

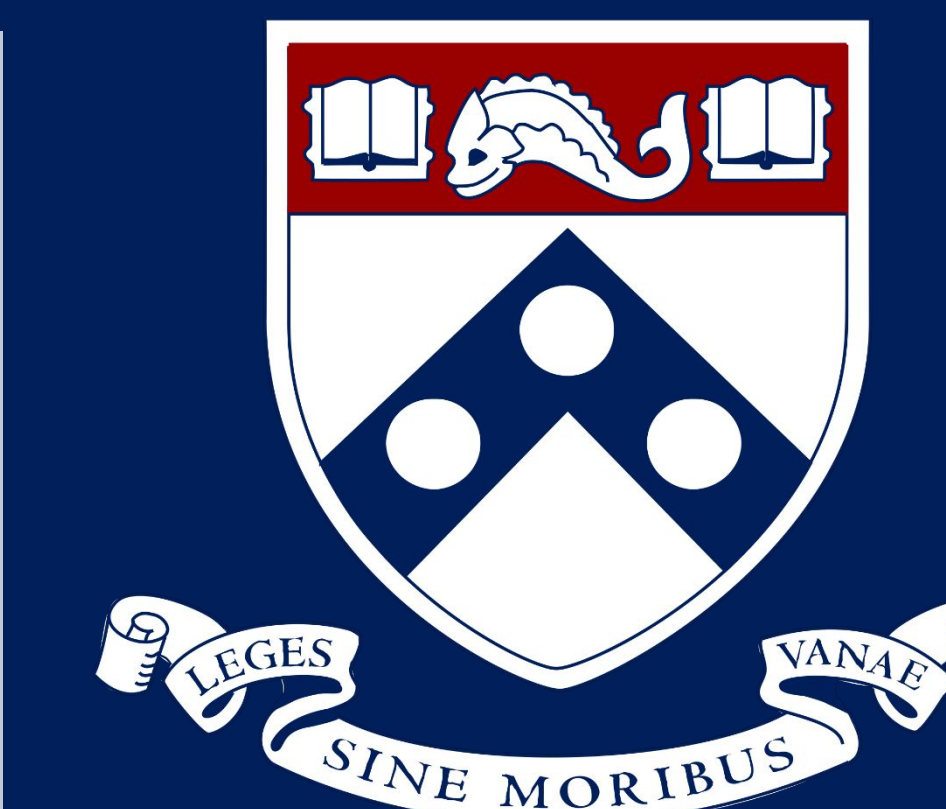


Disrupted Sleep in a Large Animal Model of Traumatic Brain Injury

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INTRODUCTION

Traumatic brain injury (TBI) is caused by mechanical insults to the head, often resulting in prolonged or permanent cognitive dysfunction.

Sleep disturbances such as difficulty falling and staying asleep are common, persistent symptoms following TBI, which can significantly complicate recovery.

ANIMAL MODELS OF TBI

To accurately model all aspects of TBI, a gyrencephalic animal model (pig) with a large brain, containing appropriate white-to-grey matter ratio, may be required.

