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SENSORY–MOTOR PROCESSING IN SUBSTANTIA NIGRA PARS RETICULATA IN CONSCIOUS CATS

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SUMMARY

1. Extracellular recordings were made with chronically implanted micro-electrodes from 109 substantia nigra neurones in conscious cats. Ninety-six of 109 neurones met the criteria of presumed non-dopaminergic pars reticulata (s.n.r.) neurones. Background discharge, in animals in a state of relaxed wakefulness and in the absence of overt movements, was in the range of 11–37 impulses/s, mean 19·2 impulses/s.

2. The discharges of fifty-two of ninety-six neurones tested were modified by innocuous mechanical skin stimulation. Neurones responded chiefly to stimuli delivered to the contralateral body side. Responses generally comprised net excitation and occurred with short latency (range 10–34 ms; mean 17·3 ms). Convergence from both forelimbs or the contralateral fore- and hind limbs was evident in a few cases.

3. One-fourth (twenty-four out of ninety-six) of the s.n.r. neurones tested were sensitive to passive manipulation of limb joints in the quiet, conscious cat and responded exclusively to angular displacement of one contralateral joint. Responses were directional and phasic.

4. None of the s.n.r. neurones tested responded to clicks and/or light flashes. However, stimuli moving across the contralateral visual field substantially modified the discharge rate of ten out of ninety-six s.n.r. neurones. Responses were directional and invariably associated with eye movements.

5. Animals were also trained to walk on a treadmill and to perform certain self-generated limb movements. S.n.r. neurones with a receptive field on a limb regularly showed modulations in discharge during locomotion, phase-related to the step cycle, and also short-latency responses during disturbance of such movements.

6. Ten out of ninety-six s.n.r. neurones discharged almost exclusively prior to and during self-generated movements of a single limb. Their most powerful modulations in firing rate occurred, whenever an animal tried to overcome an external impediment or to resist an imposed movement.

7. These observations on s.n.r. neurones, taken together with previous findings on nigral influences on spinal motor circuitry, indicate that the s.n.r. represents an output station of the basal ganglia which is involved in the subconscious processing of convergent multimodal sensory information and which participates in setting appropriate gains and biasses of spinal motor neuronal systems to adequately deal with changing motor requirements.

INTRODUCTION

Most hypotheses about the role of the basal ganglia in motor behaviour have been strongly influenced by clinico-pathological studies in patients with disorders presumed to be restricted to the basal ganglia. The symptoms described are largely 'motor' and include akinesia, rigidity, tremor, chorea, athetosis and ballism (Denny-Brown, 1962; Kornhuber, 1971; Denny-Brown & Yanagisawa, 1976). However, it is not always sufficiently stressed that these patients have inappropriate responses to somatosensory stimuli and become abnormally dependent on visual input to aid the performance of even simple motor acts (Purdon-Martin, 1976).

These clinical observations and the results of animal studies led to the suggestion that the basal ganglia include a 'receiving' area, namely the striatum (Krauthamer, 1979), and 'motor' areas, the globus pallidus and substantia nigra (s.n.), from which the output to other brain areas originates (DeLong & Georgopoulos, 1979; Marsden, 1980). In recent years the concept has arisen that non-dopaminergic cells of the reticular part of s.n. (s.n.r.) represent the main output station for striatal function, and thus a route whereby the basal ganglia may take part in the regulation of motor function (Di Chiara, Olianas, Del Fiacco, Spano & Tagliamonte, 1977; Garcia-Munoz, Nicolaou, Tulloch, Wright & Arbuthnott, 1977; Dray, 1980; Kilpatrick & Starr, 1981; Cools, Jaspers, Kolasiewicz, Sontag & Wolfarth, 1983). These conclusions, however, were based either on experimental s.n.r. lesions or the manipulation of neurotransmission within the s.n.r. To complement information derived in these ways, detailed knowledge about the firing patterns of s.n.r. neurones in normal animals was needed.

Neural recordings in partly restrained monkeys have shown s.n.r. neurones to be mainly modulated in close temporal association with voluntary movements, whereas responses to passive manipulation of limbs or to somatosensory stimuli were weak and only rarely observed (DeLong & Georgopoulos, 1979). On the other hand, reports on the behaviour of s.n.r. neurones in the anaesthetized cat and rat stressed the dominance of sensory feed-back to the nigra (Féger, Jaquemin & Ohye, 1978; Barasi, 1979; Harper, Labuszewski & Lidsky, 1979; Chiodo, Antelman, Caggiula & Lineberry, 1980; Hommer & Bunney, 1980; Maeda & Mogenson, 1981; Yoshida, 1981). In order to provide more detailed knowledge of the functioning of s.n.r. neurones as a basis for interpretation of these seemingly diverging findings we investigated the natural discharge patterns of non-dopaminergic s.n.r. neurones during a variety of somatosensory stimuli and motor tasks in the intact, conscious cat. Some of the present findings have been briefly reported elsewhere (Schwarz & Wand, 1981; Wand & Schwarz, 1982).

