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THE EFFECT OF SYMPATHETIC STIMULATION ON MAMMALIAN MUSCLE SPINDLES

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Several authors have described unmyelinated fibres entering the mammalian spindle (see Barker, 1948). These fibres are reported to degenerate on removal of the appropriate sympathetic ganglia (Hines & Tower, 1928) and are the only fibres to remain intact after complete degeneration of the somatic innervation to the spindle (Hinsey, 1927). Although the characteristics of the discharge from muscle spindle afferent fibres and the influence thereon of motor fibres to the mammalian spindle (fusimotor fibres) have been studied in detail (Matthews, 1933; Leksell, 1945; Kuffler, Hunt & Quilliam, 1951; Hunt & Kuffler, 1951), the physiological role of sympathetic fibres to the spindle has not yet been described. A preliminary report of the present results was presented at the September 1959 meeting of the American Physiological Society (*Physiologist*, **2**, 61–62).

In the present experiments the effects of stimulating sympathetic fibres on the discharge frequency in spindle afferent fibres, on the threshold to stretch of spindle receptors, and on the afferent spindle response to fusimotor stimulation, have been studied in the cat. It will be shown that sympathetic stimulation results in significant changes in threshold of spindle afferent endings in the form of an initial facilitation and subsequent depression. These threshold changes are manifest in changes in discharge frequency and in responses to fusimotor stimulation under conditions of constant muscle tension.

METHODS

Adult cats anaesthetized with sodium pentobarbital were used. With the animal lying on its side the abdominal sympathetic trunk was exposed retroperitoneally and cut in the mid-lumbar region. The distal portion was freed for subsequent placement on stimulating electrodes. Laminectomy was performed to expose the lumbosacral cord and spinal roots. Dorsal and ventral roots from L 6 to S 2 were cut close to the cord. Nerves in the limb were cut, save that to the muscle under study. The muscle tendon was cut and attached to a strain gauge or puller. Discharge in single afferent fibres from the muscle was recorded in dorsal root filaments and individual fusimotor fibres to the muscle were stimulated in ventral root filaments. Stimulation of the sympathetic trunk was carried out with rectangular

pulses of 1 msec duration. Pilomotor responses served as a useful index of the adequacy of sympathetic stimulation. Spindles from gastrocnemius, soleus and tenuissimus muscles were studied.

The device for producing muscle stretch (see Appendix) permitted a stretch to be applied which increased linearly with time and which could be controlled as to magnitude and duration. A vane attached in series between the tendon and puller was interposed between a diffused light source and a photocell. The output of the photocell was recorded on one beam of a Tektronix 502 oscilloscope. Threshold to stretch of a spindle receptor could be estimated by the amount of muscle displacement required to initiate an impulse. This was determined by simultaneous photography of a stretch-evoked impulse in an afferent fibre and the extent of muscle stretch as measured by the photocell.

Tissues were covered with pools of paraffin oil initially equilibrated with 95% O and 5% CO_2. Temperature was maintained at 37–39° C.

RESULTS

Afferent discharge at constant muscle tension

In a spindle afferent fibre showing base-line discharge at constant muscle tension, sympathetic stimulation caused an initial increase followed by a decrease or cessation of discharge. This effect occurred after a considerable latent period and depended on the duration and frequency of sympathetic

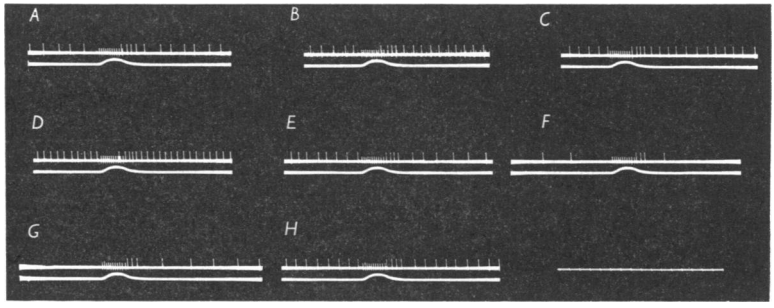

Fig. 1. Portions of continuous record from dorsal root filament (upper trace) containing one muscle spindle afferent fibre and one tendon organ fibre; lower trace, muscle tension recorded by strain gauge. *A* control. Between *A* and *B* sympathetic stimulation at 41/sec begun (total duration 16·2 sec). *B* 14·5 sec after onset of sympathetic stimulation. *C–H* at the following times after end of sympathetic stimulation: *C* 0 sec, *D* 6·7 sec, *E* 8·5 sec, *F* 10 sec, *G* 11·8 sec and *H* 17 sec. Time trace lower right, 10 msec intervals. Soleus muscle under slight initial tension.

