Supplemental Information

Supplementary Figure 1. AAB from a small subset of Long COVID participants are restricted to with CNS and PNS tissues. Confocal microscopy showing human and mouse tissues immunostained with human total IgG (green) purified from Long COVID, healthy or convalescent controls, as indicated, and nuclear DNA stain (DAPI, blue). **A** Representative images of mouse spinal cord immunostaining and mean of fluorescence intensity. **B** Mean of fluorescence for mouse thalamus plus hypothalamus, hindbrain, cerebral nuclei, cerebral cortex, hippocampus, anterior olfactory nucleous and midbrain. **C** Mean of fluorescence for human adrenal gland, breast, cervix, endometrium, gall bladder, fallopian tube, heart muscle, kidney, liver, pancreas, parathyroid, prostate, rectum, retina, small intestine, stomach, testis, urinary bladder, thyroid, placenta, ovary. Each dot in the figure represents the value obtained from an individual participant. Data are presented as the mean. Significant p-values are described in the image, as determined by One-way ANOVA with Tukey multiple comparisons test.

Supplementary Figure 2. Comparisons of meninge and sciatic nerve stain with symptoms displayed by the Long COVID participants. A Mouse meninges stain divided by symptoms displayed by the participants, as brain fog, fatigue, dizziness, tinnitus, confusion, dysautonomia, and pain. **B** Mouse sciatic nerve stain divided by symptoms displayed by the participants, as brain fog, fatigue, dizziness, disorientation, confusion, dysautonomia, pain, memory, weakness, and headache. Each dot in the figure represents the value obtained from an individual participant. Data are presented as the mean. Significant p-values are described in the image, as determined by One-way ANOVA with Tukey multiple comparisons test.

