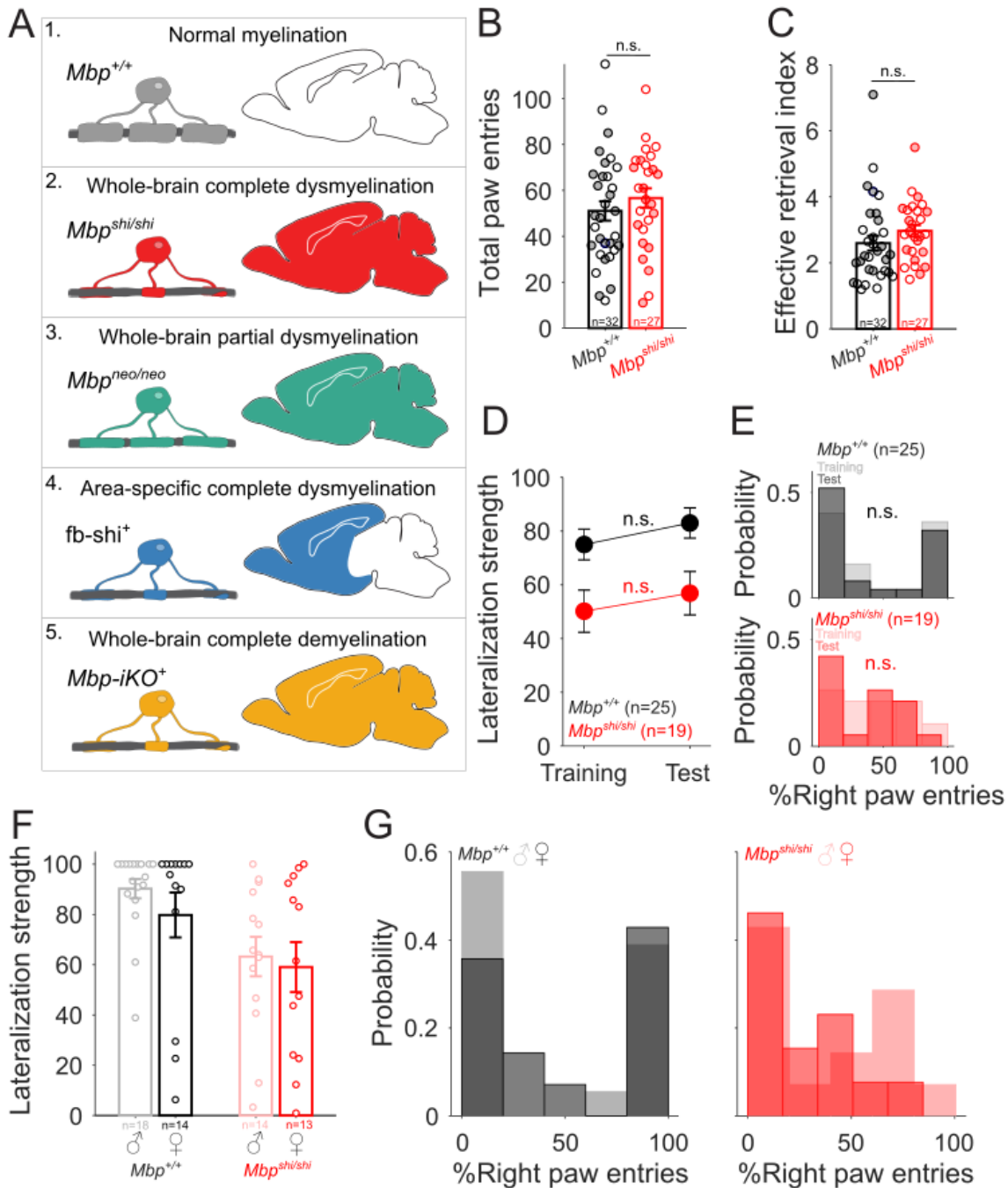


- 1 **Supporting information**
- 2 **Supplementary Figures 1-3 and Supplementary Table 1**