METHODS

Young adult female cats 2·0–2·6 kg in weight were screened for calmness and tolerance of handling. Animals were gradually familiarized with a variety of innocuous sensory testing procedures and trained not to produce detectable motor reactions. They were also trained to walk on a treadmill and to perform certain self-generated limb movements.

Surgery

During one aseptic operation under pentobarbitone anaesthesia (initially 25 mg/kg I.P., supplemented I.V. when required) implants were made of a multiple electrode assembly and miniature sockets for the connexion of a FET-headstage telemeter (Prochazka, Stephens & Wand, 1979).

The electrode assembly was stereotaxically positioned in s.n.r. through a craniotomy (target coordinates: A 3·0, L 5·0, D −4·5; Snider & Niemer, 1964). Dental acrylic was used to cement the electrode assembly, the telemeter socket and the hub of a catheter from the jugular vein to anchoring screws, and to seal over the epidural space. The scalp wounds were dressed and sutured around the implants. In order to provide fixation points for externally attached length gauges (Prochazka *et al.* 1979), small stainless-steel eyelets were attached percutaneously to the head of the tibia, lateral epicondylus of the femur, and calcaneum. Flexible, Teflon-coated wires (250 μm diam., 50 mm long), looped through the eyelets, emerged through the skin at these points. Lincomycin (Albiotic^{R}, Upjohn) was administered during the operation by I.V. injection and thereafter incorporated in the cat's normal diet during alternate weeks. After recovery from the operation, the animals bore the implants with no apparent discomfort for up to 6 weeks.

Electrode design

The multiple chronic micro-electrode assembly was a modified version of that described by Chorover & DeLuca (1972). Seven to ten fine (25 μm diameter) individually Teflon-insulated platinum–iridium monofilaments (A-M Systems, Inc., Everett, WA 98204 U.S.A.) were inserted through the lumen of a 26 gauge stainless-steel hypodermic tubing, cut to the desired length, which had been acid-soldered side-by-side to a piece of 21 gauge stainless-steel tubing emerging 5 mm from the centre of a ten-pin IC socket. The individual wires were attached to their respective contacts by carefully stripping part of the insulation and wrapping the bare wires around the pins. Solder or conductive epoxy was applied to bind each wire firmly to its contact. The electrode assembly was insulated with a coating of silicone wax (Dow Corning 630) and finally coated with non-conductive epoxy.

Using a pair of fine scissors, the probe ends of the wires were then cut in order to produce an implant of the required over-all length, the cut wires thereby protruding some 4–5 mm from the distal end of the 26 gauge tubing. Finally, the wires were fused into a single rigid shaft by coating in melted reagent-grade anhydrous dextrose, thus producing a complete, thin and uniform layer of sugar extending upward to include the distal 0·5–1·0 mm of the hypodermic tubing. After implantation the sugar gradually dissolved and units were nearly always recorded within 24 h.

Recording sessions

Starting one day post-operatively, a small capsule containing two FM transmitters was clipped to the animal's headpiece, and miniature plugs were mated with their appropriate sockets. If the chronically implanted floating electrodes happened to be favourably located, unitary activity of s.n.r. neurones could now be recorded. Unitary discharge was monitored with the use of a storage oscilloscope and earphones. In the seven cats implanted for this study, stable recordings from 109 s.n.r. neurones were obtained. Regularly units were held for between 4 and 36 h, and the most stable unit was held for 3 weeks.

During recording the animal was cradled on the experimenter's lap, so that it was gently restrained, its body weight supported and its limbs and head accessible, thus remaining quiet and relaxed for periods up to 30 min.

For a given s.n.r. neurone several forms of mechanical stimulation, e.g. stroking of fur and whiskers, light pressure to or tapping on the skin, manipulation of joints, were carried out manually. Visual and auditory stimuli were likewise applied. Subsequent to completion of sensory testing, the animals walked on a treadmill or were encouraged to produce active movements, such as self-generated flexion–extension movements of a forelimb. To enable the relation between s.n.r. neuronal discharge and active movements of different parts of the body to be assessed, a mercury-in-rubber length gauge was fixed to selected percutaneous fixation wires. A cable connecting the length gauge to the telemeter capsule was attached to the skin with adhesive tape. The electromyogram (e.m.g.) of an appropriate muscle was recorded using percutaneously inserted bipolar concentric needle electrodes. The connnecting wires also led to the telemeter capsule. Experiments were video-taped.

Recording sessions in the conscious animal generally did not exceed 1 h. Sensory testing and the movements studied depended on the s.n.r. neurone involved. Filtered neural records (band width 5 Hz–5 kHz), trigger signals, muscle length, e.m.g. and a voice commentary were stored on FM analog tape (Bell & Howell, CPR-4010). A Nicolet MED-812 digital computer was used to analyse the data directly or when it was subsequently replayed from tape (e.g. mean firing rate, interspike interval histograms, peri-stimulus time histograms, delayed averaging).