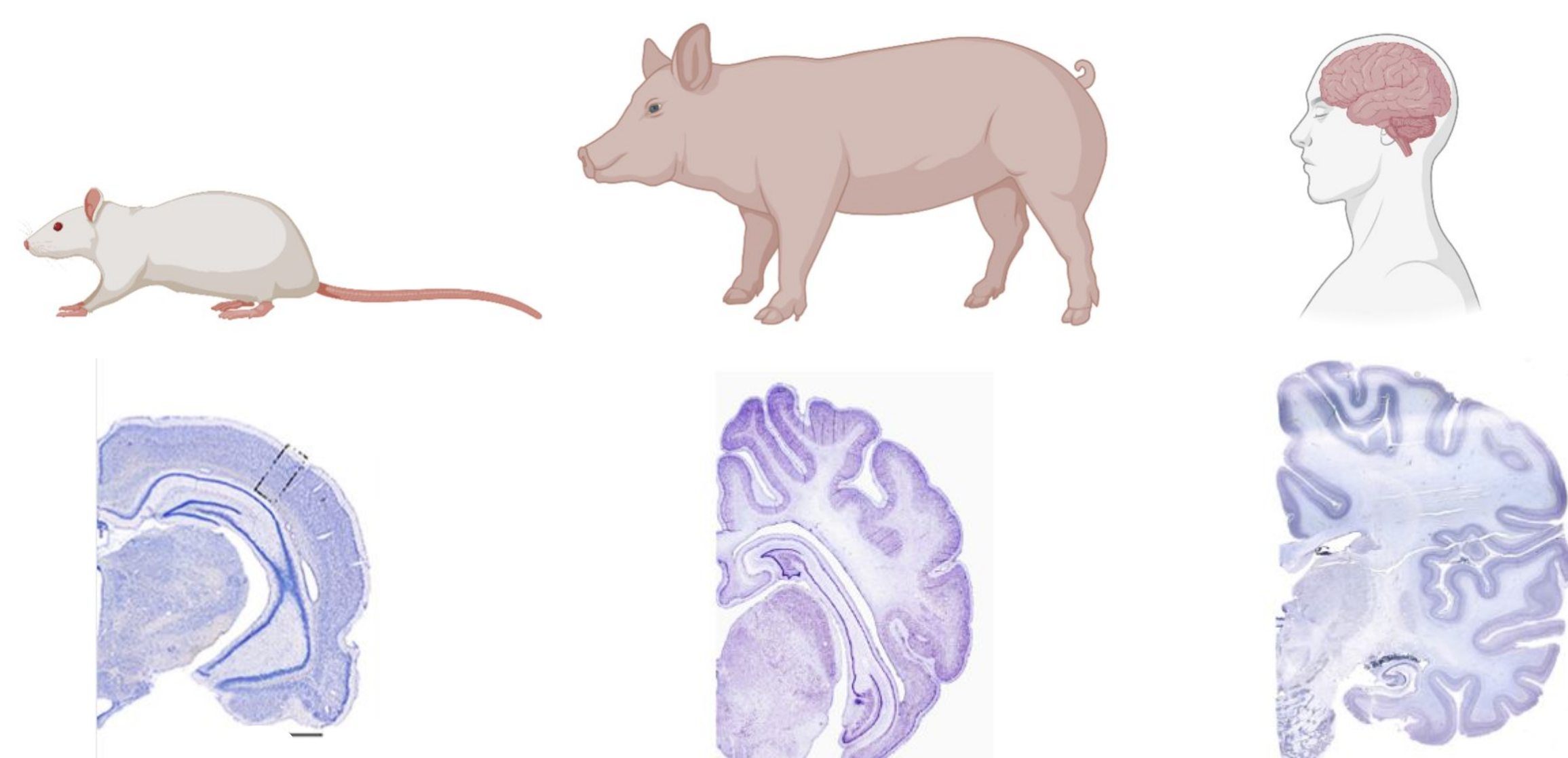


Figure 1. Coronal sections at the level of hippocampus in the rat, pig and human demonstrate the increased white matter to grey matter ratio as the cortex area expands.

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CONTROLLED CORTICAL INJURY (CCI)

Pigs are injured with an impactor going through an open skull, while the dura mater is kept intact. The animals are assessed for any neurological deficits over time post-TBI.

