Cannabidiol Aerosol Modulates Blast-Induced Cochlear Dysfunction and Auditory Pathway Injury in Rats

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Introduction

Blast-induced traumatic brain injury (bTBI) is a major cause of chronic neurological and sensory deficits, anxiety, motor dysfunction, and auditory pathway injury, particularly in military and civilian populations exposed to explosions. Effective therapeutic strategies remain limited. Cannabidiol (CBD), a non-psychoactive phytocannabinoid, has shown anti-inflammatory, antioxidant, neuroprotective, and anxiolytic effects in preclinical brain injury models, but its protective potential across both auditory and behavioral domains following blast exposure remains underexplored.

Objective

To characterize cochlear/auditory pathway function (DPOAE, ABR) and anxiety-like behavior and motor coordination (Elevated Plus Maze-EPM, Open Field Test-OFT, Grid Walking) in a rat model of blast-induced TBI, and to evaluate CBD aerosol as a candidate otoprotective and behavior-modulating intervention.

Methods

Subjects: Male Sprague-Dawley rats (n = 4/group) — Control, CBD, Blast, CBD+Blast

Blast Injury Model: Standardized shock-wave exposure under anesthesia (IACUC #202200036)

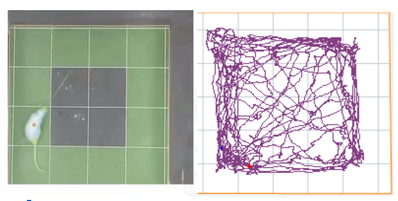
CBD Administration: 100 mg/mL (PG/VG vehicle) via aerosol inhalation, 8 hr/day for 7 post-injury days

Auditory Assessments: DPOAE (4–60 kHz) and ABR (4–32 kHz) recorded pre- and post-injury, Tucker-Davis Technologies system

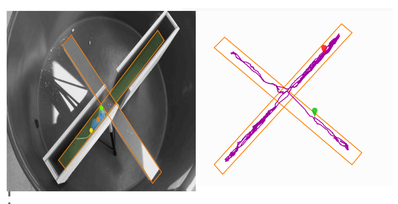
Behavioral Assessments: EPM, OFT, Grid Walking Task at Pre-injury, Post-7, Post-21, Post-45 using ANY-maze (v7.53, Stoelting Co.)

Tissue Collection: Cochlear/brain tissue + blood harvested under deep anesthesia, preserved in 4% PFA for future histopathology/molecular analyses

1a



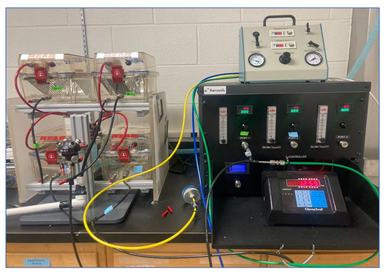
1b



1c

Figure 1a: *Open Field Test ;* ***1b****. Elevated Plus Maze ; and* ***1c****. Grid Walking*

2a



2b

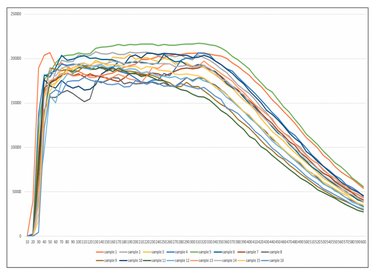


Figure 2a: CBD Exposure setup

Figure 2b : TPI 3007Sampling interval is 1 sec 2.5L/min

Distribution Statement: Approved for public release; distribution is unlimited.

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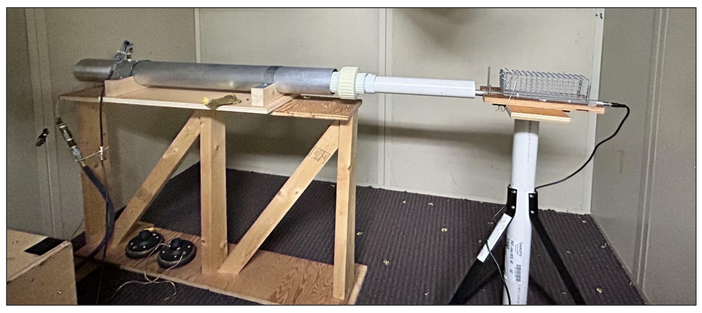
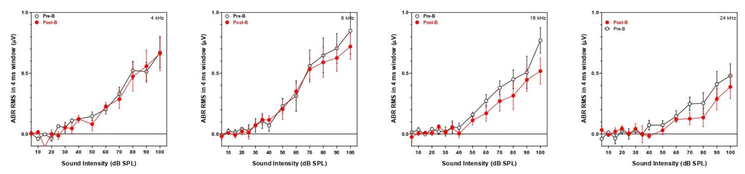


Figure 3 : Schematic of positioning the blast tube, animal, and probe tip during animal blast wave exposures.

