Genetic inactivation of SARM1 axon degeneration pathway improves outcome trajectory after experimental traumatic brain injury based on pathological, radiological, and functional measures

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• Always consult the original research paper as the true reference source for the text.

Contact Information:

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All queries, feedback or suggestions are also very welcome.

Research Paper Sections:

The sections of the research paper input text parsed in this audit.

Section No.	Headings	Sentences
Section: 1	ABSTRACT	12
Section: 2	INTRODUCTION	15
N/A	--- --- --- --- --- --- ---	0
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Title	Genetic inactivation of SARM1 axon degeneration pathway improves outcome trajectory after experimental traumatic brain injury based on pathological, radiological, and functional measures

S1 [001] ABSTRACT

S1 [002] Traumatic brain injury (TBI) causes chronic symptoms and increased risk of neurodegeneration.

> Traumatic brain injury ...
>
> ... (TBI) ...
>
> ... causes chronic symptoms ...
>
> ... and increased risk ...
>
> ... of neurodegeneration.

S1 [003] Axons in white matter tracts, such as the corpus callosum (CC), are critical components of neural circuits and particularly vulnerable to TBI. Treatments are needed to protect axons from traumatic injury and mitigate post-traumatic neurodegeneration.

> Axons ...
>
> ... in white matter tracts, ...
>
> ... such as the corpus callosum ...
>
> ... (CC), ...
>
> ... are critical components ...
>
> ... of neural circuits ...
>
> ... and particularly vulnerable ...
>
> ... to TBI. Treatments are needed ...
>
> ... to protect axons ...
>
> ... from traumatic injury ...
>
> ... and mitigate post-traumatic neurodegeneration.

S1 [004] The Sarm1 gene is a central driver of axon degeneration through a conserved molecular pathway.

> The Sarm1 gene is a central driver ...
>
> ... of axon degeneration ...
>
> ... through a conserved molecular pathway.

S1 [005] Sarm1-/- mice with knockout (KO) of the Sarm1 gene enable genetic proof-of-concept testing of Sarm1 inactivation as a therapeutic target.

> Sarm1-/- mice ...
>
> ... with knockout ...
>
> ... (KO) ...
>
> ... of the Sarm1 gene enable genetic proof-of-concept testing ...
>
> ... of Sarm1 inactivation ...
>
> ... as a therapeutic target.

S1 [006]   We evaluated Sarm1 deletion effects after TBI using a concussive model that causes traumatic axonal injury and progresses to CC atrophy at 10 weeks, indicating post-traumatic neurodegeneration.

> We evaluated Sarm1 deletion effects ...
>
> ... after TBI ...
>
> ... using a concussive model ...
>
> ... that causes traumatic axonal injury ...
>
> ... and progresses ...
>
> ... to CC atrophy ...
>
> ... at 10 weeks, ...
>
> ... indicating post-traumatic neurodegeneration.

S1 [007]   Sarm1 wild-type (WT) mice developed significant CC atrophy that was reduced in Sarm1 KO mice.

> Sarm1 wild-type ...
>
> ... (WT) ...
>
> ... mice developed significant CC atrophy ...
>
> ... that was reduced ...
>
> ... in Sarm1 KO mice.

S1 [008]   Using electron microscopy to quantify individual axons demonstrated that Sarm1 KO preserved more intact axons and reduced damaged or demyelinated axons.

> Using electron microscopy ...
>
> ... to quantify individual axons demonstrated ...
>
> ... that Sarm1 KO preserved more intact axons ...
>
> ... and reduced damaged ...
>
> ... or demyelinated axons.

S1 [009]   MRI in live mice identified significantly reduced CC volume after TBI in Sarm1 WT mice that was attenuated in Sarm1 KO mice.

> MRI ...
>
> ... in live mice identified significantly reduced CC volume ...
>
> ... after TBI ...
>
> ... in Sarm1 WT mice ...
>
> ... that was attenuated ...
>
> ... in Sarm1 KO mice.

S1 [010]   MR diffusion tensor imaging detected reduced fractional anisotropy in both genotypes while axial diffusivity remained higher in Sarm1 KO mice.