Identification of s.n.r. neurones

Units spontaneously discharging at a mean firing rate of > 10 impulses/s with short duration action potentials (< 2 ms) and small or lacking after-positivity (Bunney, Walters, Roth & Aghajanian, 1973; Guyenet & Aghajanian, 1978), which did not exhibit changes in mean firing rate after systemic injection of haloperidol (0·5 mg/kg I.P.) and/or apomorphine (0·75 mg/kg I.P.) were regarded as representing non-dopaminergic s.n.r. neurones (Steinfels, Heym & Jacobs, 1981).

Histology

Confirmation that the recorded neurones were indeed within the s.n.r. was obtained from histology. In terminal experiments, under general anaesthesia, the recording sites were marked by passing current through those electrodes which had yielded unitary recordings (40 μA, 10–30 s; electrode tip negative). Brains were perfused, *in situ*, with 10% formaldehyde solution and histologically processed. Lesions were identified in 20 μm sections stained with Nissl and Haematoxyline. In all cases, marked recording sites were within the confines of the s.n. and indicated that recordings had mainly been obtained from lateral part of s.n.r. (Fig. 1*D*).

RESULTS

Stable unitary recordings were obtained from 109 s.n.r. neurones in seven cats.

Identification of s.n.r. neurones

Background activity of s.n.r. neurones (Fig. 1*A*) was observed in the absence of overt movements, whilst the animal was gently supported in the experimenter's arms and appeared to be in a state of relaxed wakefulness. Mean discharge rate for ninety-six s.n.r. neurones, under these conditions, was 19·2 impulses/s (range 11–37 impulses/s). Mean rate was computed from consecutive interval histograms over 60 s periods, the samples containing in excess of 600 spikes (Fig. 1*C*).

Out of 109 s.n. neurones, 96 discharged faster than 10 impulses/s and had short-duration action potentials (< 2 ms; Fig. 1*A*, and *B*). When tested, background activity did not change up to 1 h after systemic injection of haloperidol (0·5 mg/kg I.P.). Administration of apomorphine (0·75 mg/kg I.P.) usually did not change resting discharge, but in a few cases slightly increased it. Neurones (13 out of 109) which did not meet the physiological, pharmacological and histological criteria described in the Methods section were excluded from the present analysis.

Response of s.n.r. neurones to sensory stimulation

Responses to skin stimulation. Ninety-six s.n.r. neurones were tested for their responses to mechanical tap stimuli applied to the main pads and dorsal surfaces of fore- and hind paws, skin of the thoracic region, head and face, to light pressure to the skin and to stroking fur and whiskers. Mechanical taps were applied manually with the use of a light rod (weight *ca.* 16 g) incorporating a photo-electric contact sensor. Average responses were derived by computation of peri-stimulus time histograms from thirty or more stimulus presentations at intervals of 1–3 s. Trials during

which motor reactions of the animal were visible or palpable were discarded from the data.

The discharge of fifty-two out of ninety-six s.n.r. neurones was modified by these stimuli. Units responded chiefly to stimuli delivered to the contralateral side of the body (with respect to the recording side; Fig. 2*A*), although a significant number of