Results

Auditory Outcomes.

- DPOAE (4–60 kHz): post-blast amplitudes dropped to noise floor at 8–16 kHz despite strong pre-blast baselines → widespread OHC dysfunction (Figure 5)
- ABR (4–32 kHz): reductions concentrated at 16–24 kHz; relative preservation at 4–8 kHz (Figure 4)
- DPOAE–ABR dissociation at lower frequencies → OHC loss as dominant acute peripheral mechanism, partial auditory nerve sparing
- CBD-only animals: maintained/slightly increased DPOAE amplitudes → no cochlear toxicity from CBD aerosol
- CBD+Blast animals: no DPOAE recovery vs. Blast-only → acute CBD did not restore OHC function at this dose/timepoint



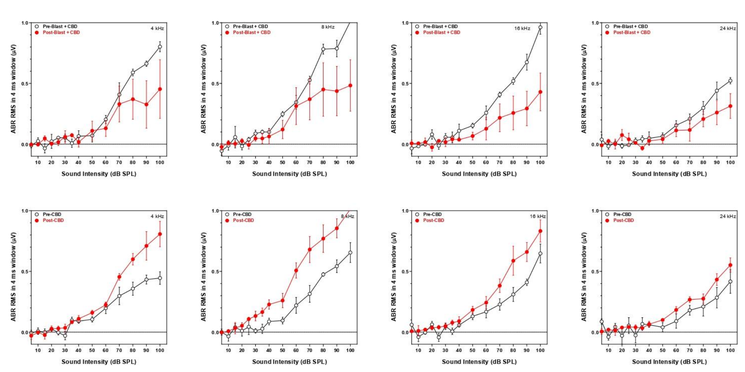


Figure 4 : ABR RMS amplitude vs. sound intensity at 4, 8, 16, and 24 kHz, pre- vs. post-recording, across all three exposure conditions (Blast, Blast+CBD, CBD).

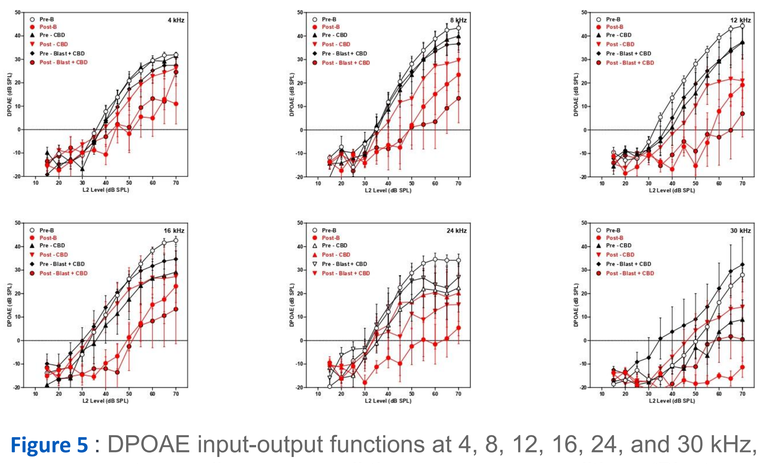
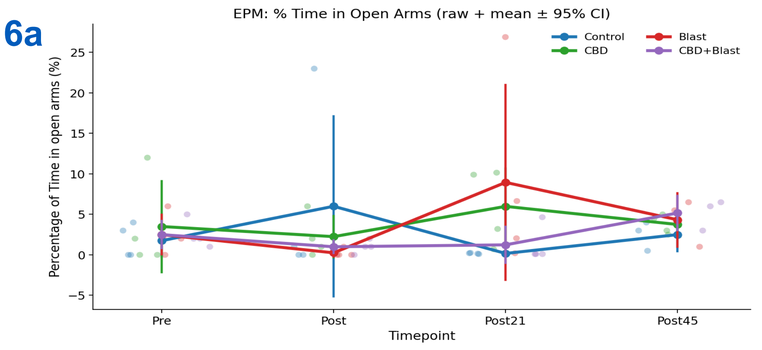