stimulation. A typical experiment is shown in Fig. 1. The discharges in a muscle spindle afferent fibre and in a tendon organ fibre (from soleus) were recorded in the same dorsal root filament on continuously moving film. Contraction of the muscle was produced by single stimuli to the ventral roots supplying the muscle. The spindle discharge showed typical cessation during the muscle twitch, whereas the tendon organ fibre showed discharge only during contraction. Record *A* represents a segment of the record in the control period. Sympathetic stimulation at 41/sec was then

applied for 16·2 sec. Record *B* was from a period near the end of sympathetic stimulation, and record *C* just after stimulation had ceased. *D*, taken 6·7 sec after cessation of sympathetic stimulation, shows an obvious increase in the frequency of the spindle afferent discharge. Later the record showed slowing or cessation of the spindle discharge (*F* and *G*), followed by return toward the control frequency (*H*). Throughout this period there was no change in the tendon organ discharge. A number of tendon organ receptors have been examined, none of which were influenced by sympathetic stimulation.

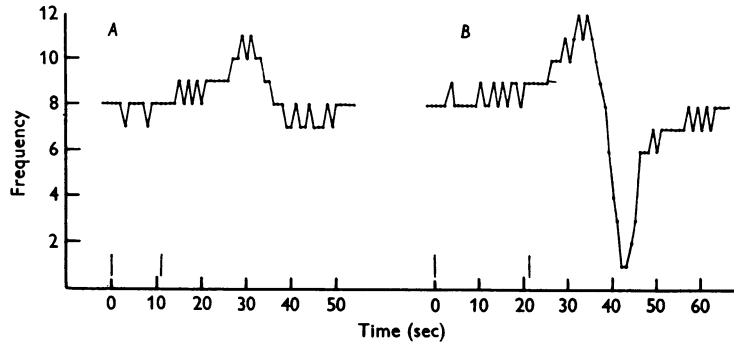

Fig. 2. Frequency changes in an afferent fibre from a muscle spindle in soleus. Sympathetic stimulation (100/sec) for 11 sec in *A* and 21 sec in *B*. Period of stimulation noted by vertical lines above abscissa.

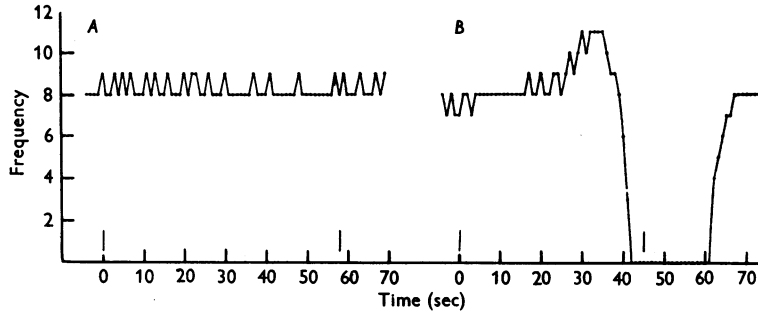

Fig. 3. Frequency changes in same fibre as in Fig. 2. In *A* sympathetic stimulation at 1·75/sec for duration indicated between vertical lines. In *B* sympathetic stimulation at 2/sec for period indicated.

The effect on the afferent discharge from muscle spindles could be graded by the frequency and duration of sympathetic stimulation. Figure 2 shows frequency plots of the response of a spindle afferent fibre (soleus) to sympathetic stimulation at 100/sec. In *A* stimulation for 11 sec was followed by an increase in discharge frequency. In *B* stimulation for 22 sec caused an initial increase followed by a decrease in frequency. More prolonged

sympathetic stimulation resulted in an initial increase, then a period of cessation of afferent discharge, followed by recovery (Fig. 3*B*). The optimal frequency of sympathetic stimulation for the production of the above changes was usually between 10 and 30/sec.