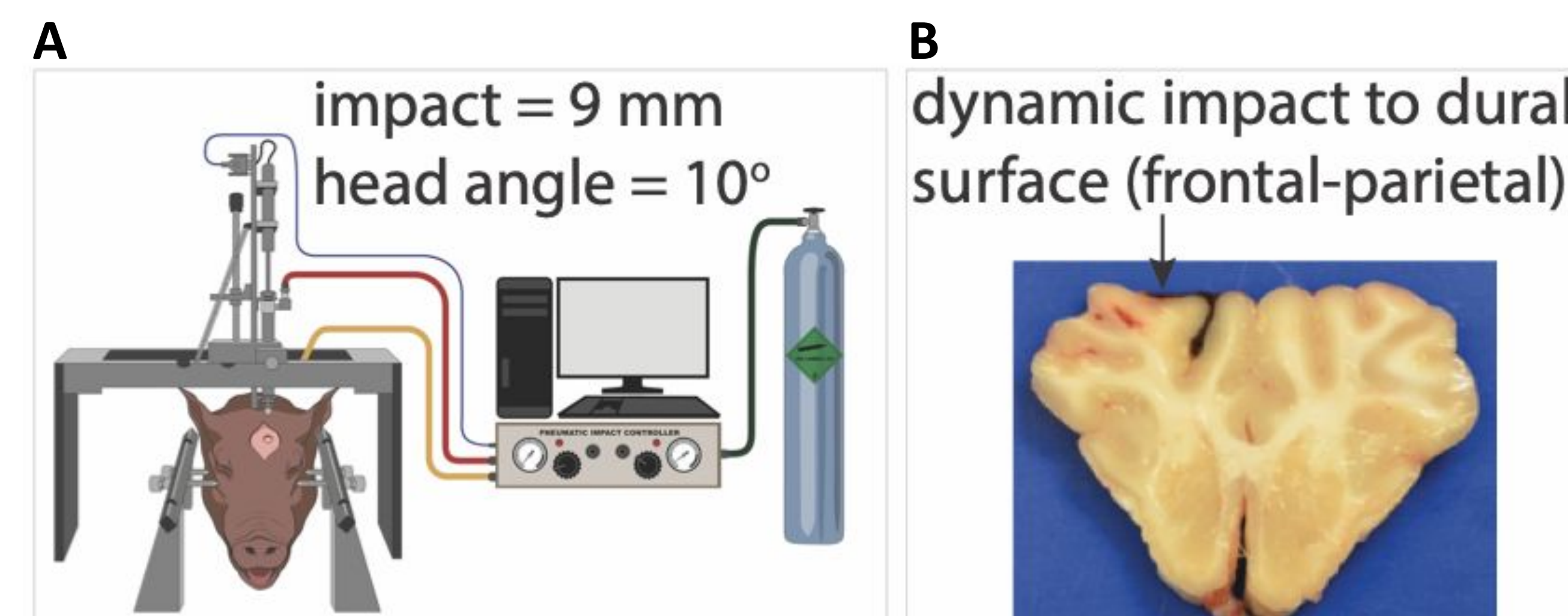


Figure 2. Male Yucatan pigs were injured via controlled-cortical impact injury at 6 months of age. A) The dynamic impact was performed at 9 mm from the brain surface. B) The injury was performed on the left side of the brain. Total number of animals: sham-injured n = 3, CCI-injured n = 4.

PIG EPILEPSY MONITORING UNIT

Following TBI, pigs are continuously monitored in home cages. Video is recorded 24/7, and EEG signals are recorded 14-16 hours every other day for the duration of the study (up to 9 months post-TBI).

