

Vacuum Erectile Device Treatment for Erectile Dysfunction after Cavernous Nerve Injury: Role of Long-term Label-retaining Cells

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Introduction

Vacuum Erectile Device (VED) therapy is a common method used in penile rehabilitation (PR) for improving spontaneous erectile function and penile size after radical prostatectomy.¹ While VED is used in the clinical setting for these indications, the mechanism by which this occurs is not fully understood.

Mesenchymal stem cells (MSCs) are non-hematopoietic, multipotent stem cells with the capacity to differentiate into mesodermal cell lineages.

Label-retaining cells (LRCs) replicate more infrequently as evidenced by retention of 5-bromo-2-deoxyuridine (BrdU) labeling.² These cells are hypothesized to be adult stem and progenitor cells. 5-ethynyl-2'-deoxyuridine (EdU) is an alternative to BrdU and has been shown to be superior in tracking MSCs.³ Studies have reported that EdU can also be used to track LRC.^{4,5}

Hypothesis

We hypothesize that VED improves erectile function by increasing long-term label-retaining cells in the penile tissues.

Materials and Methods

A cavernous nerve injury model was employed using bilateral cavernous nerve crush (BCNC) on male Sprague Dawley rats. Sham surgery was conducted on control rats. The study includes two experiments:

- Experiment 1: **Six-week-old rats**⁴ were injected intraperitoneally (IP) with 5-ethynyl-2'-deoxyuridine (EdU) (50mg/kg) 7 days after surgery to label LRCs. Groups: BCNC group (n=4), VED treatment group (n=6) and sham surgery control group (n=6).
- Experiment 2: **New born rat pups**³ were injected IP with EdU (50mg/kg) to label LRCs. Surgery was performed at 6 weeks of age. Groups: BCNC group (n=5), VED treatment group (n=7) and sham surgery control group (n=7).

Tumescence was induced for 1 minute using the VED for a total of 5 cycles under isoflurane anesthesia. Treatment was administered daily, Monday-Friday for 4 weeks. Sham and BCNC groups received the same anesthesia. Outcome measures:

- Intracavernosal pressure/mean arterial pressure ratio (ICP/MAP) for assessment of erectile function.
- Immunofluorescence of EdU+ cells using Click-iT EdU Cell Proliferation Kit (Thermofisher®) to identify LRCs.

References

1. Wang R. Vacuum Erectile Device for Rehabilitation After Radical Prostatectomy. *J Sex Med.* 2017 Feb;14(2):184-186.
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3. Lin G, et al. Labeling and tracking of mesenchymal stromal cells with EdU. *Cytotherapy.* 2009;11(7):864-73.
4. Lin G, et al. Presence of stem/progenitor cells in the rat penis. *Stem Cells Dev.* 2015 Jan 15;24(2):264-70.
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Results