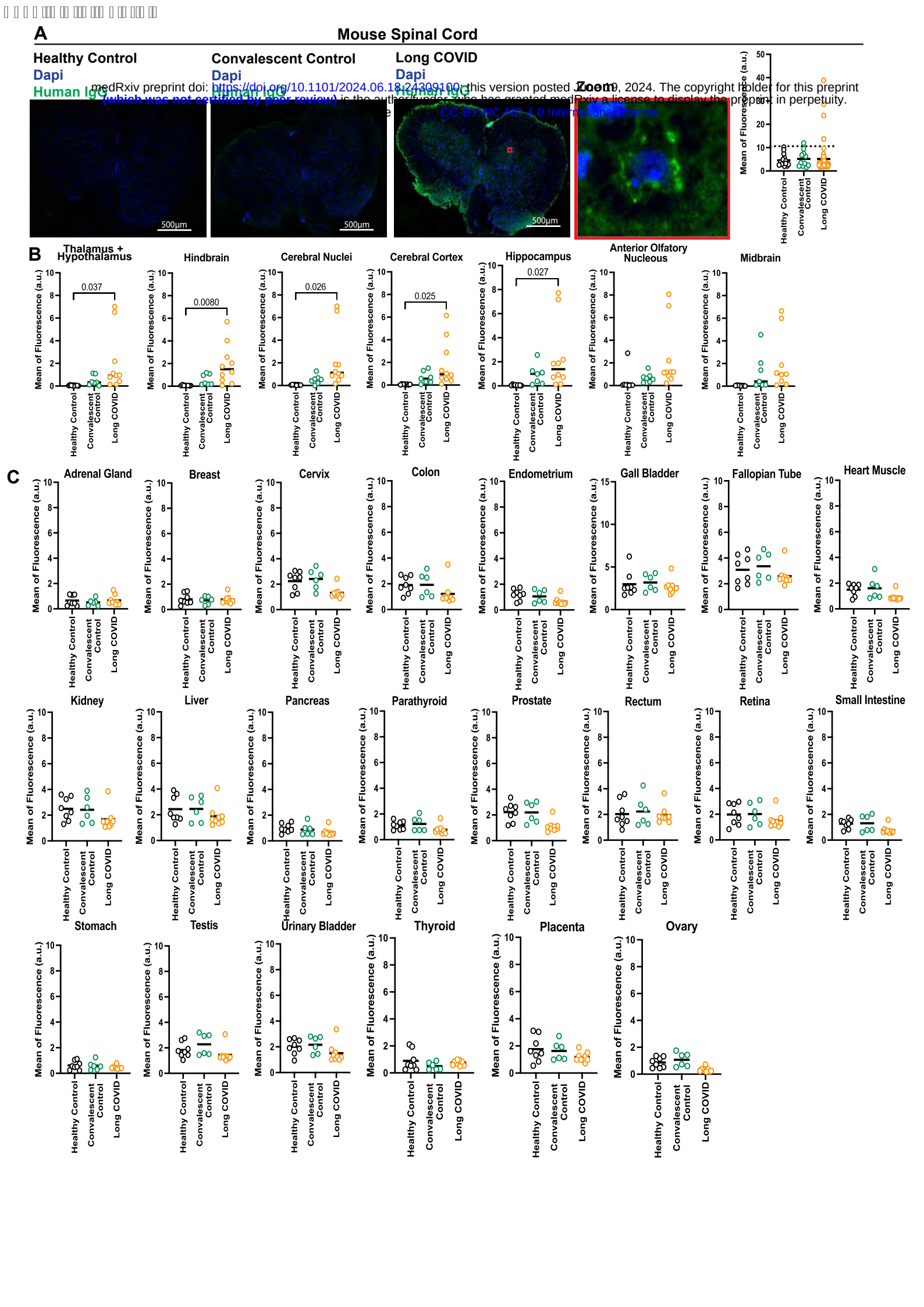
Supplementary Figure 3. Long COVID participants have increased and diverse AAB against MED and USP family proteins. A. Size-exclusion chromatography (SEC) profiles of the purified proteins run in a Fast Protein Liquid Chromatography (FPLC). Purity was determined by peak integration with the ChromLab Software. **B**. ELISA and Area Uder Curve (AUC) analysis for top hit targets identified by Huprot. **C.** Volcano plot showing differential abandance (Log_2 Fold Change) of AAB targets identified by pulldown using hIgG from healthy controls and Long COVID participants with mouse brain homogenate followed by mass spec. **D**. Time course analysis of human IgG concentration by ELISA in brain homogenate and serum for four days post-injection. Each dot in the figure represents the value obtained from an individual mouse. Data are presented as the mean ±SD. Significant p values are described in the image, as determined by T-test for two groups comparison or one-way ANOVA corrected for multiple comparisons with Tukey test for multiple groups comparison.

Supplementary Figure 4. Symptoms evaluated in the passive transfer that were not associated with hot plate test and grip strength. Dose of 38 mg/kg of total IgG purified from healthy, convalescent controls and Long COVID participants were administered to 6-8 weeks-old C57BLl/6 female mice by intraperitoneal (IP) injection, which were followed up for 5 days. **A.** Hot plate test divided by symptoms displayed by the participants as fatigue, disorientation, tinnitus, memory, confusion, dizziness, brain fog, headache. **B** Grip strength test divided by participants that displayed fatigue, disorientation, memory, confusion, weakness, dizziness, brain fog, chronic pain and dysautonomia. Each dot in the figure represents the value obtained from an individual mouse. Each mouse received antibodies isolated from a single human participant.