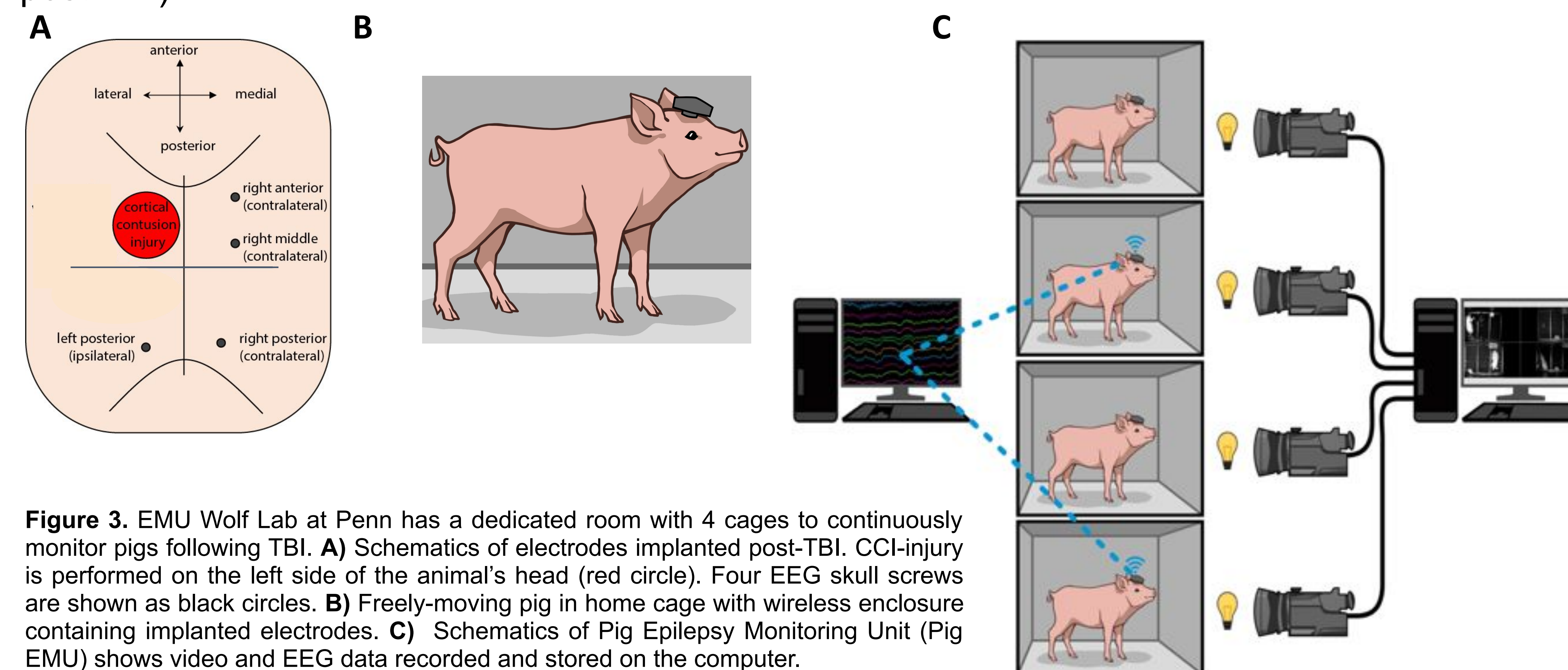


Figure 3. EMU Wolf Lab at Penn has a dedicated room with 4 cages to continuously monitor pigs following TBI. A) Schematics of electrodes implanted post-TBI. CCI-injury is performed on the left side of the animal's head (red circle). Four EEG skull screws are shown as black circles. B) Freely-moving pig in home cage with wireless enclosure containing implanted electrodes. C) Schematics of Pig Epilepsy Monitoring Unit (Pig EMU) shows video and EEG data recorded and stored on the computer.

SLEEP DISTURBANCES UP TO 6 WEEKS FOLLOWING CCI INJURY

Using automated and manual analyses of video data, disturbances in sleep and wake states were observed in CCI-injured animals up to 6 weeks post-TBI.

