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In Situ Cell Signalling of the Hippo-YAP/TAZ Pathway in Reaction to Complex Dynamic Loading in an Intervertebral Disc

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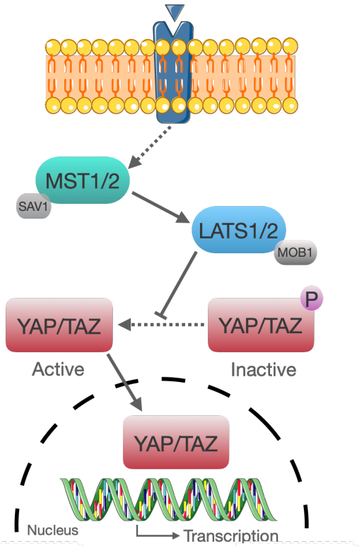
Introduction

- The Hippo-YAP/TAZ pathway is an evolutionarily conserved signalling cascade regulating numerous biological processes, including cell proliferation, differentiation, survival and mobility as well as organ size and regeneration.
- Recently, the Hippo-YAP/TAZ pathway has been correlated with intervertebral disc (IVD) degeneration.

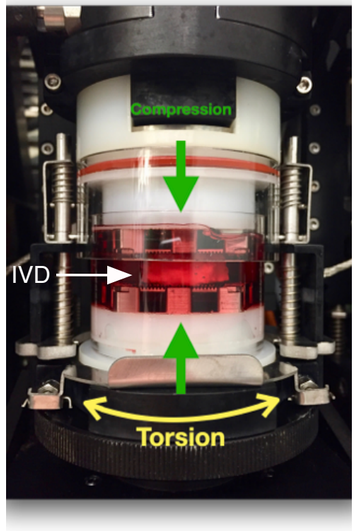
Aim

The aim of this study was to investigate the influence of i) static and ii) complex dynamic loading, more specifically of combined compression and torsion, on the intervertebral disc and on the Hippo-YAP/TAZ pathway using a bovine organ explant culture model.

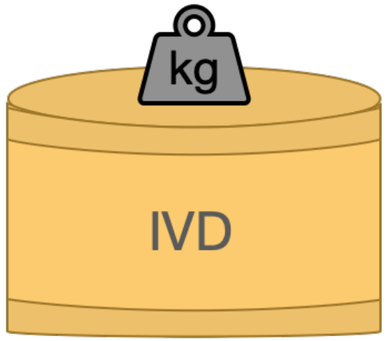
Hippo Pathway



Bioreactor



Static loading



Pressure: 0.1 MPa
Torsion: 0°

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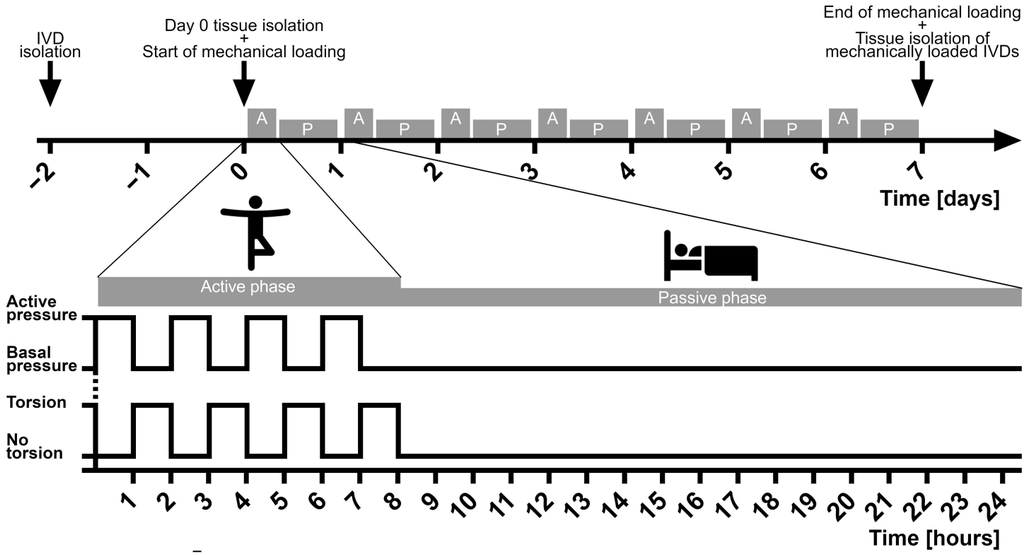
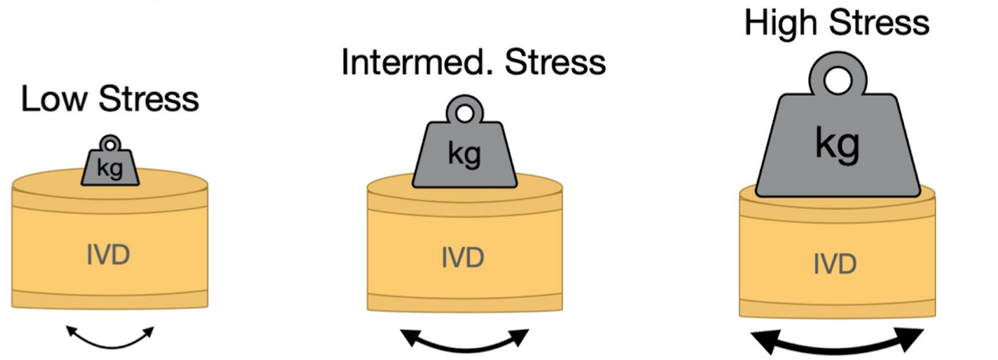
Complex dynamic loading