The lowest effective frequency of sympathetic stimulation was often quite critical. For example, the spindle afferent fibre shown in Fig. 3 showed no effect from sympathetic stimulation at 1·75/sec for 58 sec (*A*), but stimulation at 2/sec (*B*) for 45 sec caused the typical sequence of initial increase followed by cessation of afferent discharge and subsequent recovery. The lowest effective frequency of sympathetic stimulation was usually between 2/sec and 5/sec. These results suggest that the accumulation of a substance released by sympathetic stimulation is necessary to cause the alterations in sensory discharge (see Discussion).

The changes in afferent discharge from muscle spindles, as described above, were also found in the tenuissimus muscle suspended in the oil pool and devoid of circulation. This was confirmed in several experiments, in which microscopic observation showed the lack of blood flow in vessels within the muscle. This finding indicates that the changes in spindle discharge are not secondary to alterations in blood flow.

Threshold of spindle afferent endings. The threshold of spindle receptors to stretch following sympathetic stimulation was estimated by linearly increasing muscle stretch as described in Methods. Figure 4 illustrates a typical result in a fibre from triceps surae which showed no base-line discharge at the initial tension employed. Control records are shown in *A* and *B*, the impulse occurring consistently at a certain degree of stretch. Between *B* and *C* sympathetic stimulation was begun (tetanus at 10/sec lasting 28 sec). The threshold was reduced in *C*, *D* and *E*, the latter record showing two impulses as a result of the standard stretch. Records *F* and *G* show the subsequent increase in stretch threshold and in record *H* the amount of stretch applied failed to initiate an impulse. Records *I–M* show the recovery to the control stretch threshold.

The threshold to stretch was measured by noting the extent of muscle displacement as recorded in the photocell record at the time of occurrence of the impulse (conduction time was small relative to duration of stretch). The threshold was then plotted as a function of time. Figure 5 shows the threshold changes resulting from sympathetic stimulation as recorded in a single spindle afferent fibre. In *A* the sympathetic trunk was stimulated at 30/sec for 44 sec at a given stimulus strength. The stretch threshold showed an initial fall followed by a sharp rise. The receptor then failed to initiate an impulse with the degree of stretch applied by the puller. However, if a greater degree of stretch were employed, the receptor could be made to discharge during this period. After cessation of sympathetic

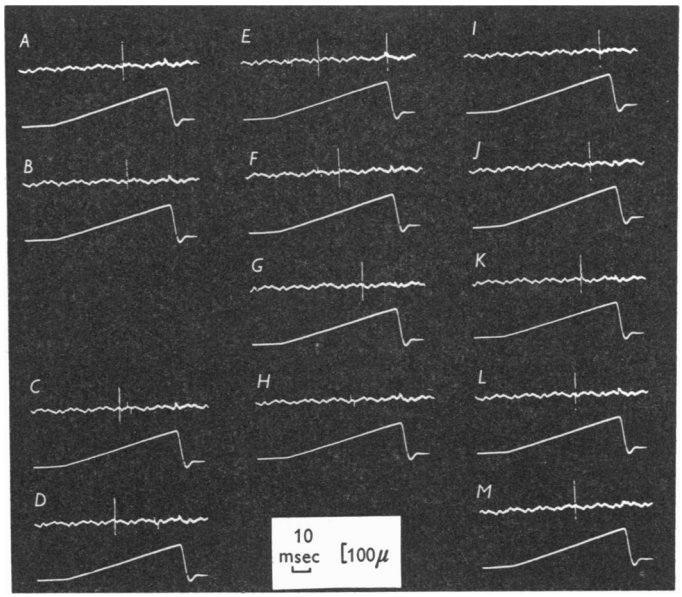

Fig. 4. Responses to stretch in a spindle afferent fibre from triceps surae. Upper record, discharge in afferent fibre; lower record, displacement of muscle. Low initial tension, no base-line discharge from spindle. *A* and *B*, controls. Sympathetic stimulation at 10/sec begun between *B* and *C*, ended between *H* and *I* (total duration 28 sec). Records *C–I* at the following times after onset of sympathetic stimulation: *C* 10 sec, *D* 14 sec, *E* 16 sec, *F* 20 sec, *G* 22 sec, *H* 26 sec. Records *I–M* at the following times after cessation of sympathetic stimulation: *I* 16 sec, *J* 18 sec, *K* 20 sec, *L* 22 sec, *M* 26 sec. Sweep duration 100 msec. Ordinate applies to lower traces.