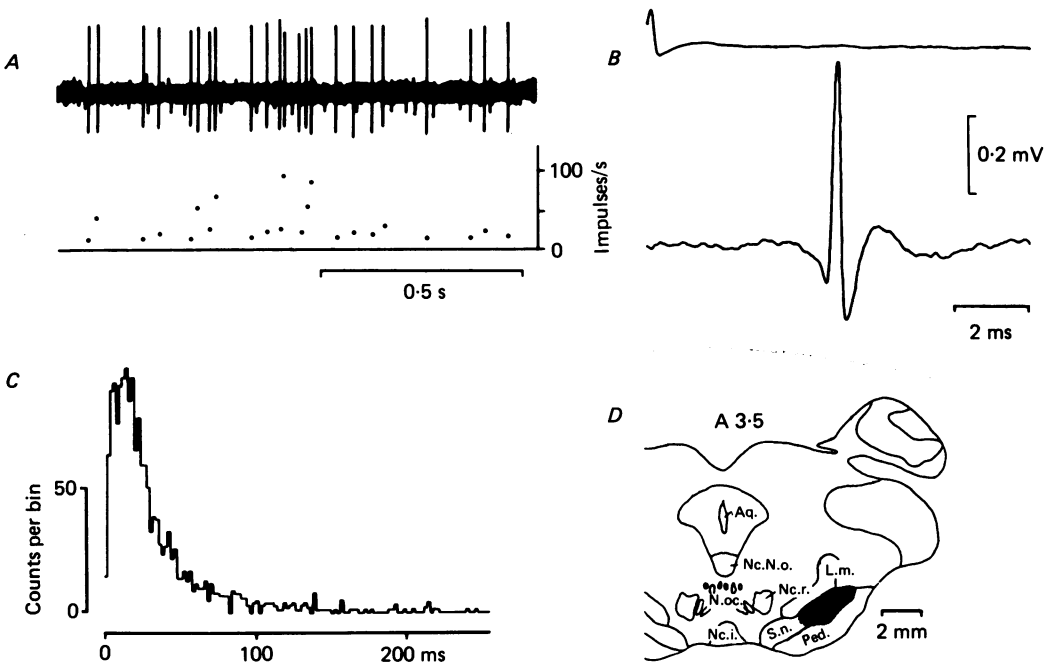

Fig. 1. Identification of presumed s.n.r. neurones. *A* shows a specimen record of a spontaneously discharging s.n.r. neurone (lower trace: instantaneous firing rate), which displayed typical attributes of a presumed non-dopaminergic s.n.r. neurone; *B*, short-duration action potentials < 2 ms (5 ms delayed average, 100 trials); *C*, background activity > 10 impulses/s as calculated from consecutive interval histograms. Total number of spikes $n = 1{\cdot}709$, mean interval = $31{\cdot}5\ \text{ms} \pm 34{\cdot}2$ S.D.; *D*, recording site within the lateral part of s.n.r. (hatched area; according to Snider & Niemer, 1964) as revealed histologically.

units responded to stimuli applied bilaterally to the body and extremities, or to stimuli delivered to mid-line structures, e.g. the nose (Fig. 2*B*). Responses generally consisted of short-latency increases in discharge rate (latency range 10–34 ms) with a tendency for the duration of these increases to be shorter (Fig. 2*C* and *D*; < 50 ms) for low background discharge rates and longer (up to 200 ms; Fig. 2*B*) for higher background discharge rates. In s.n.r. neurones responding to stimuli applied bilaterally, the response magnitude was invariably smaller and the latency longer following stimulation of the ipsilateral side (Fig. 2*C* and *D*). Receptive fields were generally large and extended over a stocking-like area of one limb, sometimes including a large region of thorax and head. Forty-eight out of fifty-two s.n.r. neurones recorded, responded to stimuli delivered to the forelegs, the thorax and head, but only a few

cells (four out of fifty-two) responded to stimuli applied to the skin of the abdomen and hind legs. Where convergence of input occurred it was usually from contra- and ipsilateral forelimbs. Convergence from the contralateral fore- and hind limbs was observed once. Convergence from both hind limbs never occurred.

When the discharge probability of s.n.r. neurones was modified by very light taps to the skin, these neurones usually also responded to stroking fur within the receptive

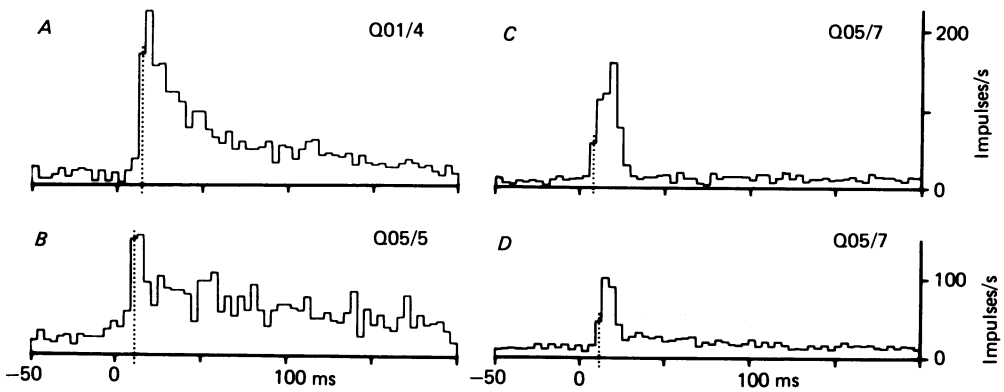

Fig. 2. Peri-stimulus time histograms for three individual s.n.r. neurones. *A*, to mechanical tap stimulation of the dorsum of the contralateral forepaw (latency: 16 ms); *B*, very light taps to the nose (latency: 12 ms). Convergence of input from the contralateral (*C*) and ipsilateral (*D*) body side elicited by tapping the toes of the forepaws in a third neurone (latencies 10 and 13 ms, respectively). All peri-stimulus time histograms in this and the following Figures were constructed with 250 μs dwell time, 16 dwells/bin, and consisted of at least thirty stimulus presentations. Latencies (represented by dotted lines) were established by using a computer program which moved a cursor along the displayed histogram, until a point was reached at which the bin content was three S.D. larger than the mean level in the 50 ms before stimulus presentation.

field for the taps. Many units responded strongly to stroking of the whiskers, usually unilaterally, but sometimes bilaterally (Fig. 3*C*). In some cases (fifteen out of twenty-one) units showed best responses being associated with a particular direction of the stimulus (e.g. higher sensitivity to vibrissae being brushed towards rather than away from the mouth). In view of the directional sensitivity of trigeminal neurones which innervate the vibrissae (Dykes, 1975), this finding in s.n.r. neurones is not surprising.

