

Effects of perindopril on the swallowing reflex in a rat dysphagia model induced by ligation of bilateral common carotid arteries (BCAO)

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Objective

Dysphagia, as one cause of aspiration pneumonia is still to be a major complication in the patients with such pathological conditions as cerebrovascular disease, Parkinson's disease, aging, and overdose of antipsychotic drugs. To evaluate the effects of the chemicals on dysphagia, we established a rat dysphagia model by ligation of bilateral common carotid arteries (BCAO).

In this study, we investigated the protective effects of perindopril against the dysfunction of the swallowing reflex in the BCAO ligation model rats.

Materials and Methods

● Animal

CrI:CD(SD), ♂, 7w

● Model preparation and evaluation method

Experiment 1

Study on the elicitation of swallowing reflexes in normal rats

Swallowing reflexes were elicited by infusion of water for injection or citric acid and were determined by recording electromyogram (EMG) of mylohyoid muscle in normal rats.

Experiment 2

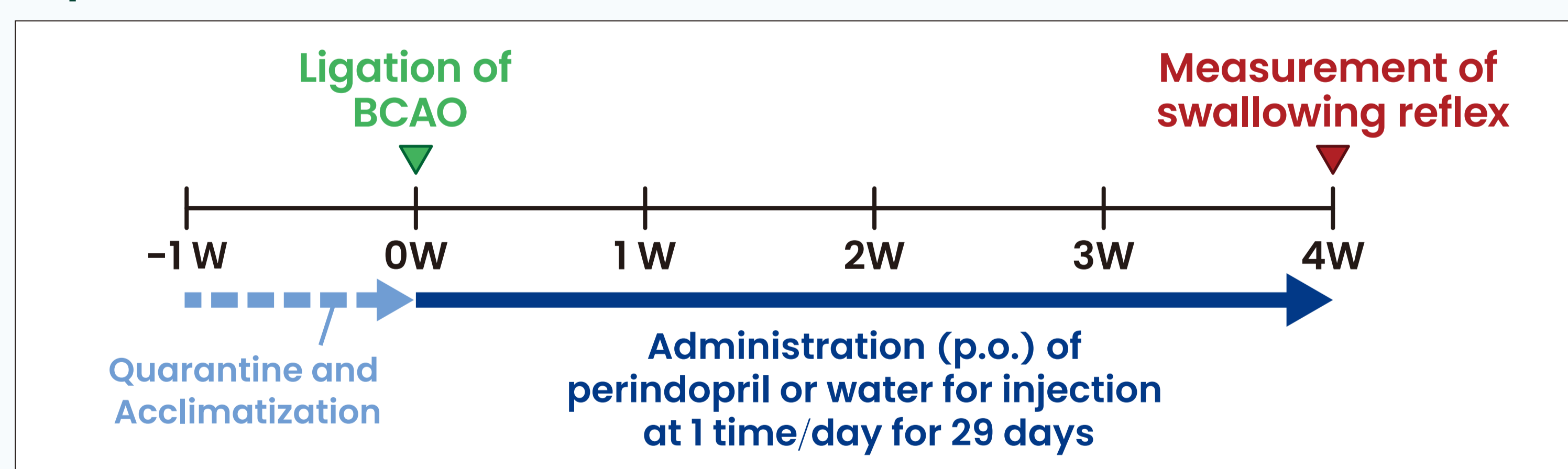
Evaluation of the effects of perindopril in BCAO rats

BCAO rats were prepared by ligation of bilateral common carotid arteries to induce dysphagia under anesthesia with isoflurane inhalation. Perindopril was continuously administered orally for 4 weeks, and the swallowing reflex was determined by recording EMG of mylohyoid muscle at 29 days post-BCAO or sham-operation.