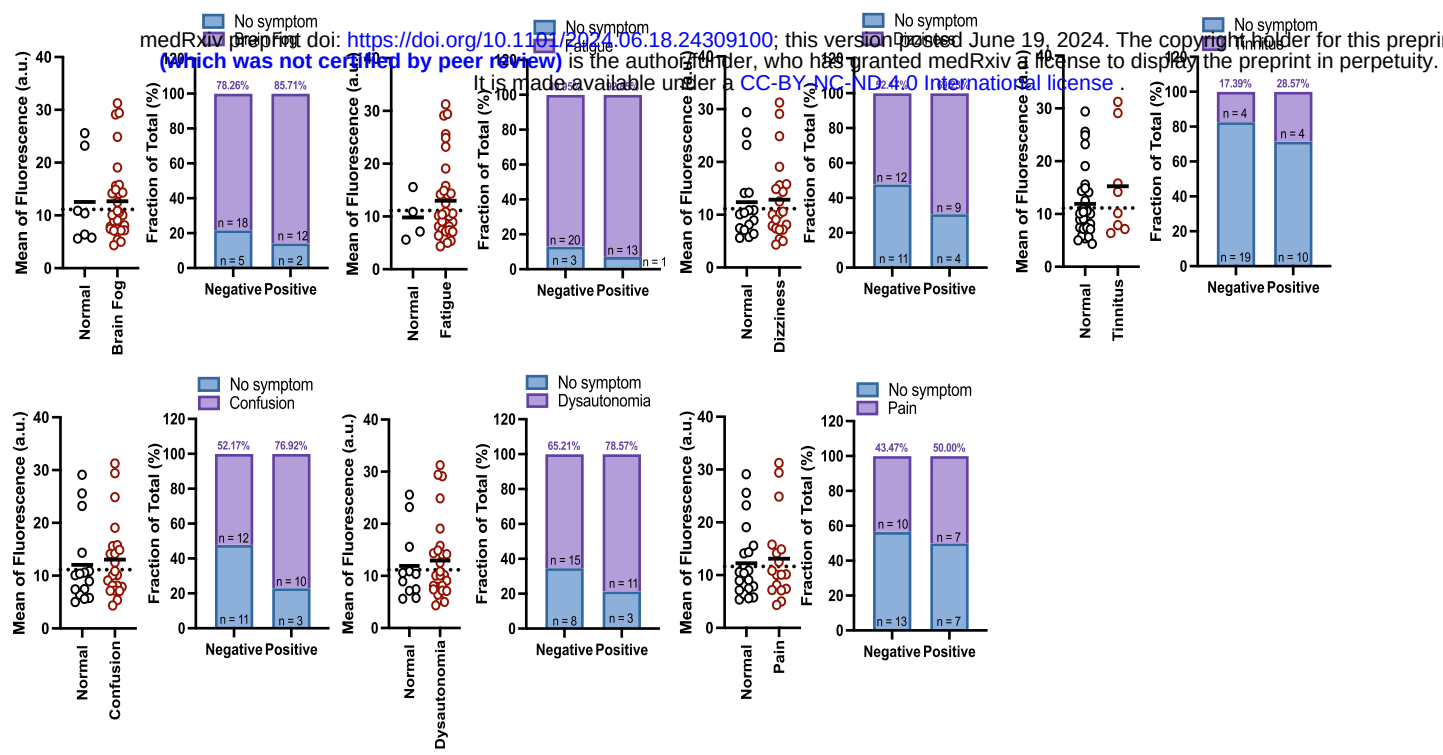
Data are presented as the mean. Significant p values are described in the image, as determined by one-way ANOVA corrected for multiple comparisons with Tukey test.

