Enhancement of electrically evoked startle-like

Medical Sciences (Beijing, China). The rats were anesthetized deeply with 10% chloral hydrate (400 mg/kg, i.p.) and placed in a Kopf stereotaxic head holder. A state of areflexia was maintained throughout the experiment by supplemental injection of the same anesthetic. Flexible wire electrodes were implanted into the hindlimb anterior biceps femoris muscles for measuring EMG responses. A midline incision

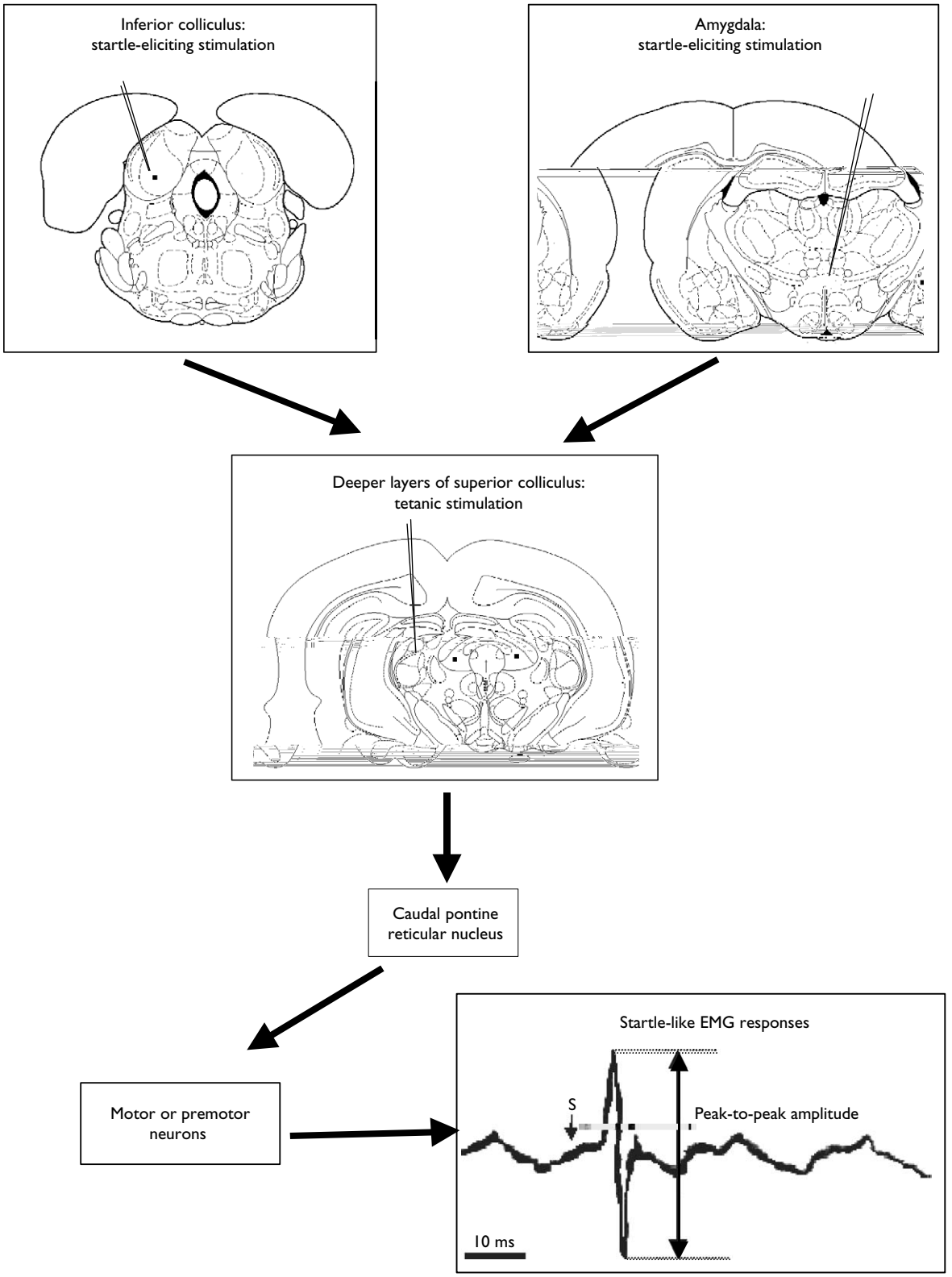

Fig. 1. Schem a ic diag an ill . a ing a n del f he al cl c i . n edia ing fea en ia i n f he . a le e e , and. h ing he n e h d . ed in he e en d . A c f EMG a ef n f n he . cill . c e. c een i di la ed in he b n anel, in hich he n e f. hl 1 . (S) i indica ed b an a in ing d n and he eak- - eak an i de i indica ed b a d ble-headed a .