1. EdU injected at different timepoint before VED treatment

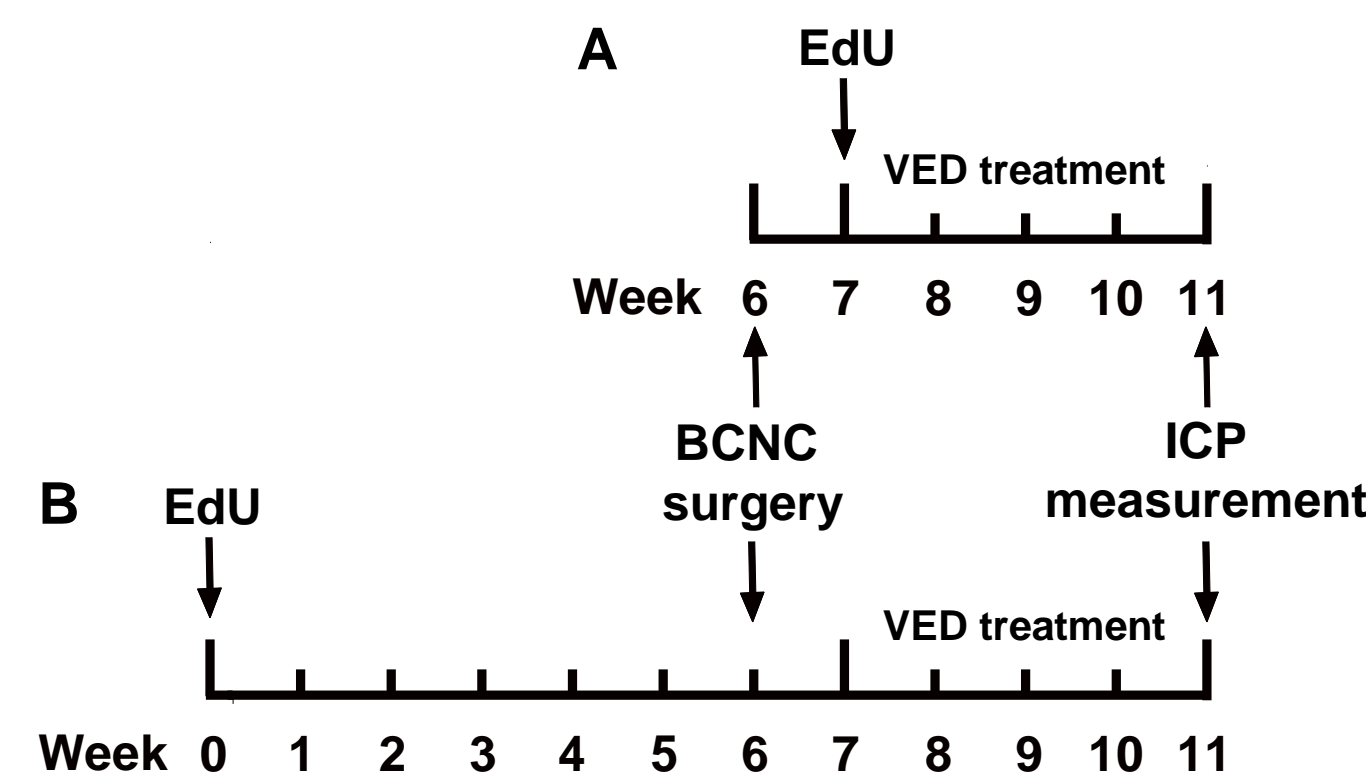


Fig 1. Schematic of two experiments. (A) Experiment 1: EdU was injected at adult stage. (B) Experiment 2: EdU was injected at postnatal stage.