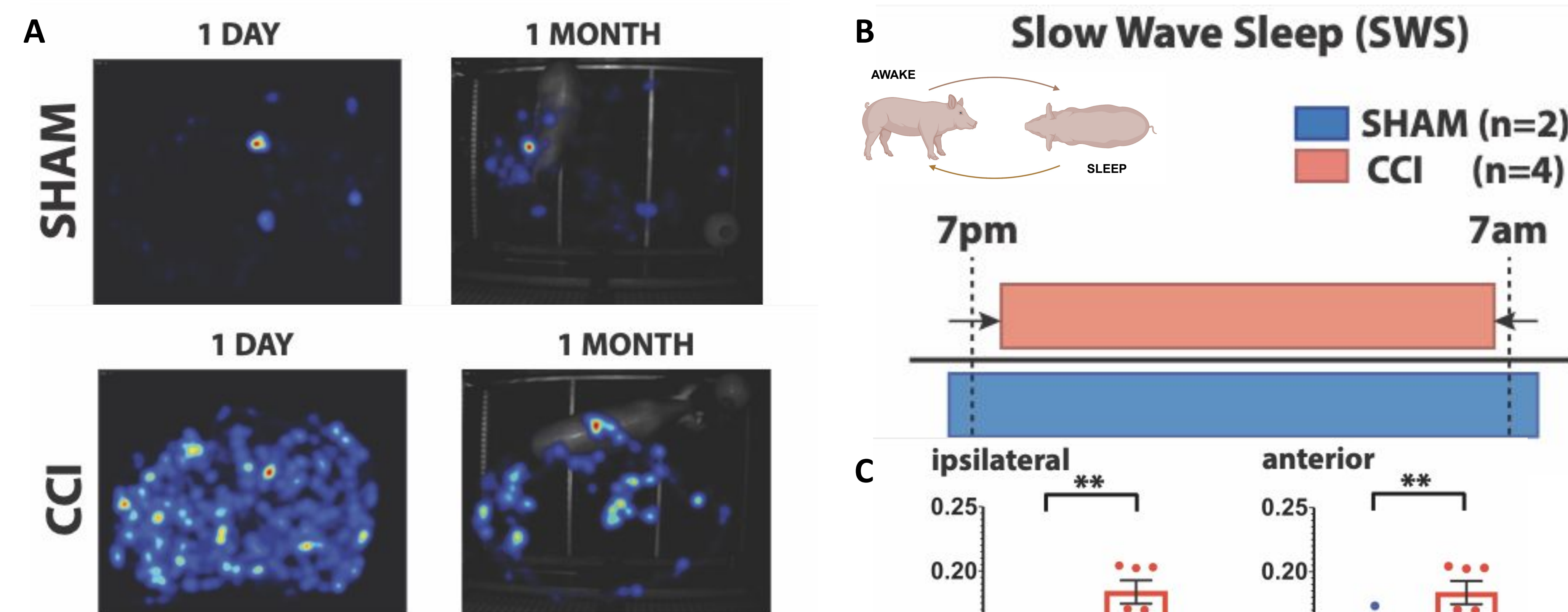


Figure 4. Sleep-wake disturbances observed in CCI-injured animals up to 6 weeks post TBI. A) Automated video analysis of home cage behavior using Noldus video tracking software shows that CCI-animals moved in their home cages more than sham animals when compared to pre-injury levels. B) Duration of sleep was significantly decreased in CCI animals. C) Percentage of Slow Wave Sleep (SWS) automatically calculated with Polyman software as percentage of delta oscillation (0.5 - 4 Hz) shows an increase in the amount of SWS detected on left (ipsilateral) as well as right (anterior contralateral) side of pig's brain relative to the CCI-injury site.

SLEEP DISTURBANCES UP TO 7 MONTHS POST-CCI INJURY

Using automated and manual analyses of video data, disturbances in sleep and wake states were observed in CCI-injured animals up to 7 months post-TBI.