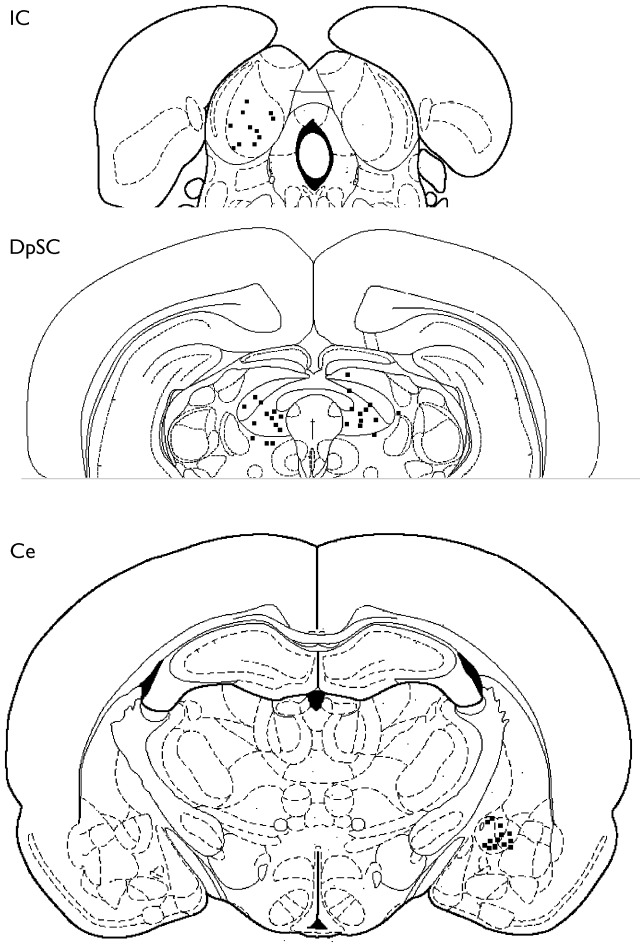

Fig. 2. L ca i n f elec de i . (a e) in he egi n f he infe i c llic l . (IC), he dee la e . f he e i c llic l . (D SC) and he cen al n cle . f he am gdala (Ce) f 25 a . . The b ain . ec i n diag am. e e ba ed n [21].

A slight increase of EMG amplitude following tetanic stimulation of the right (contralateral) DpSC was observed when EMG responses were elicited by stimulation of the left IC (Fig. 2d). ANOVA with repeated measures on the effect of tetanic stimulation revealed that the average EMG amplitude change was not significant ($F(1,4) = 1.267$, $p = 0.323$).

DISCUSSION

The amygdala and the IC are two structures where fear-like and defensive behaviors can be evoked by electrical stimulation [2,3,7]. In the present study, single-pulse unilateral electrical stimulation of the Ce or the IC elicited short latency, whole-body, bilateral, startle-like responses in chloral hydrate anesthetized rats. These results are consistent with the previous reports that electrical stimulation of the amygdala or the IC elicits startle-like responses in awake rats [4,5,6,8]. The amygdala and the IC must have close functional connections with the primary startle pathway. The stimulation currents used for Ce stimulation could have activated nearby internal capsule axons. Activation of the internal capsule axons can evoke non-startle-like unilateral forelimb flexions [25], but may not significantly influence bilateral startle-like responses of the hindlimb anterior biceps femoris muscles.

Electrical activation of the DpSC elicits fear-like behaviors in rats [11–13]. The DpSC and its immediately subjacent area, including the deep mesencephalic reticular formation and the deep mesencephalic gray, have been suggested as the relay station via which the amygdala facilitates startle [4,5,9,10]. In the present study, single-pulse stimulation of the DpSC could evoke startle-like responses. High-frequency tetanic stimulation of the DpSC markedly enhanced the startle-like EMG responses to ipsilateral Ce stimulation, and only slightly enhanced the EMG responses to contralateral Ce stimulation. This ipsilateral/contralateral difference is consistent to previous data indicating that the ipsilateral rostrolateral midbrain is more critical than the contralateral one in mediating startle-like responses evoked by unilateral amygdala stimulation [4,5]. Although the SC can show endogenous LTP in response to tetanic stimulation [17], it is not clear at this time how tetanic stimulation of the DpSC led to the potentiation of the amygdala-induced EMG responses seen here. This motor-output potentiation can be used to study the underlying neural plasticity induced by tetanic DpSC stimulation.

The EMG responses to IC stimulation are less plastic following DpSC tetanic stimulation than those to ipsilateral Ce stimulation. Tetanic DpSC stimulation augmented the

EMG responses to ipsilateral IC stimulation only to a small degree, and did not significantly change the responses to contralateral IC stimulation. Although the DpSC receives direct axonal projections from the ipsilateral external cortex of the IC [14], the present results suggest that the circuits by which IC outputs facilitate startle are not the same as those from the amygdala.

The most striking finding of the present study is that the Ce-induced startle-like responses can be markedly enhanced by tetanic stimulation of the ipsilateral DpSC. This mesencephalic synaptic relay station in the descending pathway from the amygdala to the primary startle circuit may allow for further interactions between fear outputs mediated by the amygdala and approach/avoidance outputs mediated by the DpSC. Investigation of the plasticity of this relay station would be important for understanding the dynamic processes of fear-modulated orientation and startle responses.

CONCLUSION

Unilateral electrical stimulation of either the Ce or the IC evoked unconditional startle-like responses at short latencies, suggesting functional connections of these two structures with the startle circuits. High-frequency unilateral tetanic stimulation of the DpSC had a strong enhancing effect on the startle-like EMG responses to ipsilateral Ce stimulation, but a smaller enhancing effect on the responses to contralateral Ce stimulation and those to ipsilateral IC stimulation, and even less effect on the responses to contralateral IC stimulation. The functional plasticity in the startle-like EMG responses to ipsilateral Ce stimulation following tetanic DpSC stimulation, therefore, provides a model for studying the neural substrates of emotional expression and learning.

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