> MR diffusion tensor imaging detected reduced fractional anisotropy ...
>
> ... in both genotypes ...
>
> ... while axial diffusivity remained higher ...
>
> ... in Sarm1 KO mice.

S1 [011]   Immunohistochemistry revealed significant attenuation of CC atrophy, myelin loss, and neuroinflammation in Sarm1 KO mice after TBI. Functionally, TBI resulted in late-stage motor learning and sleep deficits that were ameliorated in Sarm1 KO mice.

Immunohistochemistry revealed significant attenuation ...

... of CC atrophy, ...

... myelin loss, ...

... and neuroinflammation ...

... in Sarm1 KO mice ...

... after TBI. Functionally, ...

... TBI resulted ...

... in late-stage motor learning ...

... and sleep deficits ...

... that were ameliorated ...

... in Sarm1 KO mice.

S1 [012] Based on these findings, Sarm1 inactivation can protect axons and white matter tracts to improve translational outcomes associated with CC atrophy and post-traumatic neurodegeneration.

Based ...

... on these findings, ...

... Sarm1 inactivation can protect axons ...

... and white matter tracts ...

... to improve translational outcomes associated ...

... with CC atrophy ...

... and post-traumatic neurodegeneration.

S2 [013] INTRODUCTION

S2 [014] Traumatic brain injury (TBI) results in long term disability in more severe cases and can cause persistent symptoms even in patients who receive a "mild" diagnosis [41, 64, 69].

Traumatic brain injury ...

... (TBI) ...

... results ...

... in long term disability ...

... in more severe cases ...

... and can cause persistent symptoms even in patients ...

... who receive a "mild" ...

... diagnosis ...

... [41, ...

... 64, ...

... 69].

S2 [015] TBI may also lead to post-traumatic neurodegeneration and increase the risk for co-morbid neurodegenerative diseases, such as Alzheimer's disease [15, 18, 30, 70].

TBI may also lead ...

... to post-traumatic neurodegeneration ...

... and increase the risk ...

... for co-morbid neurodegenerative diseases, ...

... such as Alzheimer's disease ...

... [15, 18, ...

... 30, ...

... 70].

S2 [016]   In patients with moderate-severe TBI, diffuse axonal injury has been shown to predict the extent of post-traumatic neurodegeneration, based on MRI volumetric and diffusion tensor imaging (DTI) data [29].

> In patients ...
>
> ... with moderate-severe TBI, ...
>
> ... diffuse axonal injury has been shown ...
>
> ... to predict the extent ...
>
> ... of post-traumatic neurodegeneration, ...
>
> ... based ...
>
> ... on MRI volumetric ...
>
> ... and diffusion tensor imaging ...
>
> ... (DTI) ...
>
> ... data ...
>
> ... [29].

S2 [017]   The strongest relationship was found in central WM tracts, including the corpus callosum (CC).

> The strongest relationship was found ...
>
> ... in central WM tracts, ...
>
> ... including the corpus callosum ...
>
> ... (CC).

S2 [018]   The CC is one of the main structures exhibiting atrophy across patients with complicated mild to severe TBI [15, 30].

> The CC is one ...
>
> ... of the main structures exhibiting atrophy ...
>
> ... across patients ...
>
> ... with complicated mild ...
>
> ... to severe TBI ...
>
> ... [15, 30]...
>
> ... .

S2 [019]   Furthermore, DTI tractography demonstrated disrupted fiber tract continuity in anterior CC regions after concussions while broad areas of disrupted tracts were found throughout the CC in patients with MRI findings of diffuse axonal injury [37].

> Furthermore, ...
>
> ... DTI tractography demonstrated disrupted fiber tract continuity ...
>
> ... in anterior CC regions ...
>
> ... after concussions ...
>
> ... while broad areas ...
>
> ... of disrupted tracts were found ...
>
> ... throughout the CC ...
>
> ... in patients ...
>
> ... with MRI findings ...
>
> ... of diffuse axonal injury ...
>
> ... [37].

End of Sample Audit