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Spinal Cord Transcriptomic and Metabolomic Analysis after Excitotoxic Injection Injury Model of Syringomyelia

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Purpose

Syringomyelia is a condition of the spinal cord in which a syrinx, a fluid-filled cavity, forms from trauma, malformation, or general disorder. A better understanding of the underlying molecular pathways associated with syrinx formation will unveil targets for treatments and possibly prevention of syringomyelia in the future.

Methods

In this study, we performed an established surgical induction of a syrinx using quisqualic acid (QA) and kaolin injections in rats to characterize the injury at the molecular level by RNA sequencing and metabolomics techniques at three and six weeks post-injury.

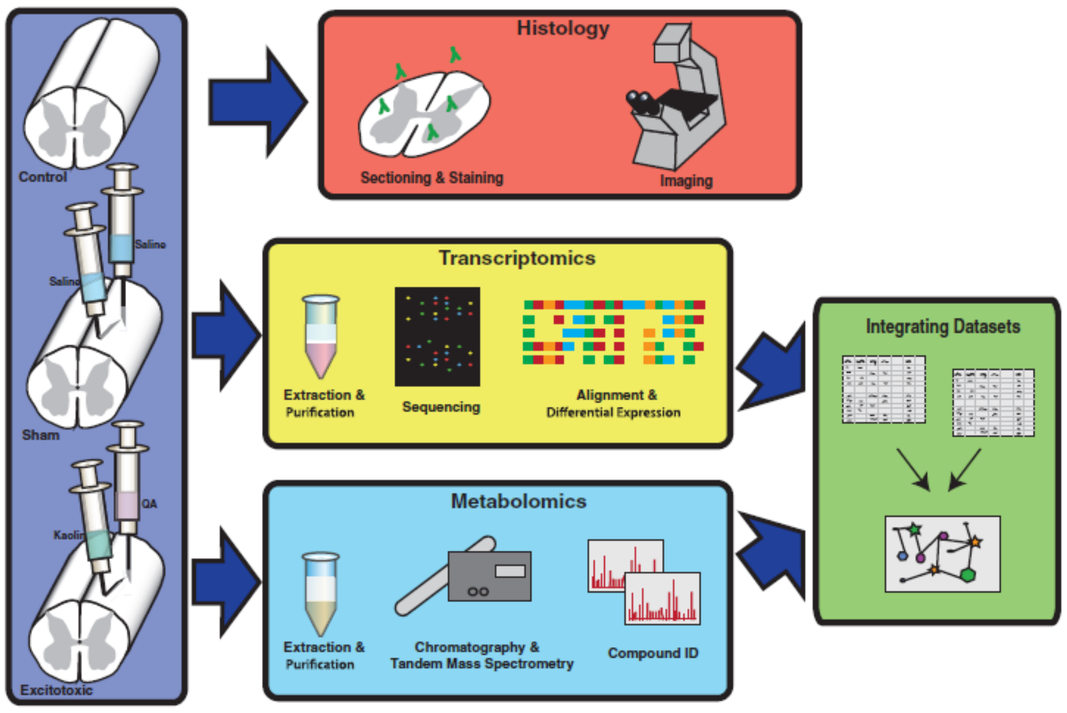
Results

Syrinxes were successfully initiated and studied at three and six weeks using surgical induction via QA and kaolin, but some cavitation was seen in saline injected SHAM animals that complicates confirmation of our interpretations. Significantly dysregulated transcript levels showed a marked immune response and a decreased population of neurons leading to transmission loss. Of note, the broad view of sequenced transcript levels and identified metabolites allowed the pinpointing of several key species including the transporters BGT-1, KCC4, and AQP1 along with highly upregulated metabolites betaine and taurine. These channels and solutes are suspected to be important in the preferential flow of fluid into the syrinx from surrounding spaces and parenchyma because of their known involvement in osmotic balance and fluid movement.

Conclusions

This study established that syrinxes can be successfully analyzed at the molecular level using an established surgical model for syrinx induction. The project also identified several targets for further study. Additional research will strive to further understand the role these targets play in syrinx formation and growth and identify counteragents which may work to limit syrinx formation and growth. The general applicability of the syrinxes in the rat model to human Chiari and trauma related syrinxes also needs to be established.

Three experimental groups were analyzed: healthy control (CTL) animals; animals receiving sham surgical treatment (SHAM) where both injections were saline; and the excitotoxic injury (EXC) group that included animals receiving surgical treatment and injections of kaolin and quisqualic acid (QA). Some of the samples were chemically fixed for histology and imaging, while in the opposing set, small molecules were isolated from tissue for transcriptomics or metabolomics.



Week six immunostaining of spinal cord sections in excitotoxic injury animals. Stars indicate syrinx.