VivaZome Proprietary Human Cell-Derived Extracellular Vesicles Enhance Recovery After Moderate Traumatic Brain Injury in a Preclinical Model

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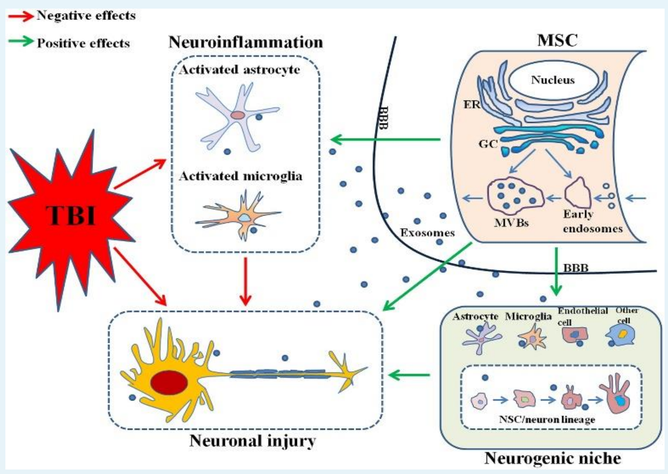
Introduction

Inflammatory mechanisms play a crucial role in the outcome of **traumatic brain injury (TBI). Extracellular vesicles (EVs)** derived from **mesenchymal stem cells (MSCs)** have been shown to modulate the inflammatory response and improve functional recovery in preclinical TBI models. **VivaZome's proprietary cells (VZT-PCs)** share key characteristics of MSCs including **cell surface markers**, **immunomodulatory properties** and **differentiation potential** (Figure 1). **VZT-PC-conditioned medium** accelerates **wound healing**, reduces **inflammation** and increases **angiogenesis. EVs derived from VZT-PCs** contain **microRNAs** known to modulate **inflammation** and demonstrate **anti-inflammatory activity** in a cell-based assay. Based on their immunomodulatory and regenerative properties, this study evaluated the **therapeutic effect of VZT-PC-derived EVs** in a **preclinical TBI mouse model** using **moderate Controlled Cortical Impact Injury (CCI).**

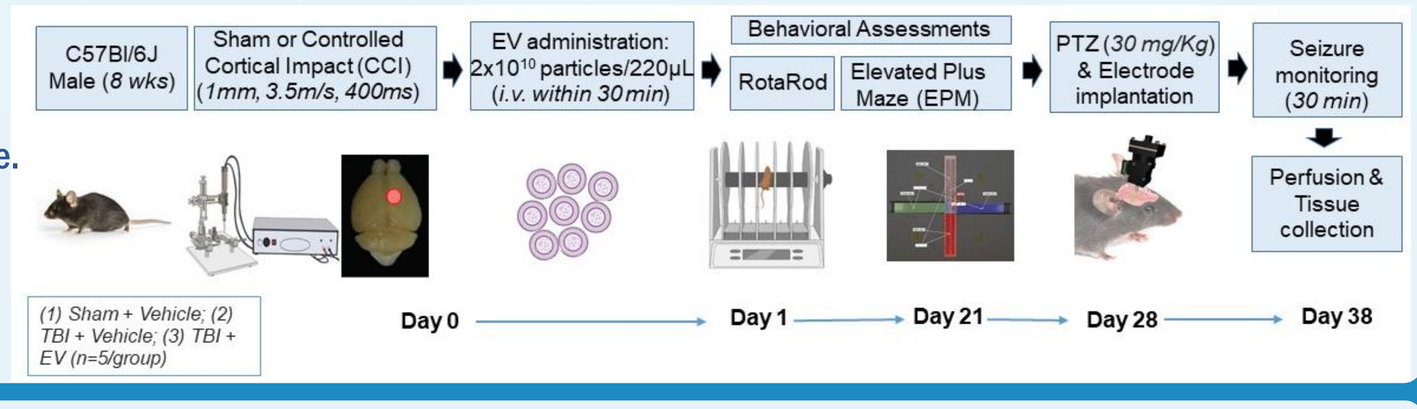
Figure 1: EVs on TBI. Probable mechanisms underlying the effects of MSC-derived EVs.



Methods

Adult C57 mice were subjected to a **moderate CCI** randomly allocated to one of three treatment groups: 1. Sham injury + Vehicle, 2. TBI + Vehicle, 3. TBI + EVs (2.19×10^{10} particles, i.v., post-injury). The Vehicle control was the "In-process control" sample collected during EV purification. Behavioural tests, including the Rotarod test, Elevated Plus Maze (EPM) were performed by investigators blinded to group to assess functional recovery. Electrode implantation was performed, followed by a PTZ-induced seizure test conducted 5 weeks post-CCI (Figure 2). Modified Racine's Scale was used to score seizure severity (ProFusion EEG 5). All statistical analyses were performed using *GraphPad Prism 10.1.2*.