Manipulation of joints and deep structures. Twenty-four out of ninety-six s.n.r. neurones showed a distinct modification in discharge by passive manipulation of joints in the quiet, relaxed cat. Of these neurones, thirteen were additionally activated by light stroking of the fur or very light taps either to hairy skin or the main pads, whilst eleven cells exclusively responded to manipulation of a single joint. In the latter case, stronger taps applied over the relevant joint and its related structures were likewise effective. The unit illustrated in Fig. 3*A* was sensitive to angular displacement in the shoulder joint. During cyclic anteversion–retroversion movements, the instantaneous firing rate approached 200 impulses/s during retroversion, whilst during anteversion discharge fell to less than 20 impulses/s. Selective

manipulation of wrist and elbow joint was ineffective in this respect. Applying strong taps to the region of the shoulder joint capsule elicited short bursts of activity (Fig. 3*B*).

Gentle taps to the main pad of the contralateral hind paw did not modify the discharge of the unit shown in Fig. 4, whereas stronger taps which caused a brisk dorsiflexion movement of the ankle joint, as evidenced by the length record of soleus muscle, resulted in instantaneous frequencies in excess of 200 impulses/s.

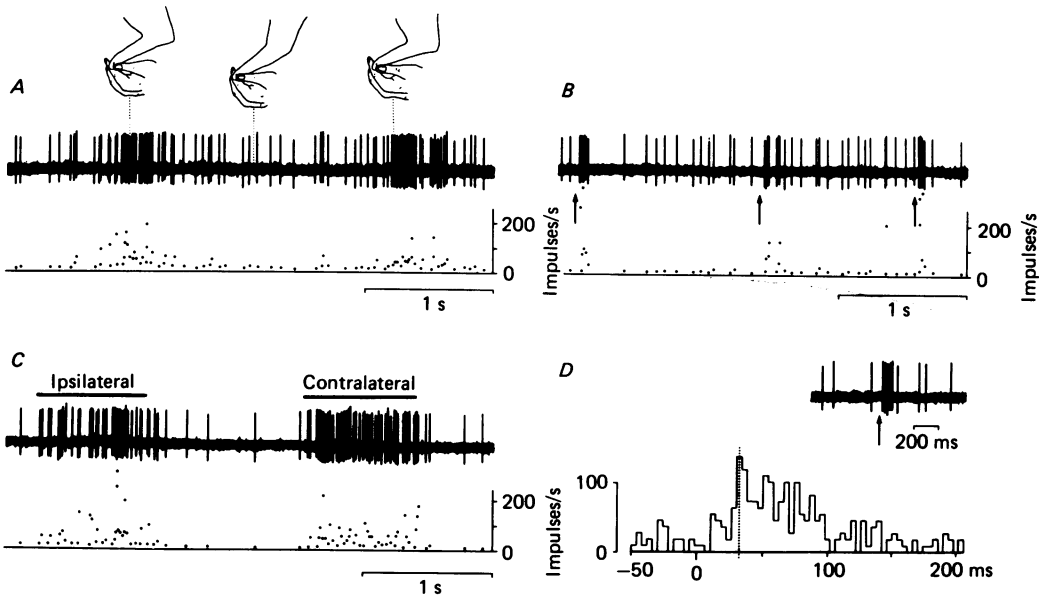

Fig. 3. Convergence of multimodal sensory input onto a single s.n.r. neurone. Imposed cyclic retroversion–anteversion movements in the contralateral shoulder joint in the non-resisting animal elicited an increase in discharge during retroversion. (*A*, tracings from a video record show the way in which the movement was applied; lower traces, instantaneous firing rate.) Stronger taps to the region of the shoulder joint capsule caused short bursts of activity (*B*), while stroking the whiskers (*C*, indicated by bars) of both sides was also a strong stimulus. Very light taps to the contralateral pinna elicited a response with a mean latency of 34 ms (peri-stimulus time histogram and inset specimen record shown in *D*).

All tested units responded exclusively to angular displacement of one joint of the contralateral fore- or hind limb. The responses were directional and phasic (ramp-and-hold movements resulted in discharge only during the ramp phase). There was no convergence from different joints.

Visual, vestibular and acoustic stimulation. None of the presumed non-dopaminergic s.n.r. neurones, the discharge of which could be modified by either skin stimulation or manipulation of joints, responded to clicks or light flashes. Stimuli moving across the contralateral visual fields, however, elicited substantial changes in the firing rate of ten out of ninety-six s.n.r. neurones, the peak firing rates occasionally exceeding 200 impulses/s. Responses varied in complexity, but generally comprised two basic patterns, namely: (i) short-latency increases in discharge of 150–250 ms duration;

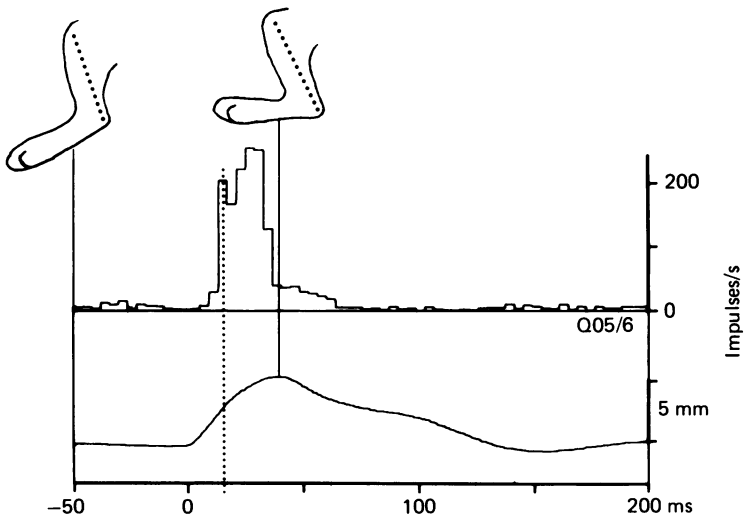

Fig. 4. Peri-stimulus time histogram of a s.n.r. neurone to strong taps of the contralateral hind paw which caused brisk dorsiflexions of the ankle joint as seen in the lower trace (length record of soleus muscle) and the video tracings. Latency indicated by dotted line.