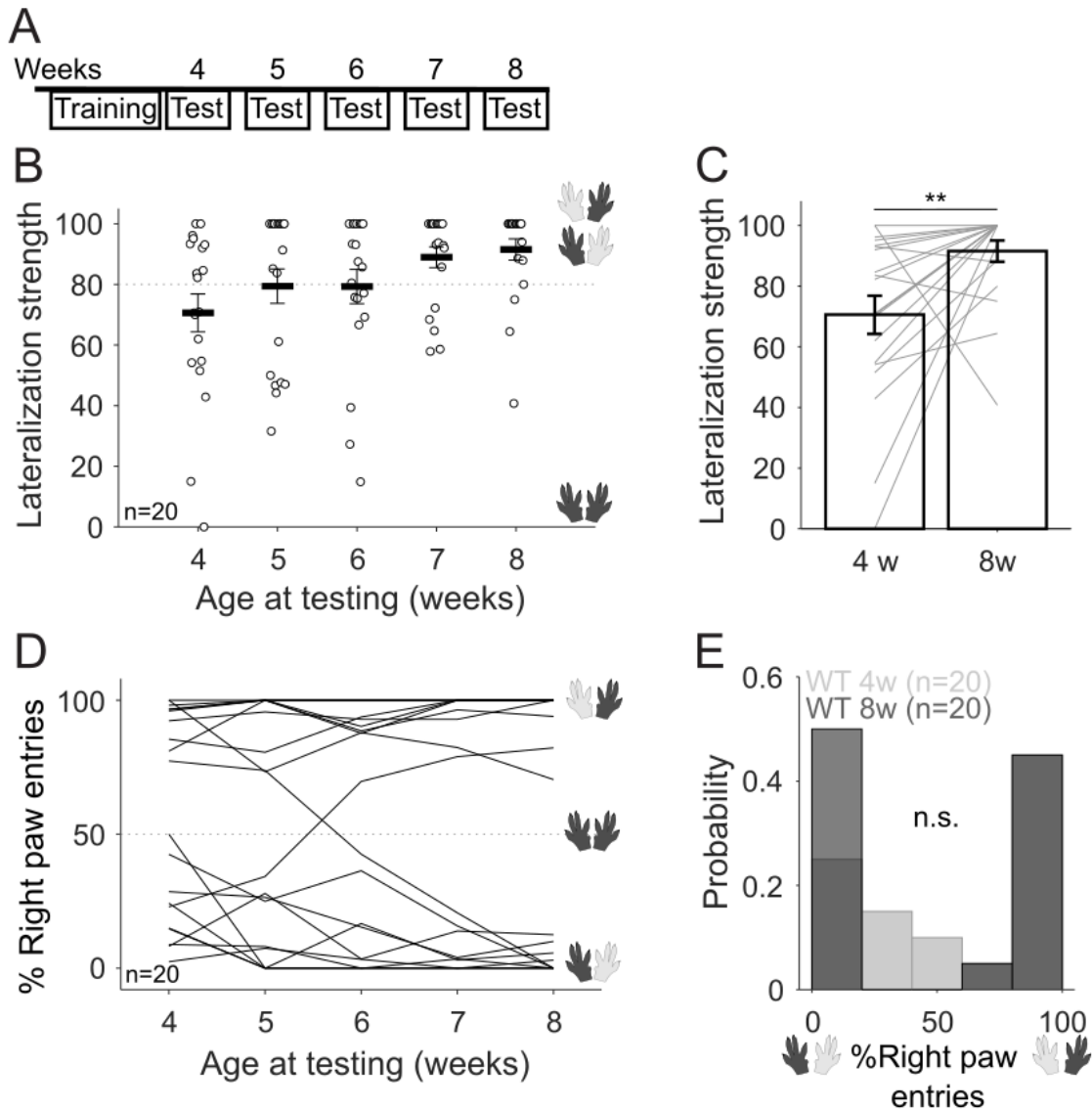


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5 **Supplementary Figure 1. *Mbp*^{shi/shi} mice can perform the paw preference task. A)** Schematic of
 6 individual mouse models used in this study. 1. Control mice (*Mbp*^{+/+}) were littermates of each mouse-line.
 7 We used three models of dysmyelination (congenital): 2. whole-brain complete dysmyelination (*Mbp*^{shi/shi}),
 8 3. whole-brain partial dysmyelination (*Mbp*^{neo/neo}), and 4. area-specific complete dysmyelination (fb-shi⁺). 5.
 9 One model of inducible adult whole-brain complete demyelination (*Mbp-iKO*⁺) was used to assess the
 10 contribution of developmental myelin in lateralized functions. **B)** *Mbp*^{shi/shi} perform a similar number of paw