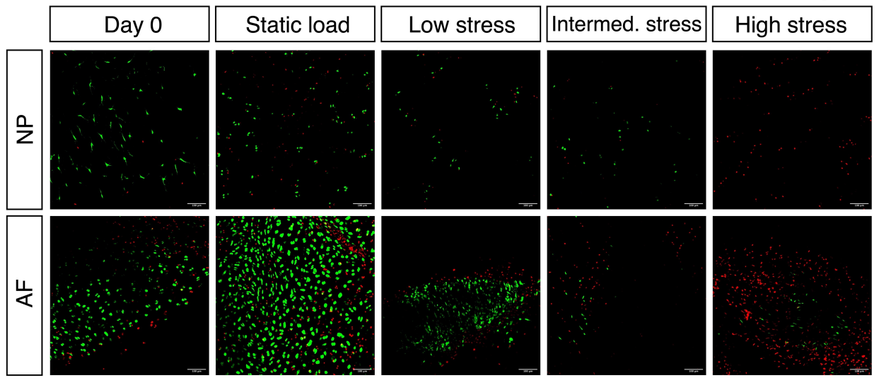


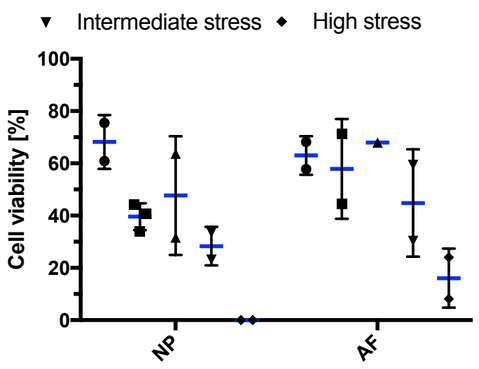
Basal Pressure: 0.1 MPa
Active Pressure: **0.2 MPa**
Torsion: **2°**

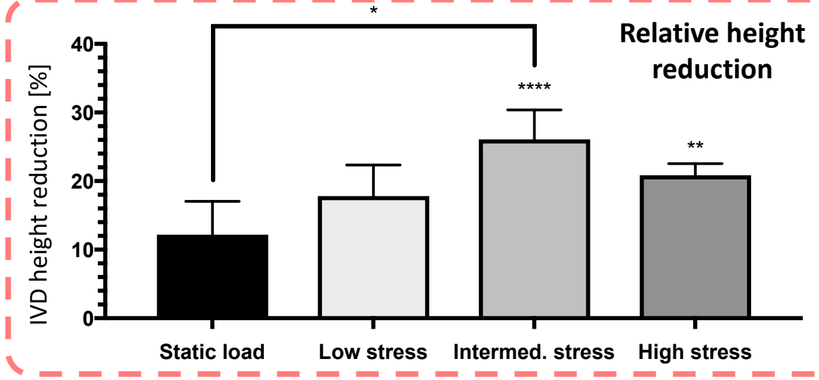
Basal Pressure: 0.1 MPa
Active Pressure: **0.4 MPa**
Torsion: **8°**

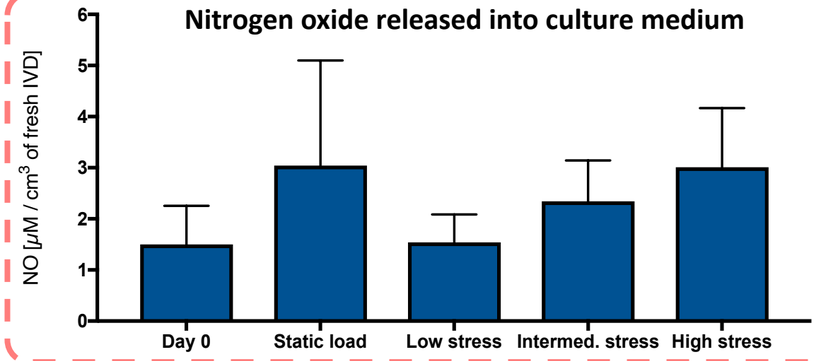
Basal Pressure: 0.1 MPa
Active Pressure: **0.6 MPa**
Torsion: **15°**