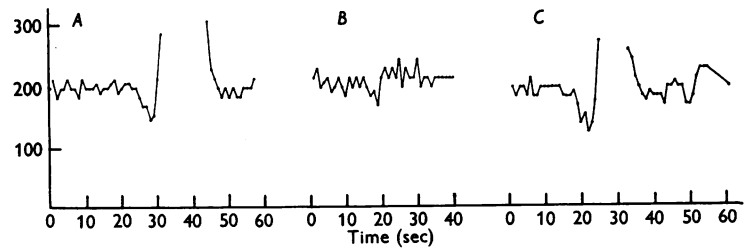

Fig. 5. Threshold changes of a spindle receptor to stretch following sympathetic stimulation. Ordinate shows extent of muscle stretch (μ) associated with impulse initiation. *A*, sympathetic stimulation 30/sec for 44 sec at strength 7 V. *B*, sympathetic stimulation 30/sec for 10 sec at strength 7 V. *C*, sympathetic stimulation 30/sec for 10 sec at strength 14 V; spindle from triceps surae (fibre conducted at approximately 52 m/sec); data derived from experiment similar to that of Fig. 4. Stimulation begins at time zero in *A*, *B* and *C*.

stimulation the threshold returned to normal. These threshold changes mirror the changes in discharge frequency described above. Figure 5*B* illustrates the effect produced by stimulation at the same strength and frequency for a shorter duration, namely, 10 sec. Only slight initial fall in stretch threshold occurred. In Fig. 5*C* stimulation was for the same duration and at the same frequency as in *B* but the stimulus strength was doubled. This resulted in striking threshold changes, comparable to those in *A*. The increase in the effect of sympathetic stimulation consequent to the change in stimulus strength between *B* and *C* indicates that convergence of more than one sympathetic efferent fibre may occur to the same spindle.

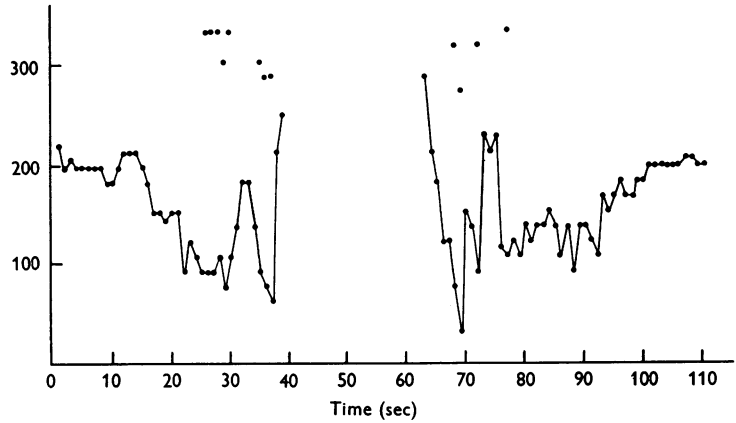

Fig. 6. Threshold changes (μ) of same unit as in Fig. 5 to intravenous injection of 200 μg adrenaline, given at time 10 sec. Dots indicate extent of muscle stretch associated with second impulse when this occurred. Stretch employed as in Fig. 4.

The effects of sympathetic stimulation on the stretch threshold of spindle receptors were similar to those occurring after intravenous injection of adrenaline although the time course was slightly different. Figure 6 shows the changes in stretch threshold of a spindle receptor that occurred following the intravenous injection of 200 μg of adrenaline. Typically a fall in threshold was followed by a marked rise in threshold. On recovery there was often a phase of enhanced excitability before the threshold returned to normal. A similar but less conspicuous second phase of decreased threshold before recovery was sometimes seen following sympathetic stimulation. The doses of adrenaline injected intravenously that were required to produce significant threshold changes were usually about 40–80 μg/kg. Intravenous adrenaline also produced changes in discharge frequency in spindle afferent fibres similar to those which followed sympathetic stimulation.