2. Erectile function was impaired by BCNC surgery, and restored after VED treatment

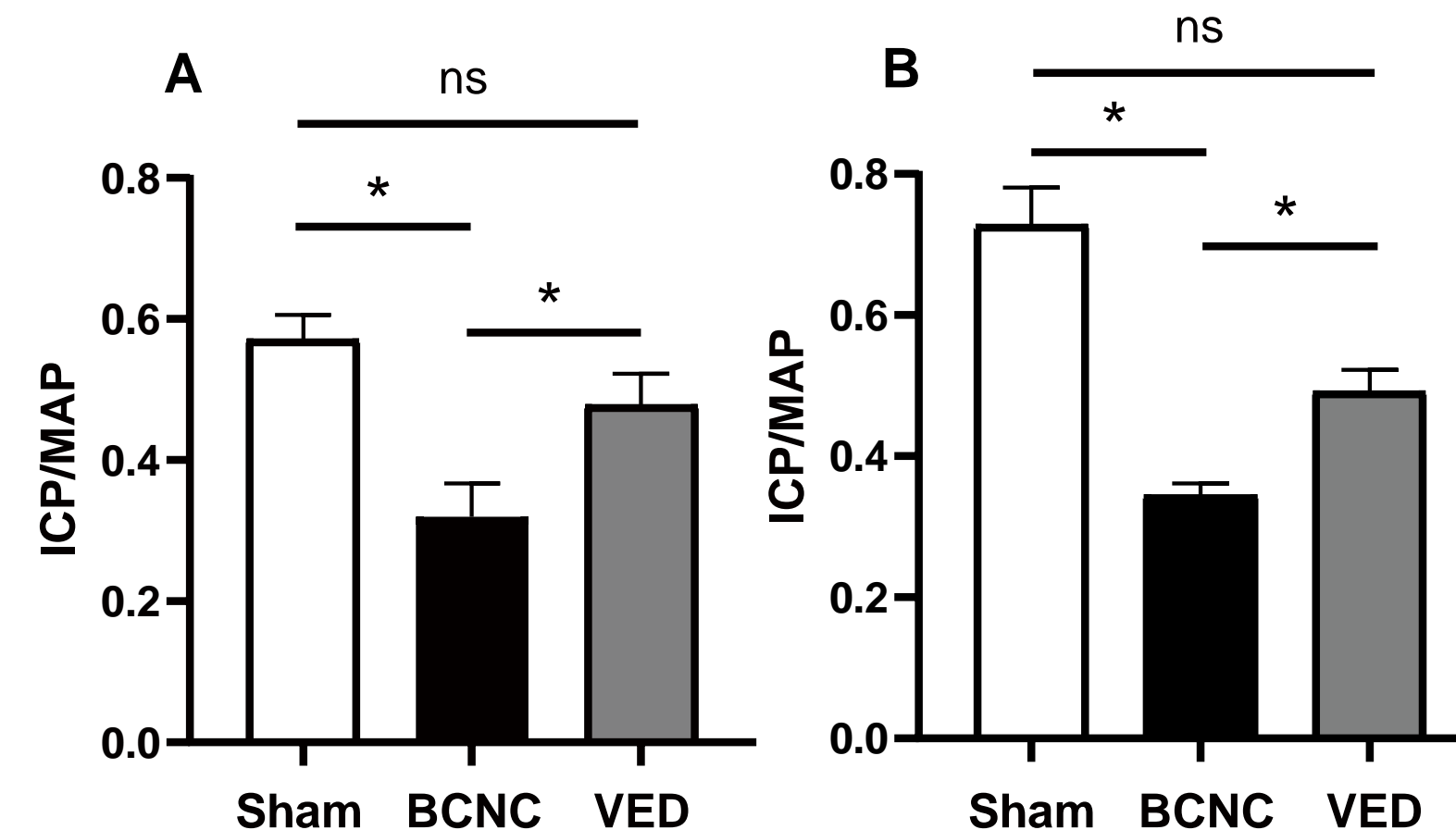


Fig 2. ICP/MAP ratio. (A) Experiment 1. (B) Experiment 2.

3. In experiment 1, LRC increased after BCNC and not changed after VED treatment. In experiment 2, LRC did not change obviously after BCNC nor after VED treatment.

