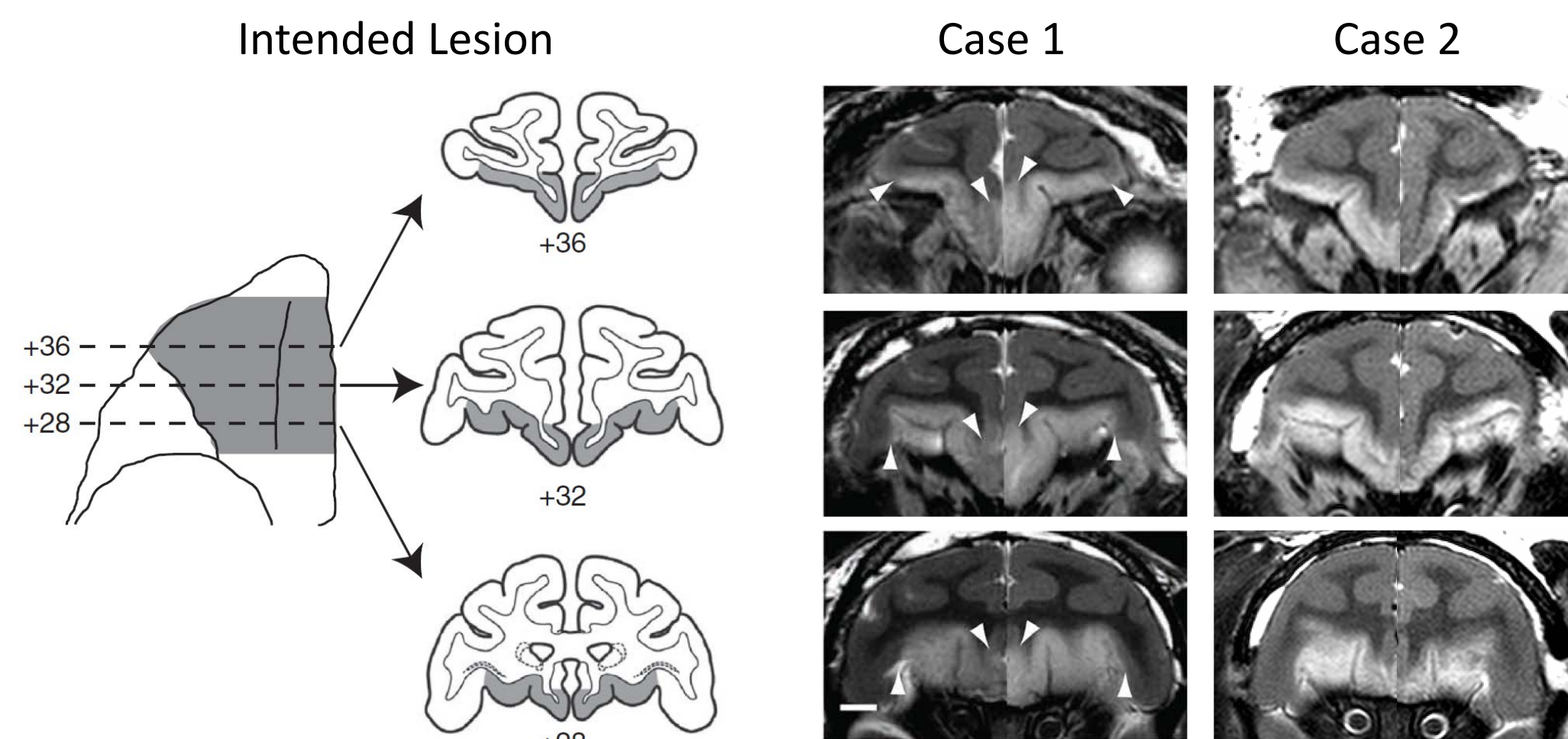


INTRODUCTION

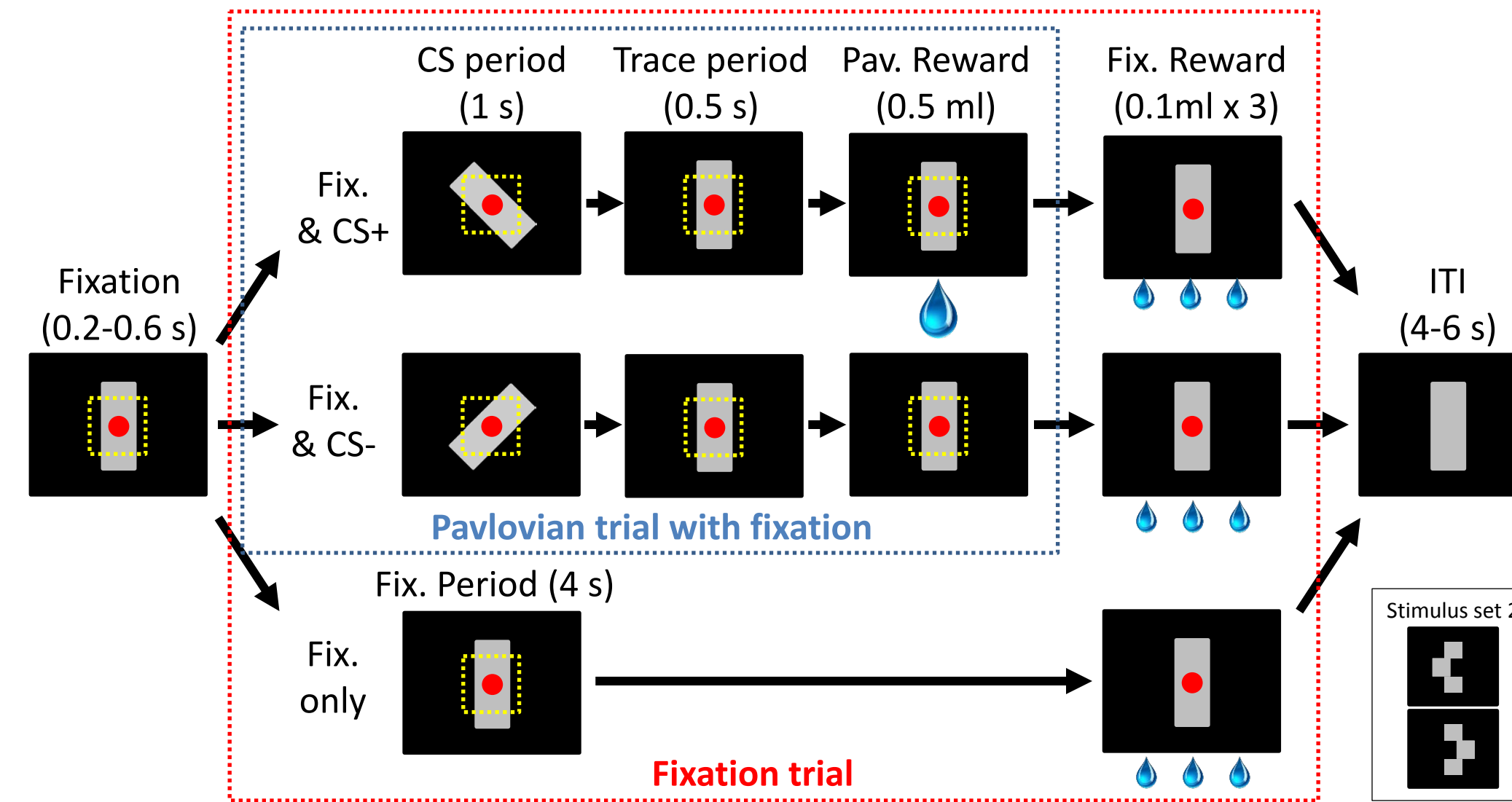
- Previous work has shown that the subgenual portion of the anterior cingulate cortex in macaques contributes to autonomic arousal during anticipation of positive rewarding events (Rudebeck et al., 2014, PNAS).
- Because orbitofrontal cortex (OFC) is involved in stimulus-based reward learning, we wondered whether this region, too, contributed to either the learning or maintenance of autonomic arousal associated with positive events.
- To answer the question, we evaluated autonomic responses in rhesus monkeys that had sustained bilateral excitotoxic lesions of OFC and unoperated controls.

SUBJECTS AND SURGERY

- A total of 7 rhesus monkeys (*Macaca mulatta*) were used.
 - 3 unoperated controls
 - 4 subjects with bilateral OFC lesions (areas 11, 13 & 14)
- The lesions were made by ibotenic acid injection and assessed with postoperative T2-weighted MRI scans. White hypersignal on T2 scans is associated with edema and indicates the extent of damage.