Figure 2: Experimental timeline.

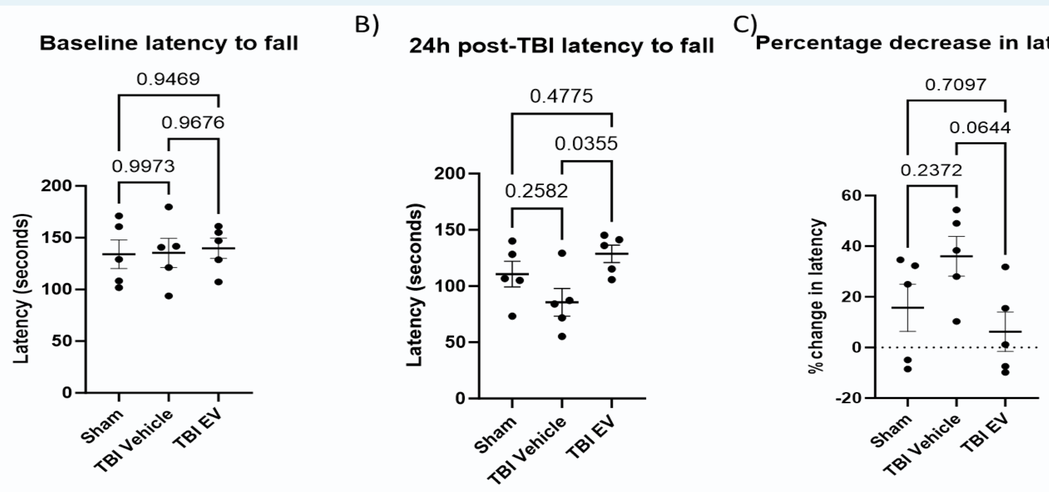


Results

◆ The Rotarod test was conducted 24 hrs post-TBI, consisting of one trial with 3 sessions (15 min inter-session intervals). The Rotarod contraption was set to Ramp mode, with initial and final speeds of 5 rpm and 60 rpm over 180 sec, respectively. Each session was for 180 sec and stopped when the mice would fall. The average latency before the animal falls from the rotating cylinder in 3 trials was calculated.

◆ Fall latency in Rotarod trials was **significantly increased** in VZT-PC-EV-treated TBI mice compared to vehicle-treated TBI mice, indicating that EV treatment effectively improved the recovery of grip strength, balance, and motor coordination after TBI.

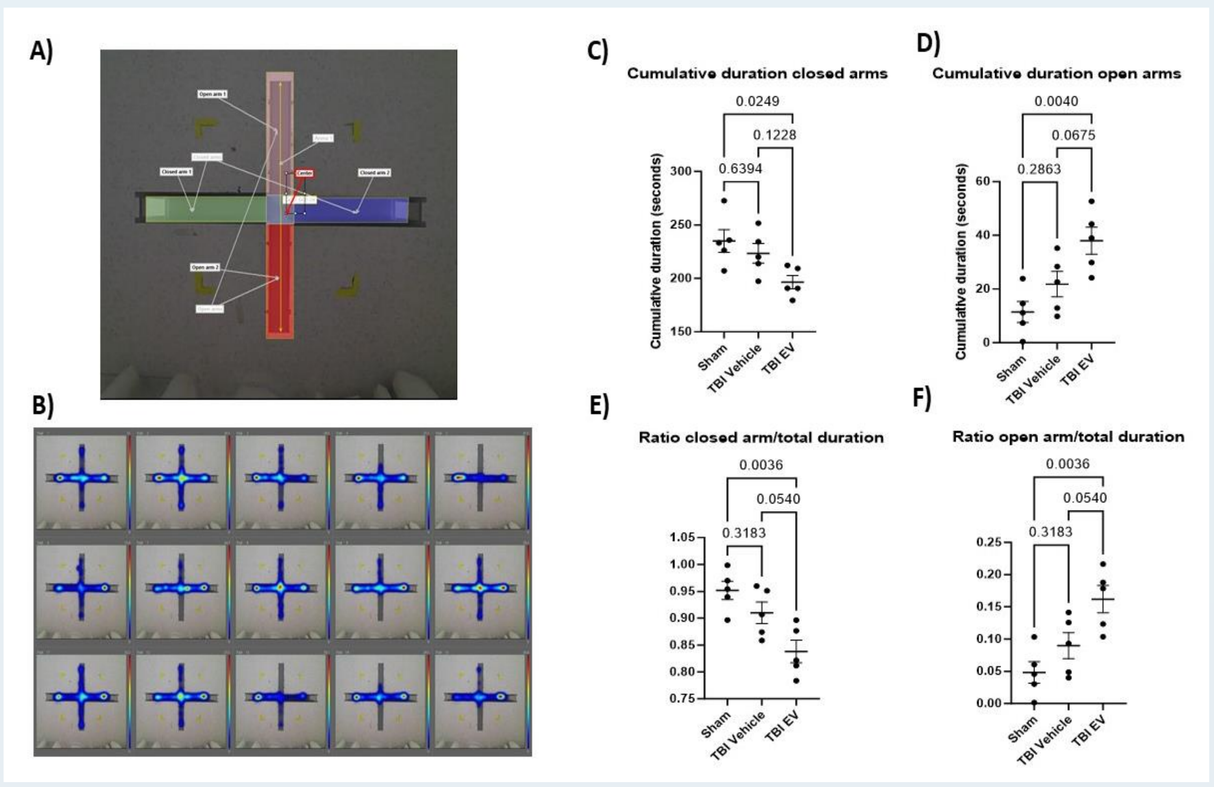
Figure 3: Latency to fall off the Rotarod apparatus comparing Sham (n=5), TBI vehicle (n=5) and TBI EV (n=5) treated mice.