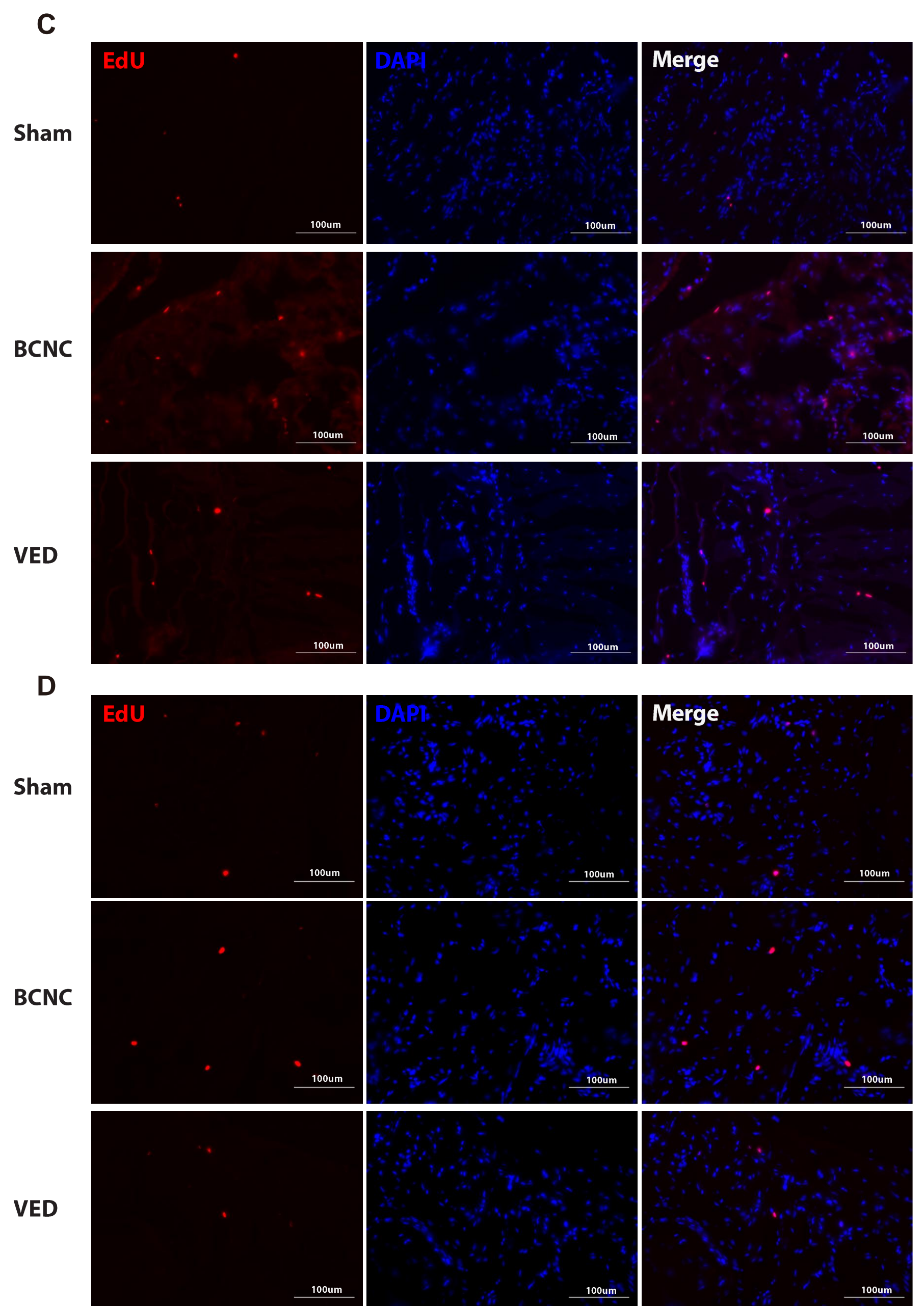
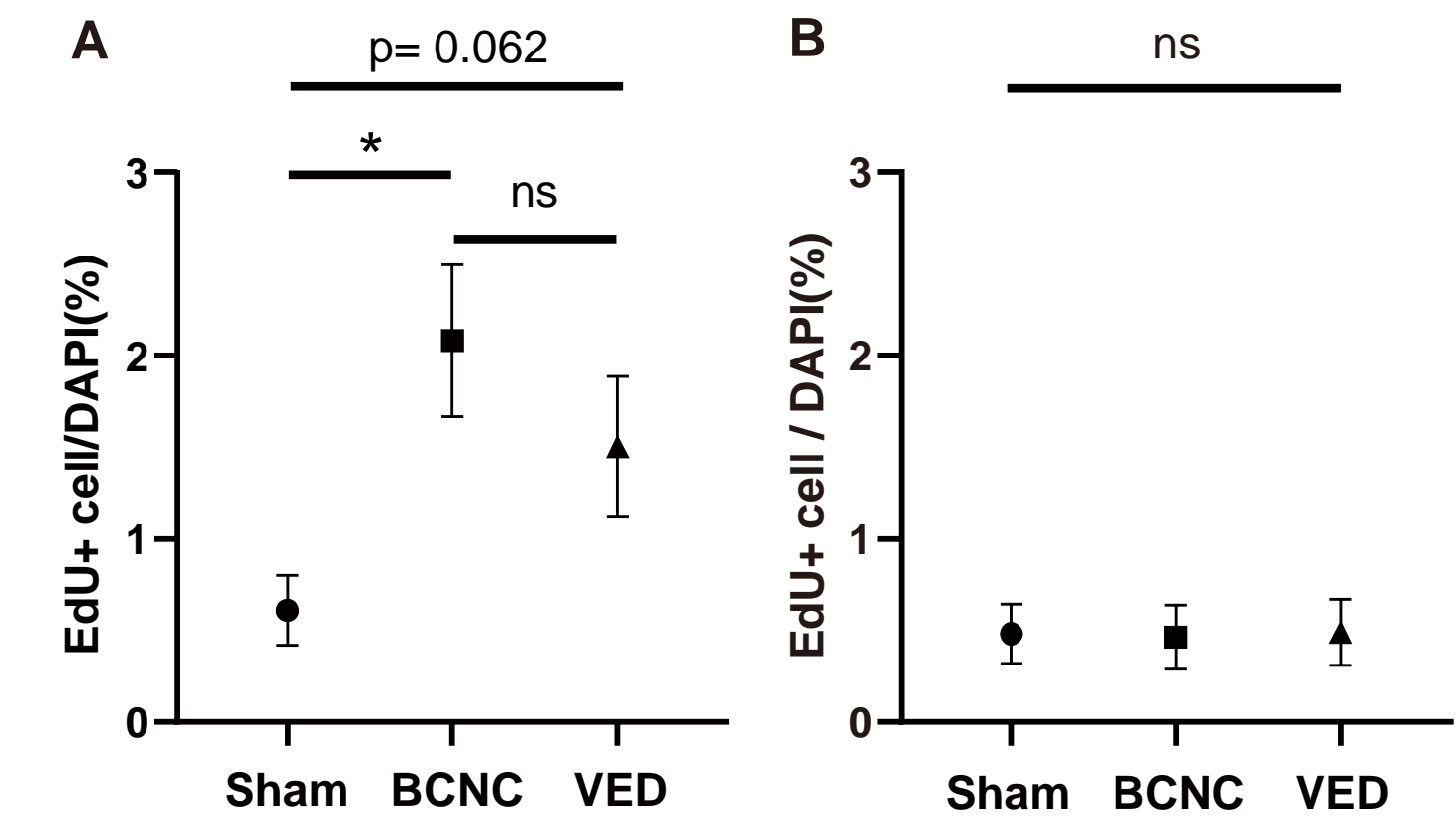


Fig 3. EdU+ cell/total cell ratio and representative images. (A) (C)Experiment 1. (B) (D)Experiment 2.

Conclusions

- VED restored erectile function in BCNC rats.
- LRCs were increased in adult-labeled BCNC rats.
- LRCs may represent different cell lineages depending on time of injection.
- BCNC may induce aggregation of certain cell lineages that are mitigated by VED.
- LRCs may play a limited role in restoring erectile function by VED.