Responses to fusimotor stimulation. As might be expected from the changes produced by sympathetic stimulation on stretch threshold of spindle receptors, alterations in the spindle response to fusimotor stimulation also occurred in response to sympathetic activity. Figure 7 shows the response to fusimotor stimulation in a spindle afferent fibre from medial gastrocnemius that has no base-line discharge. In each record 11 stimuli were delivered to a fusimotor fibre isolated to this spindle at 100/sec; no detectable contraction of the muscle could be observed. *A* and *B* represent control responses. Sympathetic stimulation (30/sec) was begun between *B* and *C* and was discontinued between *E* and *F*, the total

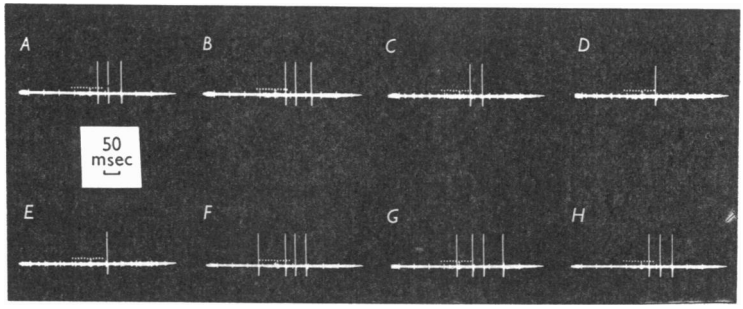

Fig. 7. Effect of sympathetic stimulation on responses in a spindle afferent fibre from medial gastrocnemius to stimulation of a fusimotor fibre (11 stimuli at 100/sec) isolated in ventral root. At the constant low initial tension employed, no base-line discharge was present in the afferent fibre. *A* and *B*: control responses. Between *B* and *C* sympathetic stimulation at 30/sec was begun (total duration 90 sec). Records *C–E* at the following times after the onset of sympathetic stimulation: *C* 60 sec, *D* 64 sec and *E* 88 sec. Records *F–H* at the following times after cessation of sympathetic stimulation: *F* 30 sec, *G* 50 sec and *H* 90 sec.

duration of stimulation being 90 sec. It may be seen that sympathetic stimulation caused a decrease in the response to fusimotor stimulation (*C* to *E*) with some possible facilitation during recovery (*F* and *G*). In *H*, taken 90 sec after cessation of sympathetic stimulation, the response has returned to normal. These changes in response to fusimotor stimulation probably reflect the changes in receptor threshold that follow sympathetic stimulation. However, an initial phase of facilitation was not as conspicuous in fusimotor responses as in threshold changes.

General comment

The great majority of spindles examined showed the effects noted. In later experiments typical effects of sympathetic stimulation were almost invariable. Some early failures were attributed to excessive cleaning of the muscle nerve. In a number of the spindle afferent fibres studied conduction velocity was determined. Typical effects of sympathetic

stimulation, as described above, were seen in spindle afferent fibres conducting at velocities characteristic of both Group I (72–120 m/sec) and Group II (30–72 m/sec) fibres (Hunt, 1954).

DISCUSSION

Sympathetic fibres are known to enter the muscle spindle and to terminate within the capsule in the region of the sensory terminals (Barker, 1948). Activity in such sympathetic fibres has been shown in the present study to cause significant changes in the threshold of spindle receptors to applied stretch. The effect of sympathetic stimulation on spindle receptor threshold is a dual one, the initial decrease in threshold being followed by an increase. The changes in discharge frequency in a spindle afferent fibre showing base-line discharge to a fixed degree of external stretch may be attributed to the threshold variations that occur in the receptor. Likewise the alterations in response to fusimotor activity following sympathetic stimulation appear to have a similar cause. An alternative explanation would be that activity in sympathetic fibres to the spindle causes a change in the intrafusal muscle fibres. This would have to occur in the absence of efferent discharge in the motor fibres to the spindle and would be analogous to the effects of the sympathetic on tonus of certain smooth muscles. However, there is no evidence to suggest that intrafusal fibres differ from extrafusal fibres by possessing such tonic properties. Furthermore, there is suggestive evidence that adrenaline may affect nerve endings. Adrenaline causes an increase in frequency of miniature end-plate potentials (Krnjević & Miledi, 1958); this could be a consequence of depolarization of the motor nerve endings. Also Lowenstein (1956) noted a lowering of threshold of receptors in frog skin on stimulating the sympathetic trunk. He also found that the effects of sympathetic stimulation could be reproduced by administration of adrenaline or noradrenaline.

