Automated Assessment of Post-Fracture Pain in Mice Using Novel Imaging and Machine Learning Tools

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Purpose: Bone fractures are one of the most common orthopaedic injuries, yet there is a paucity of research analyzing post-fracture pain. We sought to develop and validate a sensitive and unbiased methodology to measure pain following fracture in rodent models. Our work uses a novel technology, the BlackBox System, coupled with machine learning algorithms to monitor alterations in quantifiable behavioral end points of pain after bone fracture. This technology allows for the collection of continuous data streams and automatically analyzes them to assess musculoskeletal pain behaviors rapidly and objectively in a natural setting.

Methods: We performed tibia fractures in mice and longitudinally assessed pain-related behaviors and gait patterns at 4, 11, 18, and 25 days post-fracture. The BlackBox was used to perform high spatial and temporal recording of pain behaviors in freely moving mice, which captures animal pose (body position) and paw weightbearing (paw pressure). We then developed Paw Analysis Workflow (PAW), a machine learning-enabled software, which we then used to track mice and analyze changes in paw pressure and kinematic phenotypes.

Results: We observe a significant decrease in weightbearing on the fractured limb compared to the contralateral, non-fractured hindlimb when compared to unfractured mice at day 4 that resolves by day 18. Secondly, we observe guarding (raised, folded paw) of the hind paw of the fractured limb with peaks at days 4 and 11 in fractured mice, a well-characterized pain behavior in rodents. Next, we probed how pain-related posture changes translate to changes in walking gait patterns. To compensate for diminished weightbearing on the injured hindlimb, fractured mice will often hop with their uninjured hindlimb.

Conclusion: Our data demonstrate how coupling the BlackBox system with powerful, high-throughput machine learning tools (PAW) greatly enhances our ability to detect pain behaviors in mice after fracture. This allows for a more comprehensive analysis with greater sensitivity in quantifying induced and chronic pain-related behaviors than currently available methods (i.e., von Frey fibers, CatWalk/DigiGait, etc.). The BlackBox will ultimately enable us to assess the efficacy of non-opioid alternatives and therapeutics for post-fracture pain.