Figure 5 : DPOAE input-output functions at 4, 8, 12, 16, 24, and 30 kHz, pre- vs. post-recording, across all three exposure conditions (Blast, CBD, Blast+CBD)

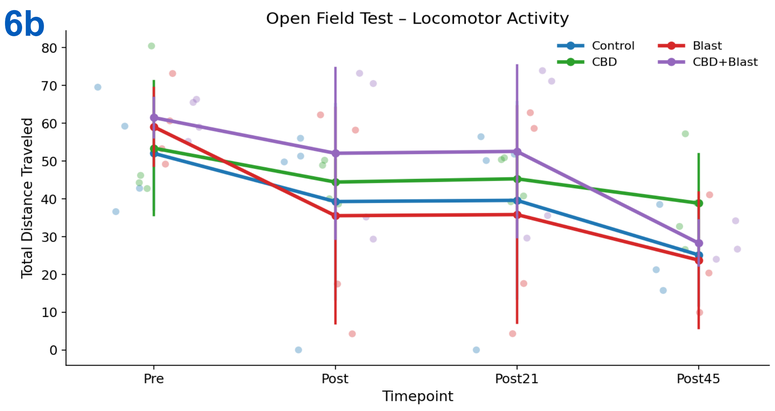
Behavioral Outcomes

- EPM: all groups low open-arm occupancy overall; Blast-only transiently elevated at Post-21 (~9%) vs. CBD+Blast (~0%); CBD+Blast suppressed at Post-21 (β=−18.03, p=.017) (Figure 6a)
- OFT: total distance declined across all groups over time; CBD+Blast highest output at all post-injury timepoints; Blast-only steepest decline, lowest at Post-45 (Figure 6b)
- GWT — *primary result*: Blast-only elevated foot slips at Post (median ~4.5/m, ~4× pre-injury); CBD+Blast lower at Post (median ~2.5/m); both trend to baseline by Post-45; GEE: blast effect β=+3.69, p=.008; CBD×Time Post-21 β=+3.47, p=.032, Post-45 β=+2.55, p=.011 (Figure 6c)

6a



6b



6c

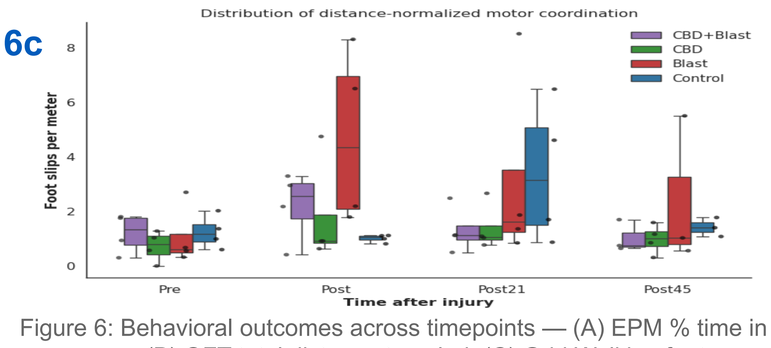


Figure 6: Behavioral outcomes across timepoints — (A) EPM % time in open arms, (B) OFT total distance traveled, (C) Grid Walking foot slips/meter

Inferences

- Blast exposure produced a frequency-specific cochlear injury profile (OHC-dominant, partial nerve sparing) alongside selective, time-dependent behavioral effects most robust on sensorimotor coordination and locomotor preservation, more modest on anxiety regulation.
- CBD aerosol was cochlear-safe but did not acutely restore auditory function; behaviorally, CBD narrowed the injured-vs-uninjured performance gap during the subacute window, positioning it as recovery-facilitating rather than a neuroprotective cure or otoprotective agent at this dose/timepoint.

Conclusion

- Inhaled CBD aerosol selectively modulated blast-induced anxiety dysregulation and motor coordination deficits most pronounced subacutely, while cochlear/auditory pathway dysfunction persisted despite CBD's safety profile.
- This dissociation suggests CBD's neuromodulatory benefits are behavioral/central rather than peripheral/cochlear at this dose. Archived tissue will support future histopathological and neuroinflammatory analysis to guide dose optimization..

References

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2. Aravind, A., Ravula, A. R., Chandra, N., & Pfister, B. J. (2020). Behavioral deficits in animal models of blast traumatic brain injury. Frontiers in Neurology, 11. https://doi.org/10.3389/fneur.2020.00990

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