Activity in Cerebellar Purkinje Cells Changes after Paired Mossy Fibre and Inferior Olive Stimulation.

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Experimental set-up

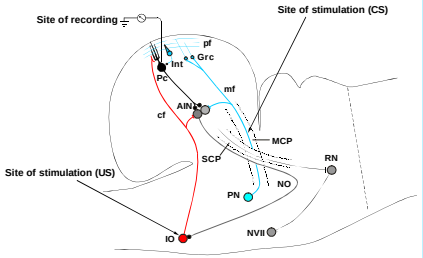

Fig.1
Experimental set-up and wiring diagram of the cerebellar cortex, deep cerebellar nuclei and the inferior olive. Purkinje cell (Pc), Interneuron (Int), Climbing fibre (cf), granule cell (Grc), mossy fibre (mf), parallel fibre (pf), anterior interpositus nucleus (AIN), inferior olive (IO), nucleo-olivary fibres (NO), red nucleus (RN), facial nucleus (NVII), superior cerebellar peduncle (SCP), middle cerebellar peduncle (MCP), pontine nuclei (PN).

Introduction

The cerebellar cortex has been shown to be critically involved in classical conditioning of motor responses. Purkinje cells (Pc) and interneurones in the cerebellar cortex receive convergent input from pontine nuclei via mossy fibres (mf) and from the inferior olive (IO) via climbing fibres (cf). Previous investigations of eye blink conditioning have demonstrated a suppression of Pc activity in trained animals when using electrical forelimb stimulation as conditioned stimulus (CS) and periorbital stimulation as unconditioned stimulus (US). Also, repeated presentation of the CS alone (extinction) returned Pc activity during the CS-period to normal. Furthermore, it has been shown that direct stimulation of mf can serve as a CS instead of forelimb stimulation to elicit conditioned eyelid responses.

If the mf are part of a CS-pathway and the cf are part of a US-pathway, then direct stimulation of these afferents would be expected to produce suppression of Pc activity following paired presentations, reversible by mf stimulation alone.

Sample record

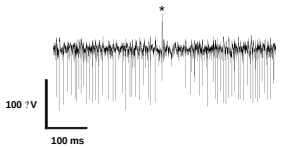

Fig. 2
Sample record of the Purkinje cell reported here. Complex spike indicated by *.

Purkinje cell activity during paired and unpaired stimulation

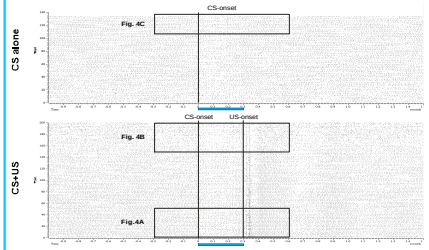

Fig. 3
Raster plot of Purkinje cell activity during paired (CS+US) and unpaired (CS alone) stimulation. Each dot indicates a Pc spike. One row indicates one trial. Onset of CS and US stimulation indicated by vertical lines. CS duration is indicated by the blue line. Boxes indicate spike activity data presented in Figure 4.

Methods

The experiments were performed on decerebrate male ferrets (Fig. 1). Direct stimulation of cerebellar afferents was applied in a delay conditioning paradigm. Direct stimulation (300 ms train, 15 pulses, 60 ?A) of mf in the middle cerebellar peduncle was used as CS and direct IO stimulation (45 ms train, 3 pulses, 250 ?A) was used as US. Paired stimulation was presented for 200 trials and was then followed by 135 trials of CS stimulation alone. The activity of a single Pc in the c3 zone of the cerebellar cortex was recorded (cf. Fig 2 and Fig 3).

The results presented are preliminary in the sense that they were obtained from a single experiment. Data has so far been collected in only a few experiments and the effects reported here have not been observed in every Pc studied so far.

Effects of paired and unpaired stimulation

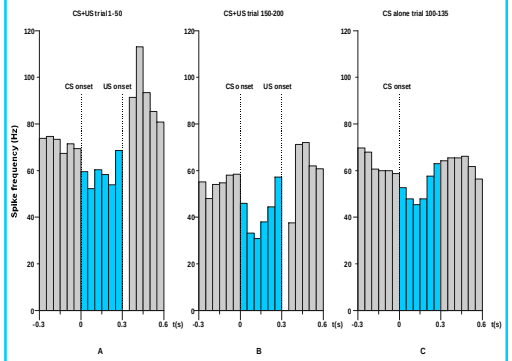

Fig. 4
Histograms of Purkinje cell activity during (A) the first 50 trials of paired stimulation, (B) the last 50 trials of paired stimulation, and (C) the last 35 trials of unpaired stimulation. In each histogram, activity during CS stimulation period is indicated in blue, pre- and post-stimulation activity in grey. The first 50 ms after US stimulation were excluded due to stimulation artefacts.

Results

Pc activity during the CS-period (mf stimulation) was gradually reduced when paired with the US (IO stimulation). During the first 50 trials Pc activity was in the range of 52-69 Hz (Fig. 4A). During the last 50 trials, Pc activity decreased to a range of 31-57 Hz (Fig 4B). This effect was almost completely reversed during unpaired mf stimulation (CS alone), when Pc activity increased to a range of 46-63 Hz (Fig 4C).

Interestingly, also the Pc background activity range was lowered, from 67-75 Hz to 48-58 Hz (Fig 4A and 4B) during paired stimulation, while mf stimulation alone increased background spike frequency to 59-70 Hz (Fig 4C). Furthermore, a reduction in Pc activity in response to the US (IO stimulation) was observed (Fig 4B and 4C) after paired stimulation.

Conclusions

As predicted, Pc activity in response to mf stimulation was reduced after repeated trials of paired stimulation. Furthermore, this reduction was almost completely reversed by presenting mf stimulation alone.

These observations are in good agreement with previous investigations and support the hypothesis that classical conditioning involves changes in cerebellar Pc activity, induced by converging mf and cf input to the cerebellar cortex. These changes in Pc activity may involve synaptic changes both at Pc dendrites and at inhibitory interneurones.

The observed decrease in Pc background activity after paired stimulation, and its partial reversal after mf stimulation alone, may also be relevant for cerebellar mediated conditioned responses. Reduced Pc background activity may contribute to disinhibition of the deep cerebellar nuclei, thus fascilitating the expression of a conditioned response. Conversely, increased Pc background activity may contribute to suppressing cerebellar mediated motor responses.

Aknowledgement

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