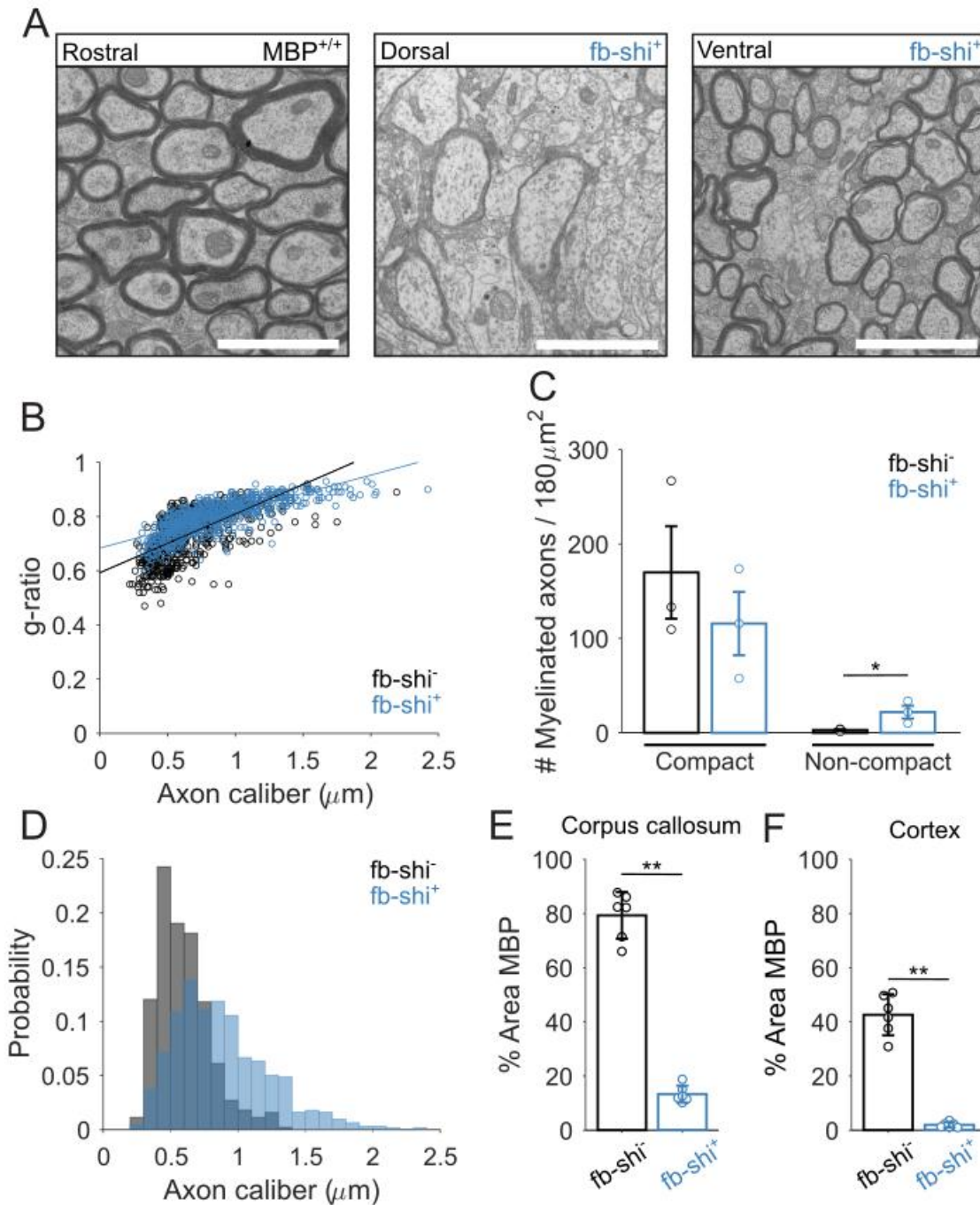
11 entries during the test session compared to *Mbp^{+/+}*. A two-way ANOVA revealed no significant effect of
12 genotype ($F(1,55)=0.9$, $p=0.35$), no effect of sex ($F(1,55)=3.17$, $p=0.081$) and no genotype x sex interaction
13 ($F(1,55)=0.95$, $p=0.33$). Open circles represent individual female mice and colored circles represent males.
14 **C)** Mice are also retrieving pellets with similar efficiency. A two-way ANOVA revealed no significant effect
15 of genotype ($F(1,55)=1.86$, $p=0.18$), no effect of sex ($F(1,55)=0.92$, $p=0.34$) and no genotype x sex
16 interaction ($F(1,55)=0.61$, $p=0.44$). Open circles represent individual female mice and colored circles
17 represent males. **D)** The reduced lateralization scores in *Mbp^{shi/shi}* mice are not due to spontaneous
18 alternation in one session but demonstrate a change in the established laterality pattern, as we see similar
19 scores between Training and Test sessions (a two-way ANOVA revealed a significant effect of genotype
20 ($F(1,84)=14.35$, $p=0.0003$), no effect of training stage ($F(1,84)=1.2$, $p=0.28$, and no genotype x training
21 stage interaction ($F(1,84)=0.01$, $p=0.92$). **E)** The biased directionality scores in *Mbp^{shi/shi}* mice are not due
22 to spontaneous alternation in one session but demonstrate a change in the established laterality pattern, as
23 we see similar directionality scores between Training and Test sessions (top plot (*Mbp^{+/+}*), Monte-Carlo χ^2
24 test, $\chi^2(4) = 1.12$, $p = 0.72$, Cramér's $V = 0.15$; bottom plot (*Mbp^{shi/shi}*), Monte-Carlo χ^2 test, $\chi^2(4) = 2.97$, p
25 $= 0.58$, Cramér's $V = 0.28$). **F)** Independent visualization of the strength of lateralization for males and
26 females from each genotype. A two-way ANOVA revealed a significant effect of genotype ($F(1,55)= 9.97$,
27 $p=0.0026$), no effect of sex ($F(1,55)=0.94$, $p=0.34$) and no genotype x sex interaction ($F(1,55)=0.17$,
28 $p=0.67$). Bonferroni-corrected post-hoc tests revealed that *Mbp^{+/+}* males were significantly different from
29 *Mbp^{shi/shi}* females (adjusted $p=0.026$) whereas all other pairwise comparisons were not significant ($p>0.05$).
30 For the complete statistical outcome refer to Supplementary Table 1. **G)** Independent visualization of the
31 directionality of lateralization for males and females from each genotype. Directionality distribution did not
32 differ between males and females of neither control *Mbp^{+/+}* (left plot, Monte-Carlo χ^2 test, $\chi^2(4) = 5.33$, $p =$
33 0.080 , Cramér's $V = 0.41$) or *Mbp^{shi/shi}* (right plot, Monte-Carlo χ^2 test, $\chi^2(4) = 3.97$, $p = 0.39$, Cramér's $V =$
34 0.38).