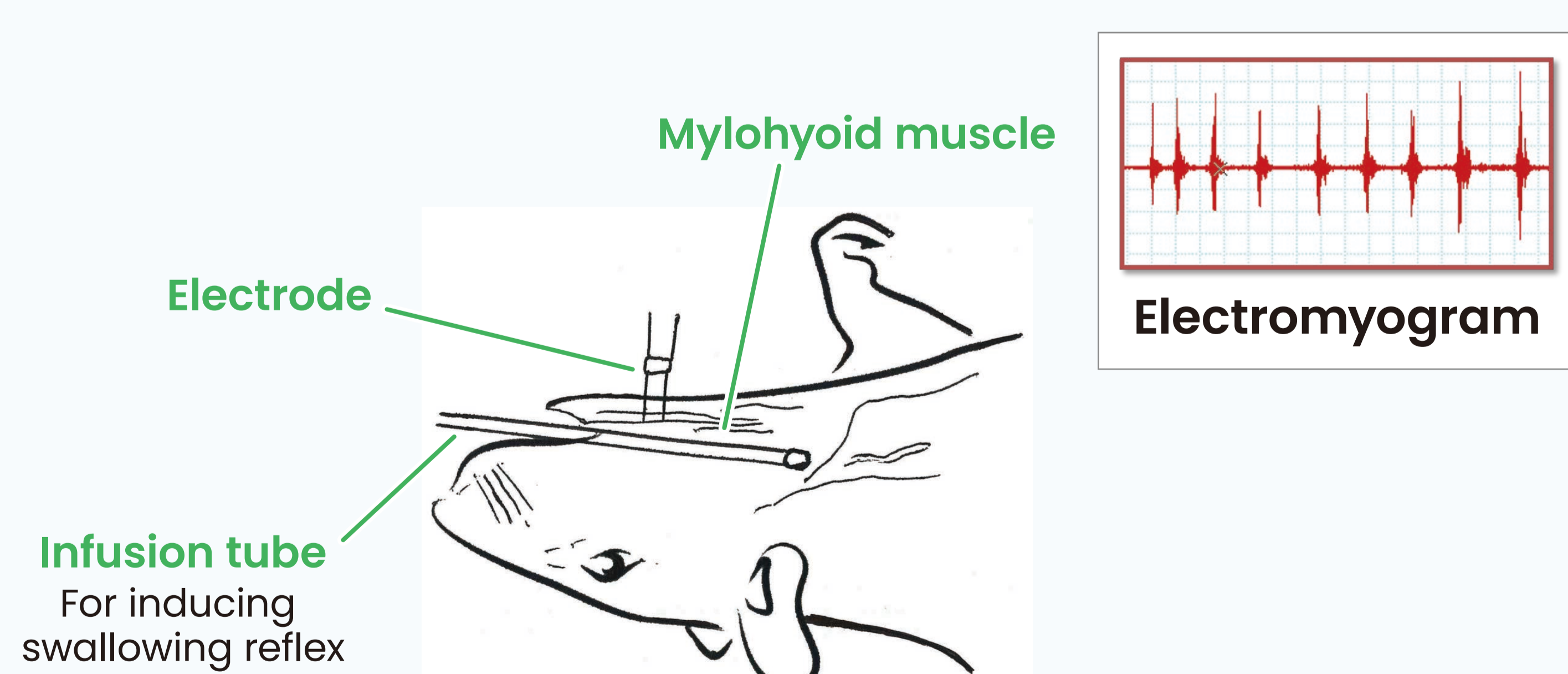
● Group composition

Test Group	Dose level	Dose volume	Dose route	Animal number
Sham group	-	-	-	7
BCAO group (Control)	0	5 mL/kg	p.o.	11
Perindopril group	0.4 mg/kg			12

● Experimental schedule



● Image diagram of swallowing reflex measurement



Summary in Japanese

誤嚥性肺炎の原因の一つである嚥下障害は、脳血管疾患、パーキンソン病、加齢、抗精神病薬の過剰摂取の患者にとって、依然として主要な合併症である。化合物の嚥下障害に対する効果を評価するために、両側総頸動脈 (BCAO) の結紮によるラット嚥下障害モデルを作製した。

この研究では、ラットのBCAOにおける嚥下反射の機能不全に対するペリンドプリルの効果を検討した。BCAOラットは、イソフルラン吸入による麻酔下で、両側総頸動脈を結紮して作製し、嚥下障害を誘発した。BCAOラットにペリンドプリルを4週間経口投与し、BCAOまたは偽手術後29日目に顎舌骨筋の筋電図 (EMG) を記録することによって嚥下反射を測定した。BCAOラットでは、ペリンドプリルの4週間経口投与により、嚥下反射の減少が改善された。これらの結果は、BCAOによって嚥下障害モデルが確立され、ラットのBCAO誘発嚥下障害モデルを用いて嚥下反射に対する化合物の効果を評価できることが示している。