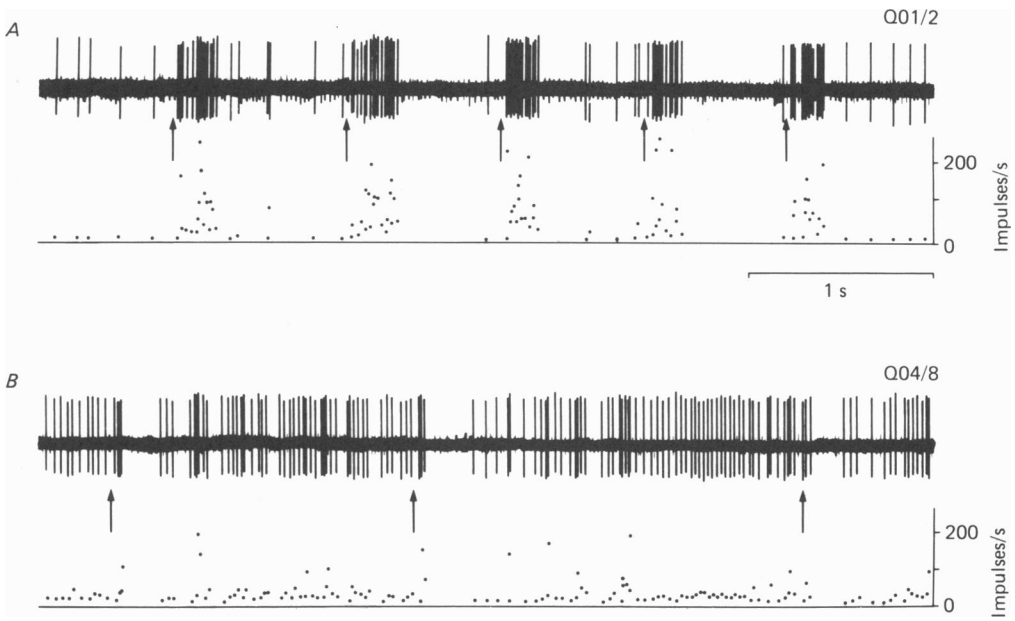

Fig. 5. Unitary records of two s.n.r. neurones illustrating the basic discharge patterns elicited by moving visual stimuli. *A*, short-latency increase in firing lasting for about 150–250 ms in a s.n.r. neurone with low background activity; *B*, short-latency increase immediately followed by a 150–250 ms period of reduced firing in a s.n.r. neurone discharging with higher frquency at rest (arrows indicate beginning of stimulus presentation; lower trace in each record shows instantaneous firing rate).

(ii) short-latency bursts of 3–4 spikes followed by a 150–250 ms period of silence, sometimes followed by a period of enhanced discharge.

The two s.n.r. units depicted in Fig. 5 illustrate these two basic patterns and show an additional feature, in that units which discharged a longer burst of activity always discharged at rest with low frequencies (around 10 impulses/s; Fig. 5*A*), whilst neurones displaying the more complex pattern (Fig. 5*B*) had a higher background activity (around 30 impulses/s). All units which responded to moving visual stimuli were directionally sensitive and responded best when the stimulus moved in a sagittal plane. During this mode of stimulation eye movements were regularly observed but not quantified.

Role-tilt of the whole animal or rotation of the animal's head resulted in a change of discharge rate of two s.n.r. neurones, neither of which had a detectable input from skin and limb joints. Therefore, an influence of macular labyrinthine receptors and neck afferents onto some s.n.r. neurones cannot be excluded, yet it was difficult to establish in the conscious cat. Linear accelerations of the whole animal in a vertical plane led to distinct directionally sensitive changes in discharge rate of three other s.n.r. neurones comprising both increases and decreases in discharge rate. However, it cannot be concluded that the cells responded specifically to these stimuli rather than any other, e.g. due to air movement on skin or the light pressure on skin exerted by the experimenter's arms supporting the cat.

In summary, most of the s.n.r. neurones recorded so far received a multimodal input from the somatosensory system, sometimes associated with visual input. Responses occurred with latencies of 10–34 ms (mean 17·3 ms) to light tactile stimulation of the skin of the forelimbs, thorax and head preferentially of the contralateral body side, and to passive manipulation of contralateral joints preferentially of the forelimbs. The multi-modal nature of s.n.r. input is illustrated by the unit shown in Fig. 3 (see above), which had a convergence of inputs from joints (*A*, *B*) whiskers (*C*) and hairy skin of the pinna (*D*).