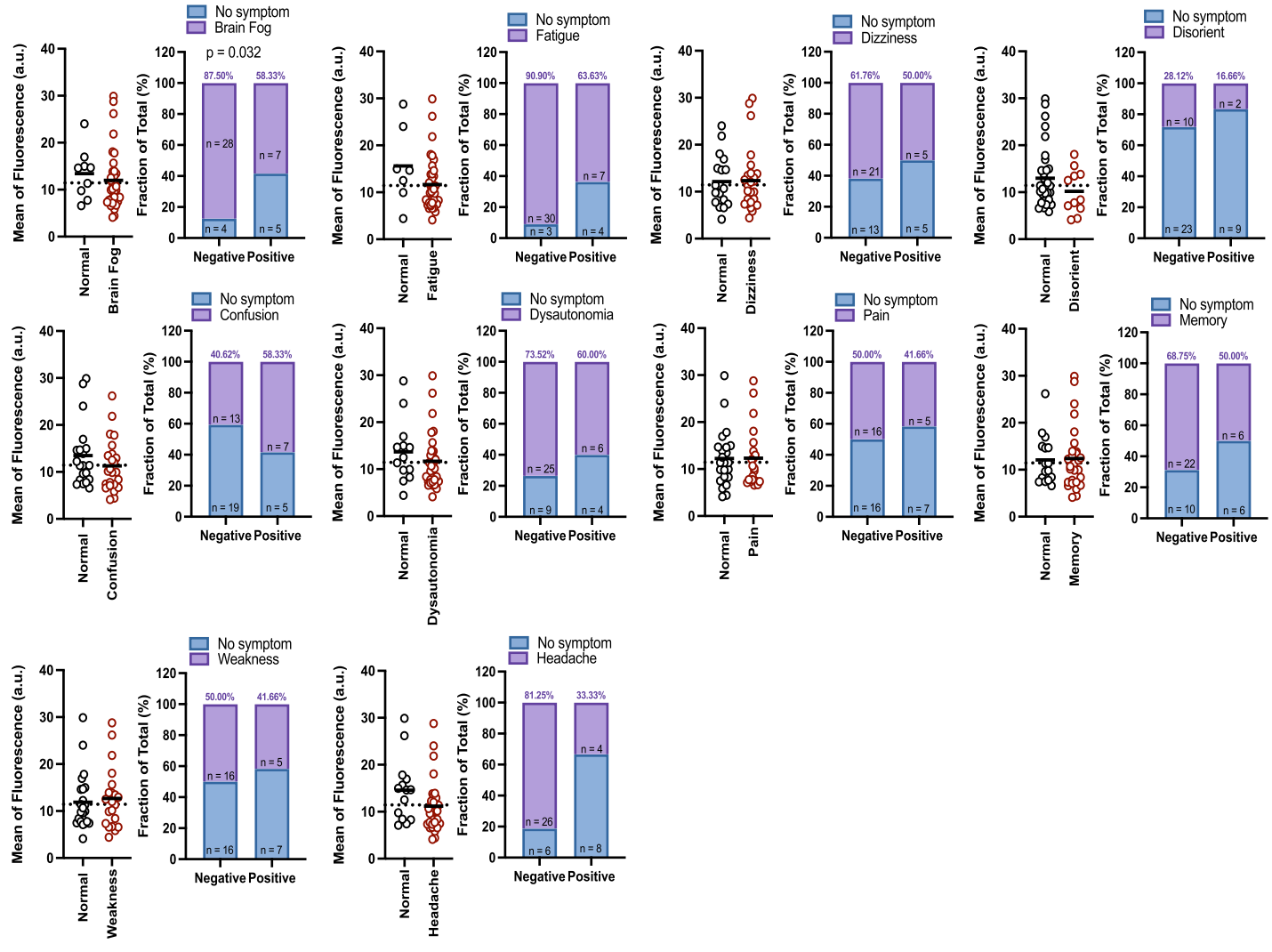
Supplementary Figure 5. Symptoms evaluated in the passive transfer that were not associated with rotarod. Dose of 38 mg/kg of total IgG purified from healthy, convalescent controls and Long COVID participants were administered to 6-8 weeks-old C57BL/6 female mice by intraperitoneal (IP) injection, which were followed up for 5 days. **A.** Rotarod test divided by symptoms displayed by the participants as fatigue, disorientation, tinnitus, brain fog, confusion, weakness, memory, chronic pain, headache, and dysautonomia.

Supplementary Figure 6. Passive transfer does not induce anxiety like behavior, locomotion and cardiovascular function symptoms in mice. Dose of 38 mg/kg of total IgG purified from healthy, convalescent controls and Long COVID participants were administered to 6-8 weeks-old C57BL/6 female mice by intraperitoneal (IP) injection, which were followed up for 5 days. **A**. Cumulative time spent in the cente, cumulative time spent in the border and representative heat map showing mice movement in the open field test. **B**.Mean velocity, distance moved and time moving during the open field test. **C**. Cumulative time in open arms, cumulative time in closed arms and representative heatmap showing mice movement in the elevated zero maze test. **D**. Heart rate, mean blood pressure, systolic blood pressure and diastolic blood pressure measurements. Each dot in the figure represents the value obtained from an individual mouse. Each mouse received antibodies isolated from a single human participant. Data are presented as mean. Significant p values are described in the image, as determined by one-way ANOVA corrected for multiple comparisons with Tukey test.