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39 **Supplementary Figure 2. Lateralization strength develops with age.** **A)** Wild-type animals were tested
 40 weekly between week 4 and 8. **B)** At 4 weeks of age lateralization was weak but it strengthened with age,
 41 passing a threshold of 80% at 5 weeks. $n=20$ mice. **C)** 4-week old mice are significantly less lateralized
 42 than 8-week-old mice (Wilcoxon signed rank test, $p=0.0055$). **D)** Directionality of preferred paw is constant
 43 throughout in most animals (only 2/20 mice switched directionality) and **E)** the distribution of directionality
 44 scores is comparable between 4- and 8-week-old mice. (Monte-Carlo χ^2 test, $\chi^2(4) = 6.67$, $p = 0.091$,
 45 Cramér's $V = 0.41$) ($n=20$ mice).



46

47 **Supplementary Figure 3. Characterization of the fb-shi mouse model. A)** Representative EM pictures
 48 of a control (fb-shi⁻), and fb-shi⁺ CC, showing preferential dysmyelination of the dorsal CC. Scale bar: 1 μm .

49 **B)** G-ratio quantification. (n=3 fb-shi⁻ mice and n=3 fb-shi⁺ mice) (CC). **C)** Number of myelinated axons in
 50 the CC. (n=3 fb-shi⁻ mice and n=3 fb-shi⁺ mice). **D)** Axon caliber distributions in the CC (n=3 fb-shi⁻ mice
 51 and n=3 fb-shi⁺ mice).

52 **E)** Significant reduction of the % area covered by MBP in the CC (Wilcoxon rank-
 53 sum test p=0.00028, n=6 datapoints from 3 mice and 2 slides quantified per mice for fb-shi⁻ and n=6
 datapoints from 3 mice and 2 slides quantified per mice for fb-shi⁺) and the **F)** cortex (Wilcoxon rank-sum

54 test p=0.00028, n=6 datapoints from 3 mice and 2 slides quantified per mice for fb-shi⁻ and n=6 datapoints
55 from 3 mice and 2 slides quantified per mice for fb-shi⁺).

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57 **Supplementary Table 1. Complete list of multiple comparisons for Figure S1F.**

Group comparison	Mean difference	P value
Mbp ^{+/+} females x Mbp ^{shi/shi} females	20.72	0.40
Mbp ^{+/+} females x Mbp ^{+/+} males	-10.46	1.00
Mbp ^{+/+} females x Mbp ^{shi/shi} males	16.55	0.81
Mbp^{shi/shi} females x Mbp^{+/+} males	-31.18	0.026
Mbp ^{shi/shi} females x Mbp ^{shi/shi} males	-4.17	1.00
Mbp ^{+/+} males x Mbp ^{shi/shi} males	27.01	0.066

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