Results

Experiment 1

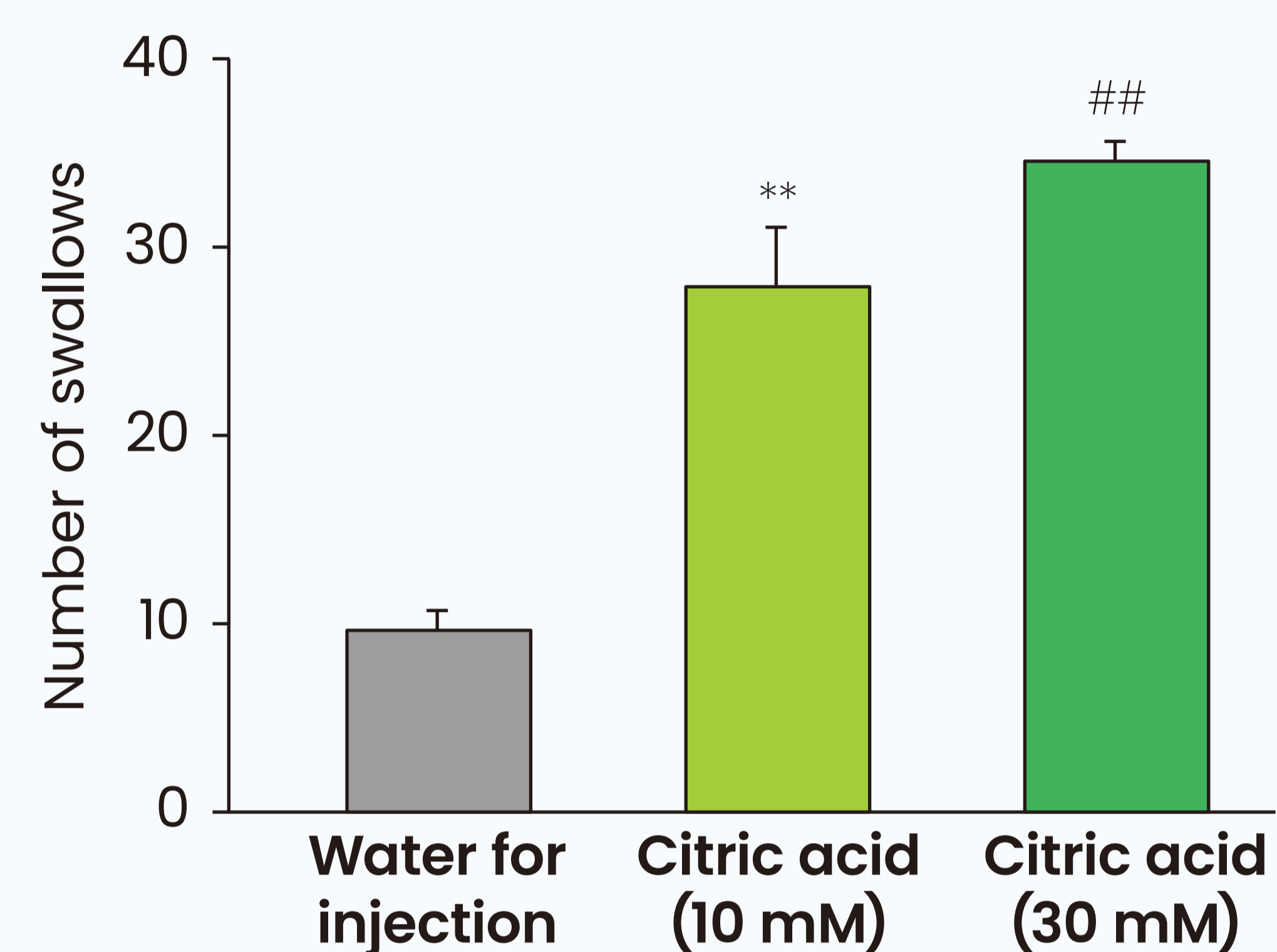


Figure 1 Elicitation by water for injection or Citric acid

**p<0.01 vs water for injection group; ## p<0.01 vs Citric acid 10mM group (Student's t-test)

Experiment 2

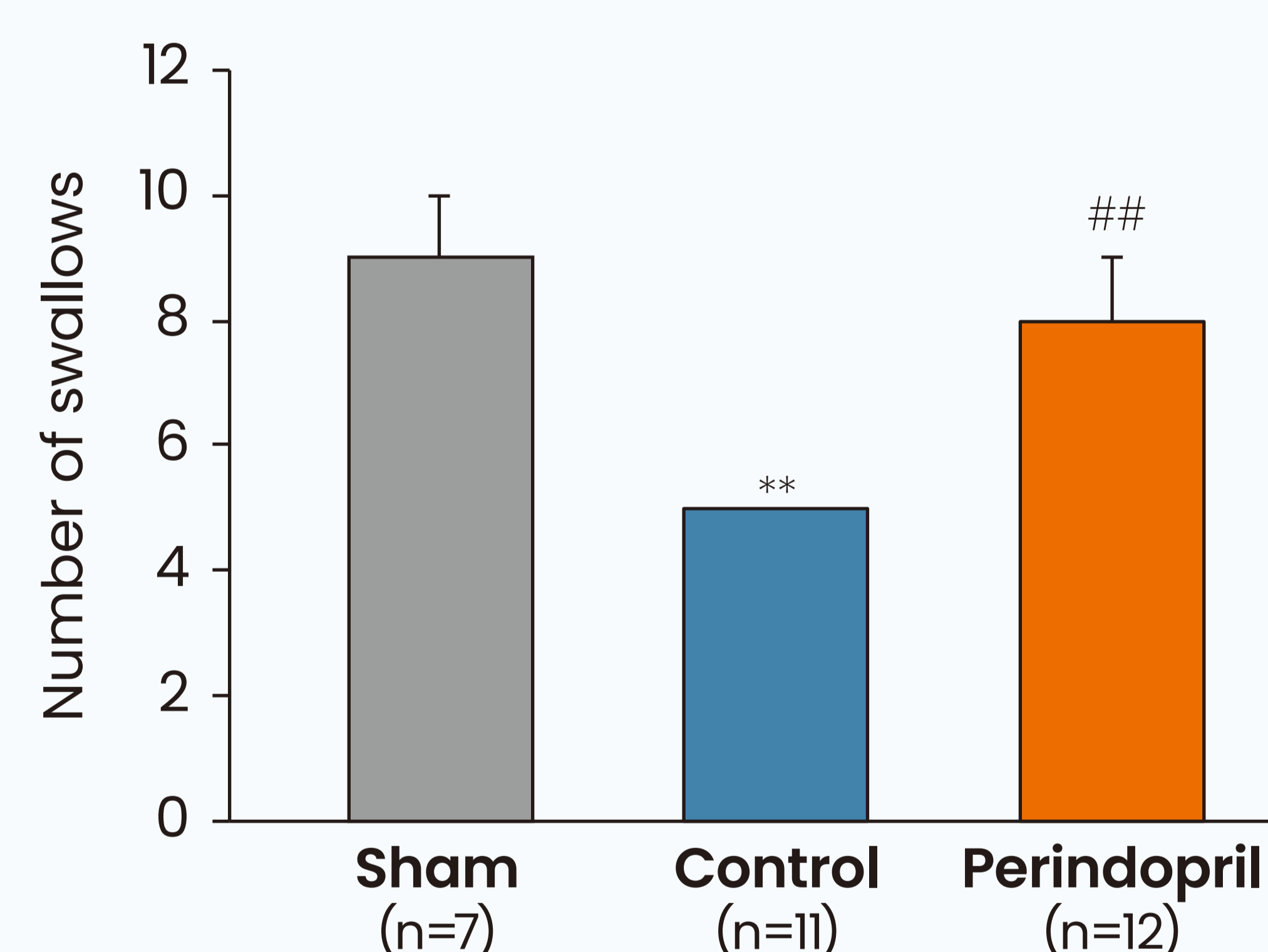


Figure 2 Elicitation by water for injection

**p<0.01 vs sham group (Student's t-test); ## p<0.01 vs Control group (Student's t-test)

Conclusion

- (1) In the rats stimulated by citric acid, the number of the swallowing reflexes was significantly increased compared to those stimulated by water for injection.
- (2) The number of the swallowing reflexes was significantly decreased in the BCAO (control) group compared to the sham group. By administration of perindopril, the number of swallowing reflexes was significantly increased compared to the control group.

In conclusion, BCAO treatment induced dysphagia in rats. Perindopril improved the swallowing reflexes in the BCAO-induced dysphagia in rats, indicating that BCAO-induced dysphagia model in rats is useful in the development of therapeutic drugs on dysphagia.