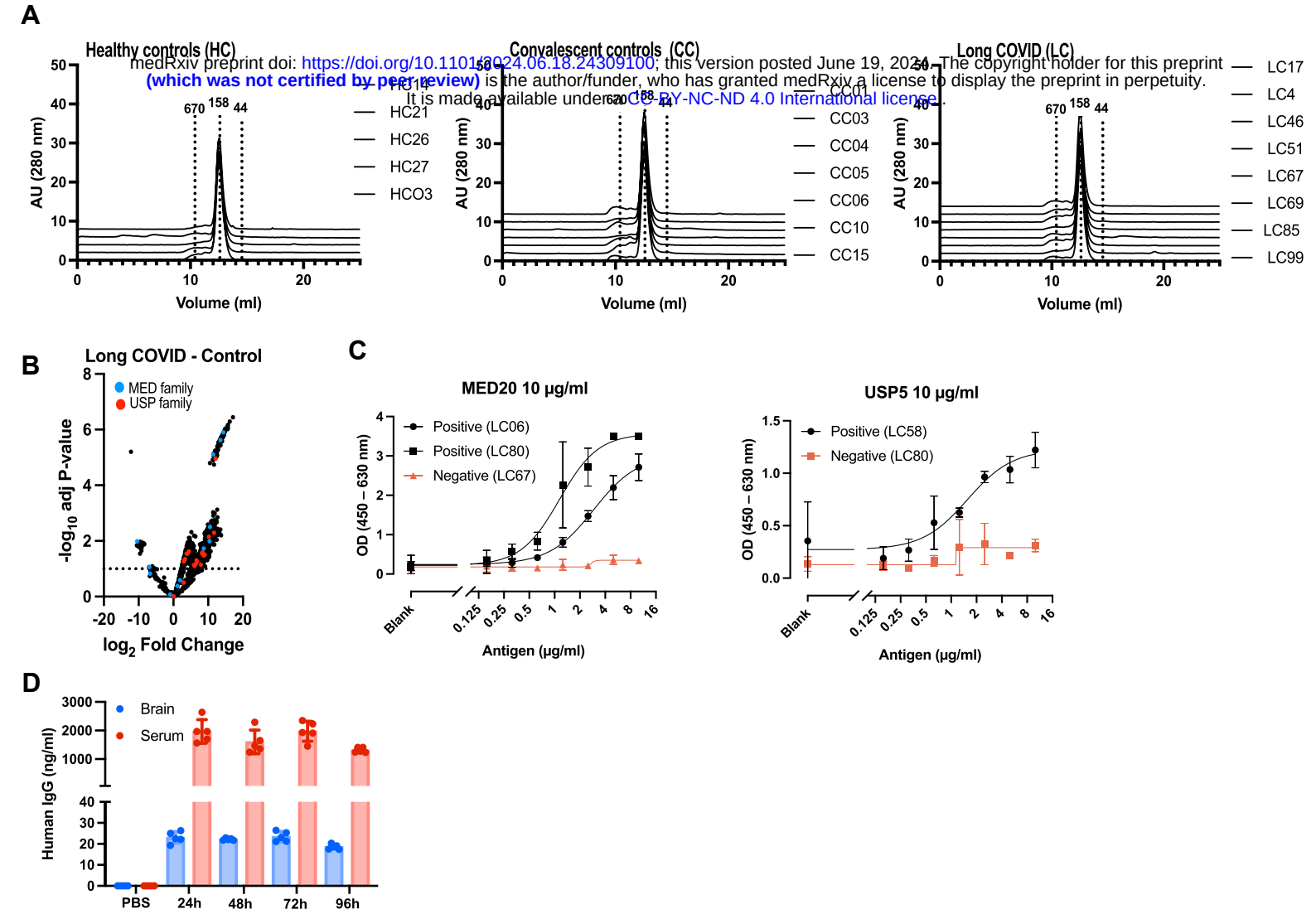


Supp. Fig. 2. Sá et al.