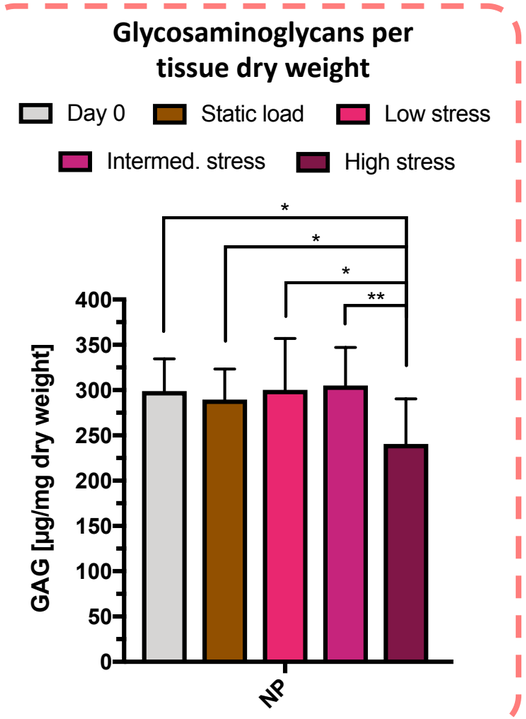
Cell viability











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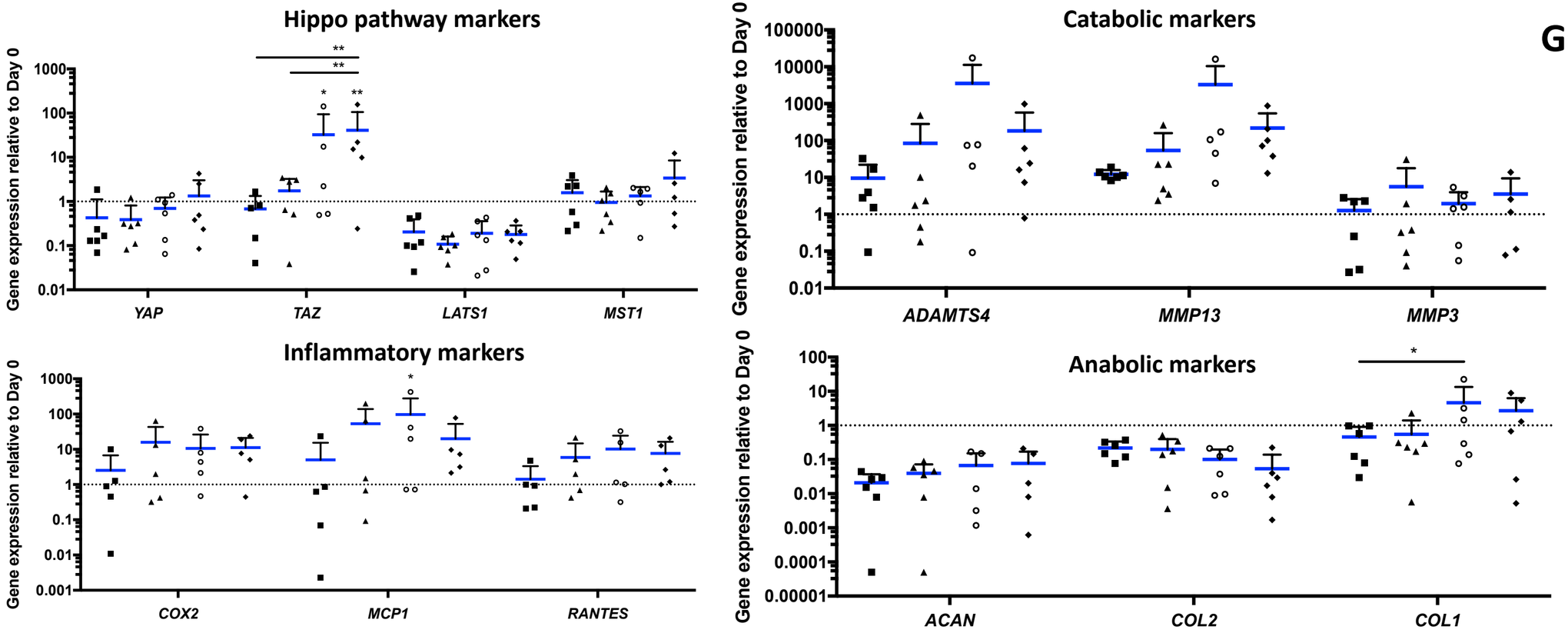
NP: Nucleus Pulposus
AF: Annulus Fibrosus

Gene expression



Conclusion

- Intense complex dynamic loading overloads the intervertebral disc and leads to key features of intervertebral disc degeneration.
- Overloaded intervertebral discs react to complex loading by unsuccessfully trying to activate endogenous repair mechanisms by upregulating *TAZ*.

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