Comparison of latency to fall between vehicle and EV-treated mice was performed using one-way analysis of variance (ANOVA). All values are expressed as mean ± standard error of the mean. The threshold for statistical significance is set at $p \leq 0.05$ for all analyses.

◆ In the elevated plus maze test, EV treatment enhanced exploratory behaviours in TBI mice compared to Vehicle, as evidenced by the increased duration in the open arms.

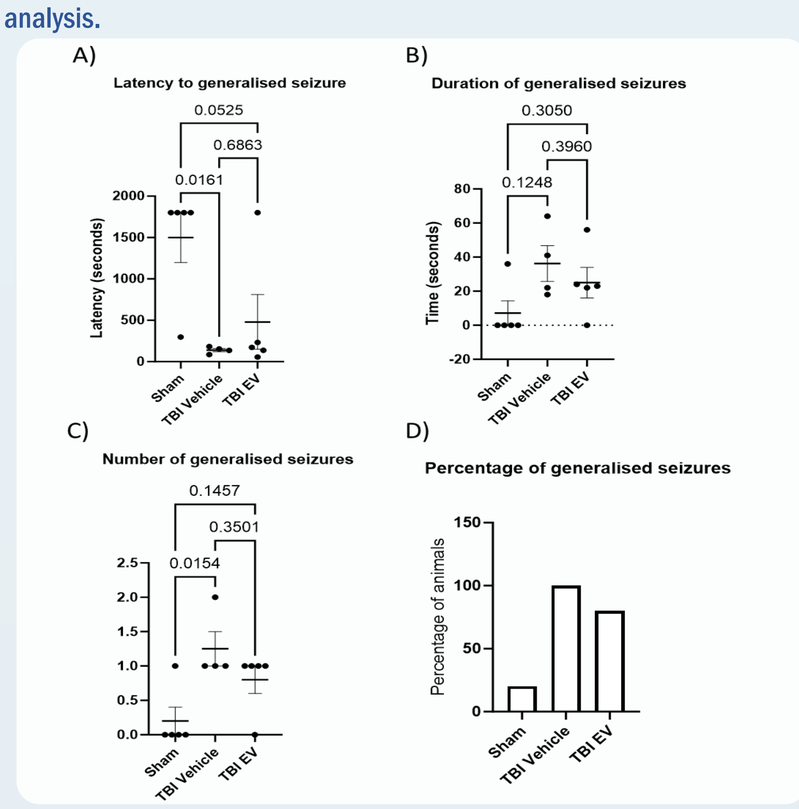
Figure 4: (A) EPM arena indicating different established zones (B) Heat map track visualisation of mice. (C) Cumulative duration in closed arms. (D) Cumulative duration in open arms. (E) Ratio of cumulative duration in closed arms/ total test duration. (F) Ratio of cumulative duration in open arms/ total test duration.



Comparison of each parameter between Vehicle and EV-treated mice was performed using one-way ANOVA. All values are expressed as mean ± standard error of the mean. The threshold for statistical significance is set at $p \leq 0.05$ for all analyses.

◆ A trend was observed where EV treated mice had a lower number of generalised seizures along with a higher latency to generalised seizure than vehicle treated mice.

Figure 5: PTZ induced seizure susceptibility data for measuring (A) Latency to generalised seizure. (B) Duration of generalised seizure. (C) Number of generalised seizure. (D) Percentage of generalised seizures. Duration of analysis was 30 mins and ProFusion EEG 5 platform was used for data analysis.



Comparison of each parameter between Vehicle and EV-treated mice was performed using one-way ANOVA. All values are expressed as mean ± standard error of the mean. The threshold for statistical significance is set at $p \leq 0.05$ for all analyses.

Conclusion

VZT-PC-derived EVs improved motor function, enhanced exploratory behavior and promoted balance 24 hours post moderate TBI . Furthermore, VZT-PC-derived EVs may reduce seizure susceptibility post-TBI.

These findings, along with the accessibility and high proliferative potential of VZT-PCs, position them as a promising source of EVs for treating TBI.

Acknowledgements

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