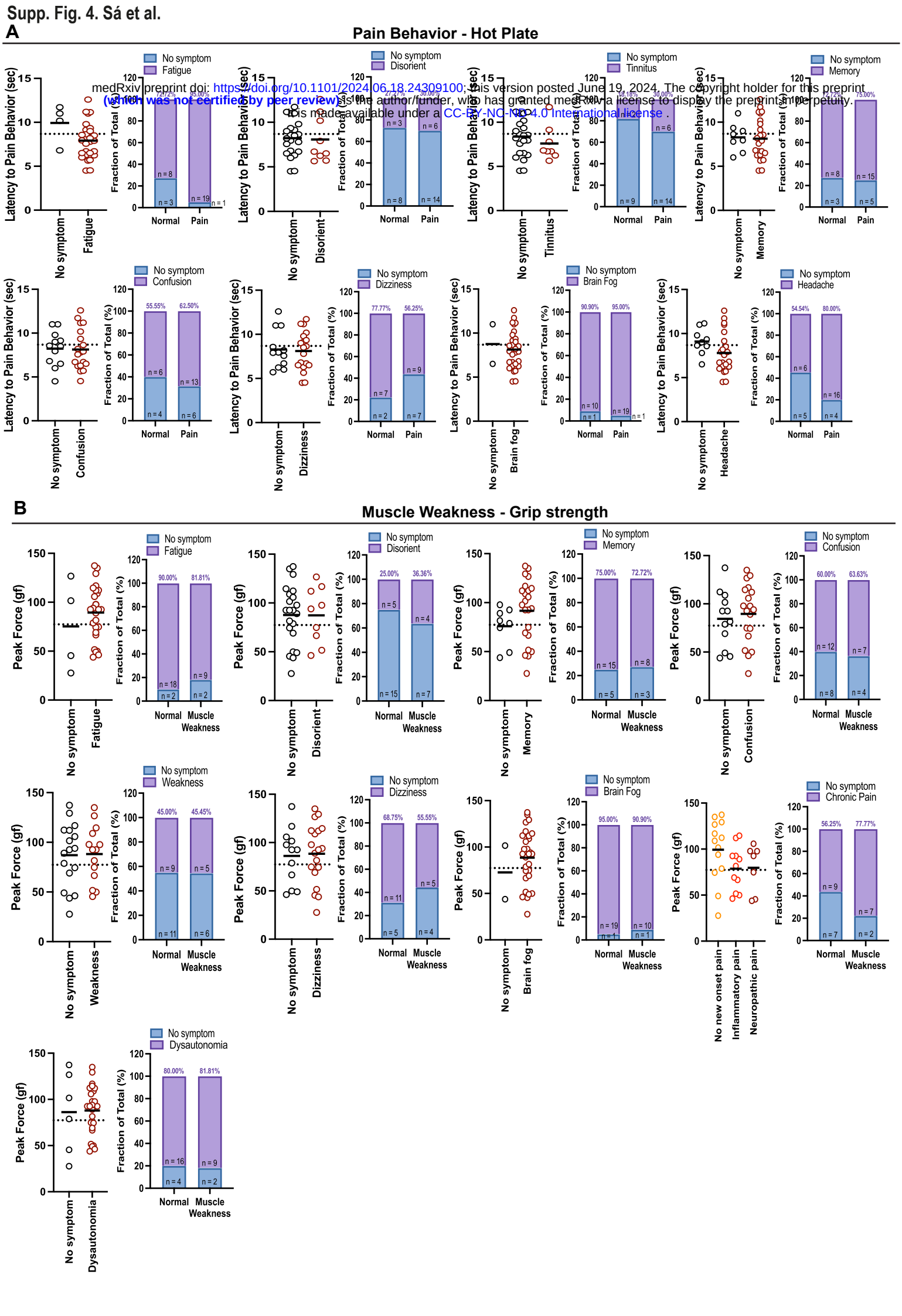




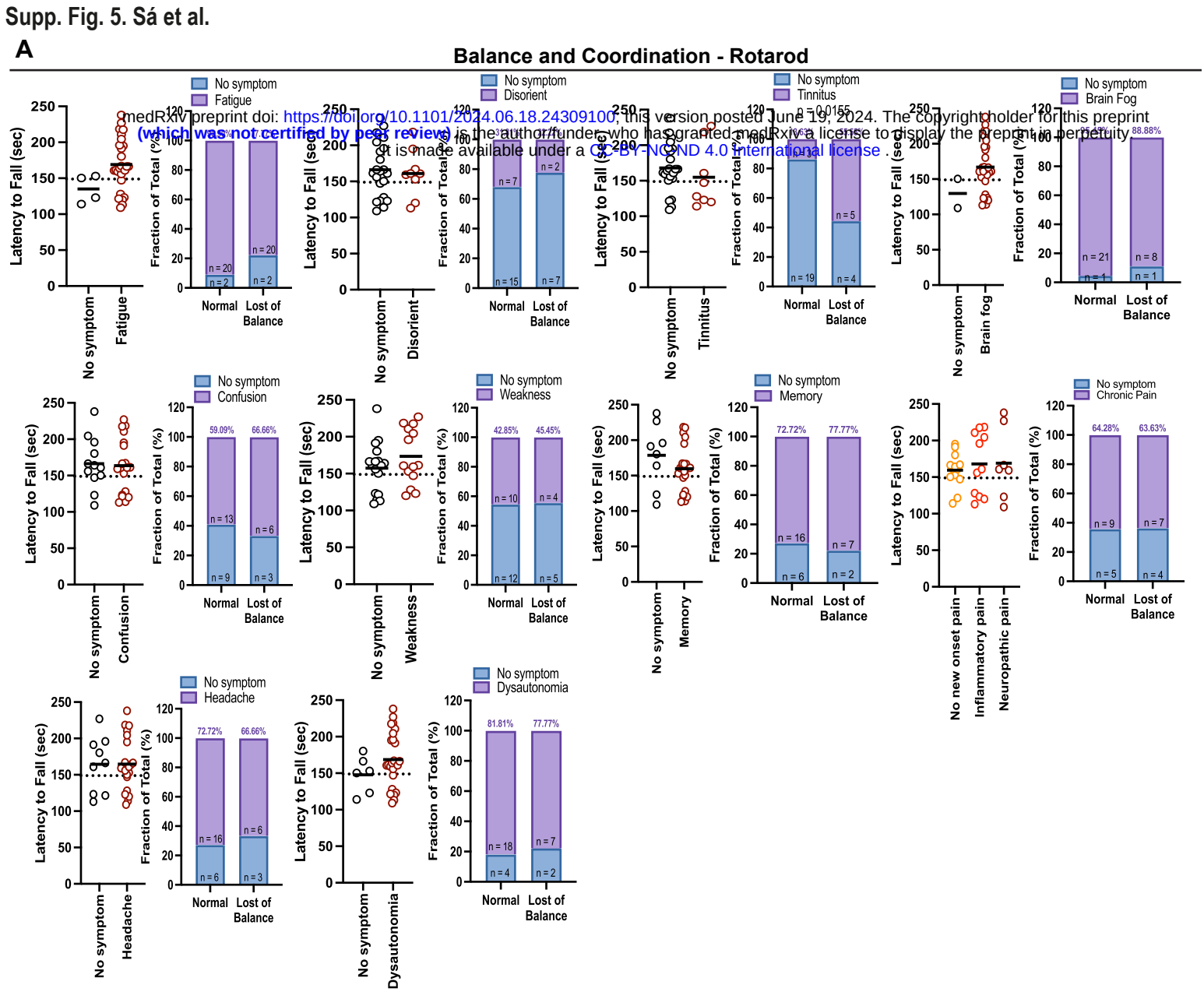
Supp. Fig. 3. Sá et al.



Supp. Fig. 4. Sá et al.



Supp. Fig. 5. Sá et al.



Supp. Fig. 6. Sá et al.