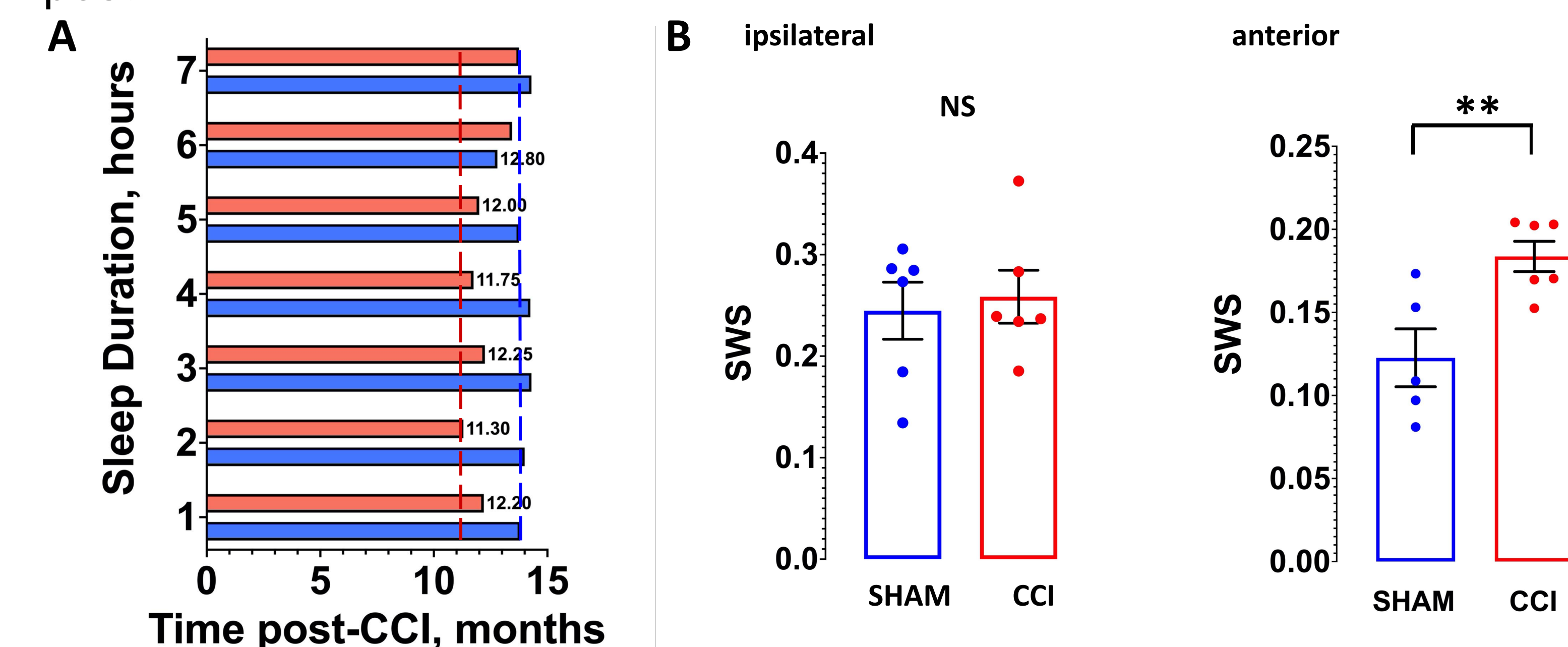


Figure 5. Sleep disruptions observed in CCI-injured animals up to 7 months post TBI. A) Duration of sleep was significantly decreased in CCI animals up to 5 month post-CCI. B) Percentage of Slow Wave Sleep (SWS) automatically calculated with Polyman software as percentage of delta oscillation (0.5 - 4 Hz) shows a significant increase in the amount of SWS detected on anterior contralateral screw only (up to 6 months post-CCI).

CONCLUSION

1. CCI-injured animals had a significant decrease in duration of sleep compared to SHAM animals at 6 weeks and up to 4 months following TBI.
2. CCI-injured animals had a significant increase in Slow Wave Sleep (SWS) calculated as a percentage of delta oscillation (0.5 - 4 Hz) at 6 weeks post-CCI and up to 4 months following TBI.

ACKNOWLEDGEMENTS

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Note: Data used for this project has not yet been published.