Modulation of discharge of s.n.r. neurones during active movements

Many of the s.n.r. neurones which responded to imposed movements and discrete sensory stimuli in the relaxed, partly restrained animal (see Methods) also showed a modulation of discharge during and related to active movements.

Treadmill locomotion. S.n.r. neurones whose receptive fields covered a particular limb, regularly exhibited a rhythmic discharge during periodic active movements like treadmill locomotion. The unit illustrated in Fig. 6 responded strongly to fast passive abduction and flexion (i.e. retroversion) in the shoulder joint, but had no detectable input from the skin. Five steps on the treadmill (speed 0·3–0·5 m/s) are shown, with rhythmic bursts of activity just prior to and during the flexion phase. To conform with the previous literature (Philippson, 1905; Goslow, Reinking & Stuart, 1973) the step cycles in Figs. 6 and 7 have been divided into a flexion phase (F) and three extension phases (E_1, E_2, E_3). On the surface of the treadmill belt, small obstacles made from stiff paper (height approx. 1·5 cm) were glued in a pseudo-random manner. Normally, in F and E_1 the animal swings the limb forward and contacts the ground again at the end of E_1. Towards the end of the third swing phase, when the cat would normally have placed its forepaw on the treadmill surface, it came into contact with

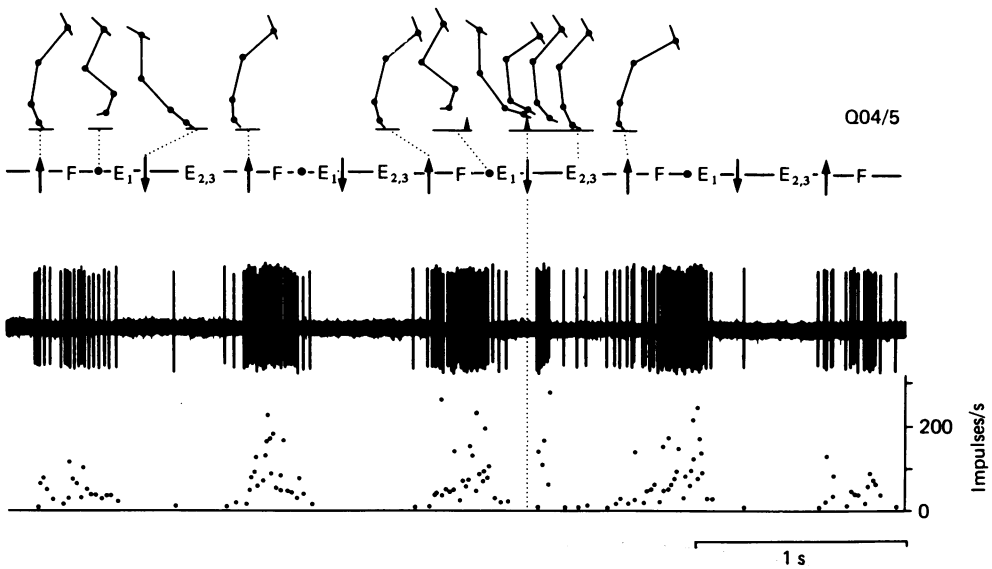

Fig. 6. Discharge train of s.n.r. neurone (middle trace; bottom trace: instantaneous firing rate) which was related to angular displacement in the contralateral shoulder joint during five steps on a treadmill, the third of which included a contact placing reaction. Consistent modulations in firing freqency included: increase towards the end of stance (E_3) and during the early phase of swing (F); pause during the latter phase of swing (E_1) and stance (E_2, E_3); rapid firing some 40–60 ms after foot contact during placing reaction (dotted vertical line). Phases of step cycle (F, E_1, E_2, E_3) after Philippson (1905). Forelimb joint angles schematically drawn by stick figures (after Sontag, Cremer, Meseke, Ropte & Inst. Wiss. Film, 1978).