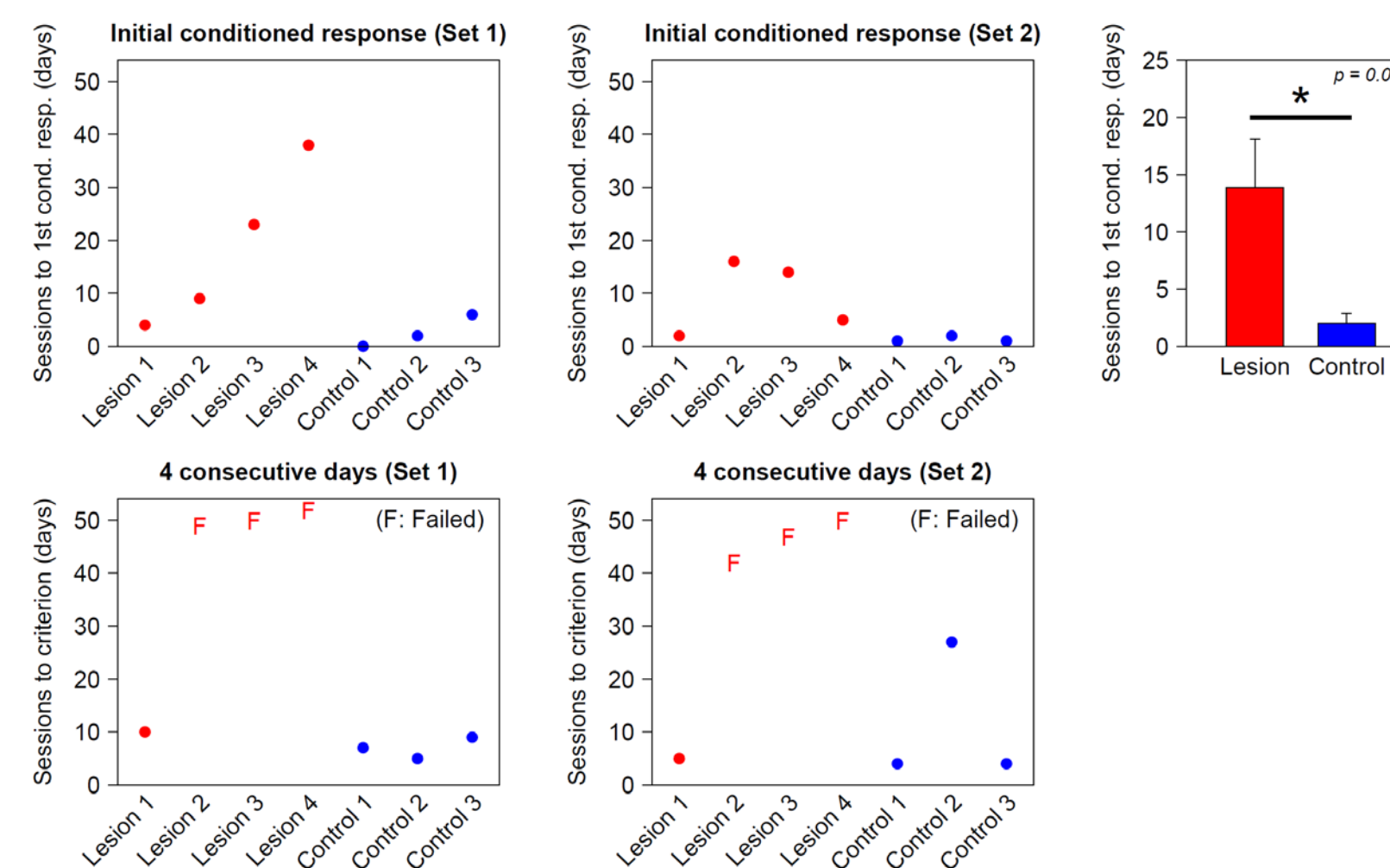


PAVLOVIAN CONDITIONING



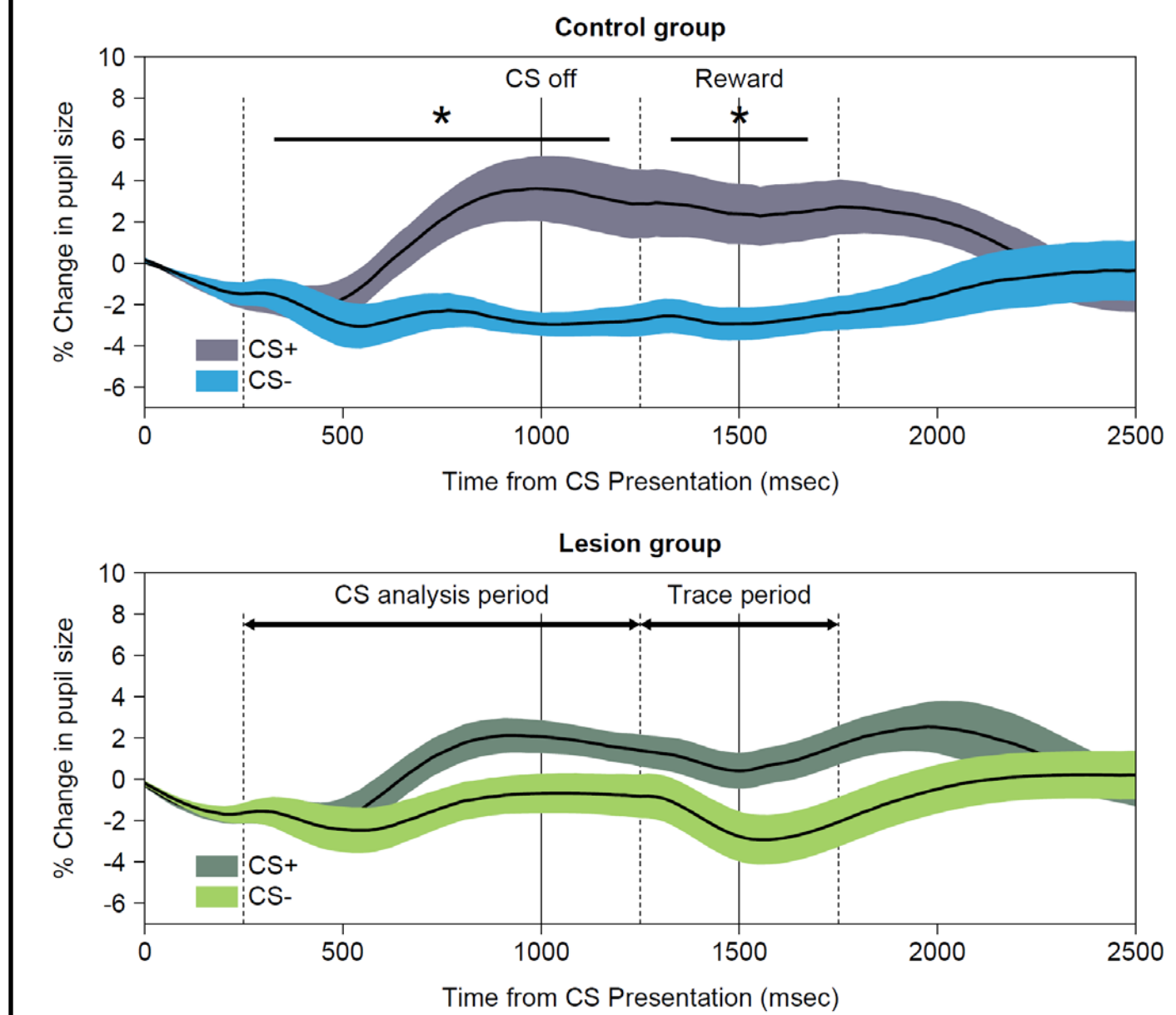
- We superimposed Pavlovian conditioning trials on fixation trials. Pavlovian conditioning proceeded independently of the fixation task.
- On a subset of trials, one of two Pavlovian stimuli (CS+, CS-) was presented. Pupil size was recorded with an eye tracker as a measure of the autonomic response.

RESULT 1: DAYS TO CRITERION



- The control group acquired a conditioned pupil response to the CS+ within a couple of training sessions and continued to show it across at least 4 consecutive sessions.
- The lesion group required more sessions to acquire a conditioned autonomic response and three out of four subjects failed to sustain it for 4 consecutive sessions in one or both training sets.

RESULT 2: PUPILLOMETRY



- Controls exhibited an increased pupil size to the CS+, compared to the response to the CS-, and continued to show the conditioned pupil response in anticipation of reward.
- By contrast, in monkeys with OFC lesions, the pupil response to the CS+ was not significantly different from that to the CS- in both CS and trace analysis periods.

SUMMARY

- Monkeys with OFC lesions were impaired in acquiring a conditioned pupil response. In addition, 3 out of 4 failed to maintain the acquired autonomic response across days, unlike unoperated controls.
- In line with a previous finding that the primate OFC is important for regulating cardiovascular arousal upon omission of reward (Reekie et al., 2008, PNAS), the present results suggest that OFC is involved in acquiring appropriate autonomic responses to cues predicting positive events.

REFERENCES

- Rudebeck PH, Putnam PT, Daniels TE, Yang T, Mitz AR, Rhodes SE, Murray EA (2014) A role for primate subgenual cingulate cortex in sustaining autonomic arousal. *Proc Natl Acad Sci U S A* 111:5391-5396.
- Reekie YL, Braesicke K, Man MS, Roberts AC (2008) Uncoupling of behavioral and autonomic responses after lesions of the primate orbitofrontal cortex. *Proc Natl Acad Sci U S A* 105:9787-9792.