One may postulate that the sympathetic endings in the spindle release a substance on activity and that this substance, possibly adrenaline and/or noradrenaline, on reaching an appropriate concentration, causes a decrease in receptor threshold, and at higher concentrations causes an increase in threshold. Repetitive stimulation of the sympathetic would then be necessary to permit the accumulation of a sufficient concentration of the substance released. Such a scheme could explain the critical minimal effective frequency of sympathetic stimulation, and the dependence of the effects on frequency and duration of sympathetic stimulation

While prolonged sympathetic activity is required to affect spindle receptor threshold, the effective frequences are low. Hence tonic discharge in sympathetic efferent fibres could produce significant effects on spindle

receptors. The functional role of this accessory innervation to the muscle spindles is not clear. While some role could be attributed to the decrease in receptor threshold as a consequence of general sympathetic activity, it is difficult to deduce a meaningful function for the increase in threshold which usually follows.

SUMMARY

1. The effect of stimulation of the sympathetic trunk on muscle spindles has been studied in the cat.

2. Repetitive sympathetic stimulation of relatively long duration but of low or moderate frequency results in an initial lowering of threshold to stretch followed by an increase of threshold that may last for many seconds. The magnitude of the changes depends upon the frequency and duration of the tetanus applied to the sympathetic fibres.

3. With the muscle under constant tension, sympathetic stimulation produces an initial rise followed by a fall in discharge frequency in spindle afferent fibres. This effect parallels the changes in stretch threshold of spindle receptors.

4. Sympathetic stimulation alters the response of spindle afferent fibres to fusimotor stimulation, the most conspicuous change being a reduction in the number of responses to a standard tetanus to a fusimotor fibre. This effect is also attributed to receptor threshold changes.

5. The above effects of sympathetic stimulation can be imitated by injection of adrenaline intravenously.

6. No changes in tendon organ discharge have been found following sympathetic stimulation.

7. The effects of sympathetic stimulation on muscle spindles also occur in the tenuissimus muscle deprived of its circulation, and hence are not attributable to alterations in blood flow.

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APPENDIX

A control circuit for an electromagnetic puller

By H. Fein

The electromagnetic puller (Goodmans Industries Ltd. Model V47) is excited by a saw-tooth potential obtained from a Tektronix (162) waveform generator (Fig. 8). This wave form is resistively added and attenuated against a negative 170 V potential (obtained from a Tektronix 160 A power supply) so that at junction point 1 a negative saw tooth of approximately 5 to 6 V amplitude is obtained. The amplitude control R_5 applies

a selected amount of this saw tooth to the Goodmans puller via a transistor compound emitter follower (its function being similar to a vacuum tube cathode follower). Since the emitter follower responds to a negative signal, application of negative pulses of other wave forms could be employed with suitable adjustment of the reference potential. Minimum displacement time depends upon characteristics of the electromagnetic puller. Displacement of the puller is recorded by a vane interposed between a diffused light source and an International Rectifier Corp. B-10 photocell.

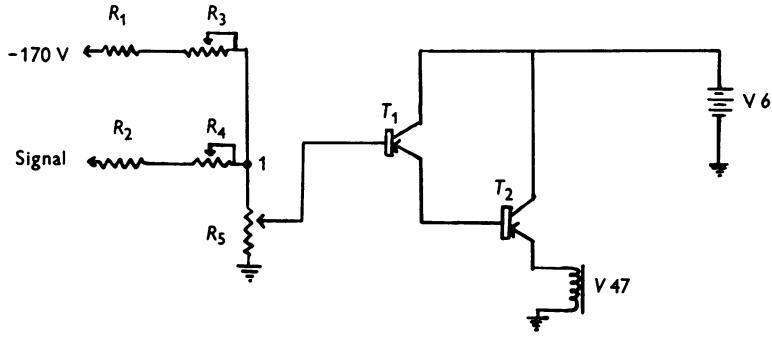

Fig. 8. Transistor control circuit for puller. R_1, R_2 = 22 kΩ; R_3, R_3 = 50 kΩ; R_4 = 1 kΩ. T_1 = Texas Instruments 2N291. T_2 = CBS 2N155. $V47$ = Goodman's Puller.

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