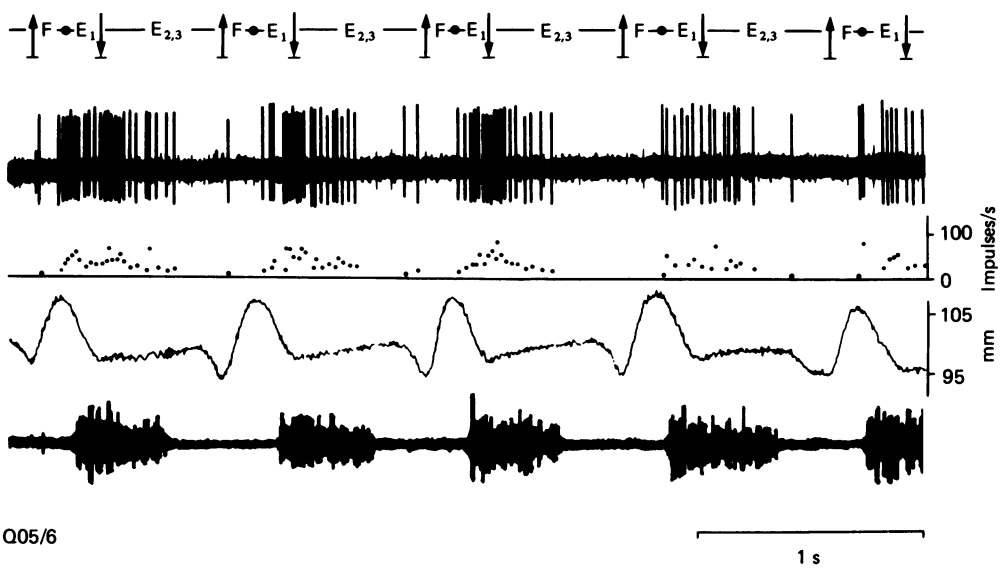

Fig. 7. Discharge of a s.n.r. neurone which was related to angular displacement in the contralateral ankle joint during five steps on a treadmill. Length and e.m.g. (lower traces) refer to soleus muscle. Modulation in discharge was closely related to ankle extensor e.m.g. during the extension phases E_1, E_2.

one of the obstacles. The limb was immediately flexed and then placed in front of the obstacle. 40–60 ms after contact (third video frame) the s.n.r. unit discharged a burst concomitant with the rapid flexion of the forelimb.

One of the few units responding to stimulation applied to deep structures of a hind limb (unit of Fig. 4, see above), was observed during stepping (Fig. 7). This neurone

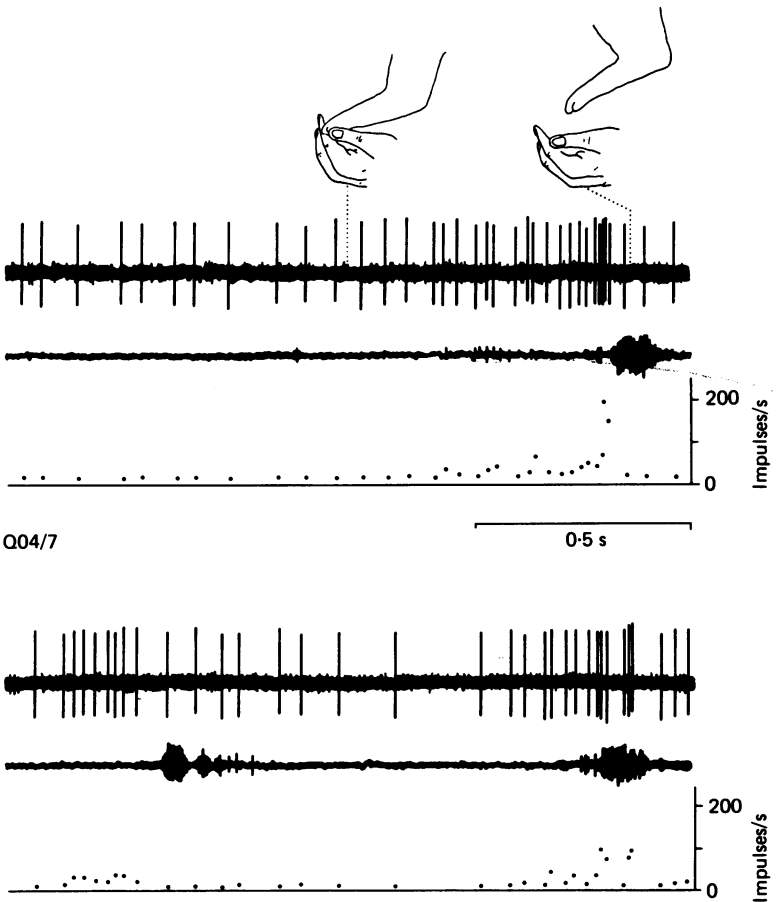

Fig. 8. Discharge pattern of a s.n.r. neurone during three self-generated unobstructed flexion–extension movements of the contralateral forelimb. Despite some variability the unit showed a constant increase in firing rate prior to and during self-generated flexions; e.m.g. (middle trace) refers to elbow flexor muscle.

discharged bursts of activity in E_1 and E_2 during slow treadmill walking (speed 0·3 m/s), the modulation of discharge being reasonably correlated with the e.m.g. of lateral gastrocnemius. This unit had not exhibited any significant input from the skin. Passive manipulation of various joints, however, had resulted in a moderated change in firing rate. Careful re-examination revealed an almost exclusive sensitivity of this s.n.r. unit to angular displacement in the contralateral ankle joint.

Self-generated movements. Ten out of ninety-six s.n.r. units discharged almost exlusively in close temporal association with active movements of a single limb. These

cells lacked detectable sensory input from skin, and were only rarely responsive to passive manipulation of single joints in the relaxed, non-resisting animal. A typical example of a s.n.r. neurone which discharged prior to and during self-generated movements is shown in Fig. 8. Here, the cat produced three flexion–extension movements of the contralateral forelimb. The cat's forepaw was gently held by the

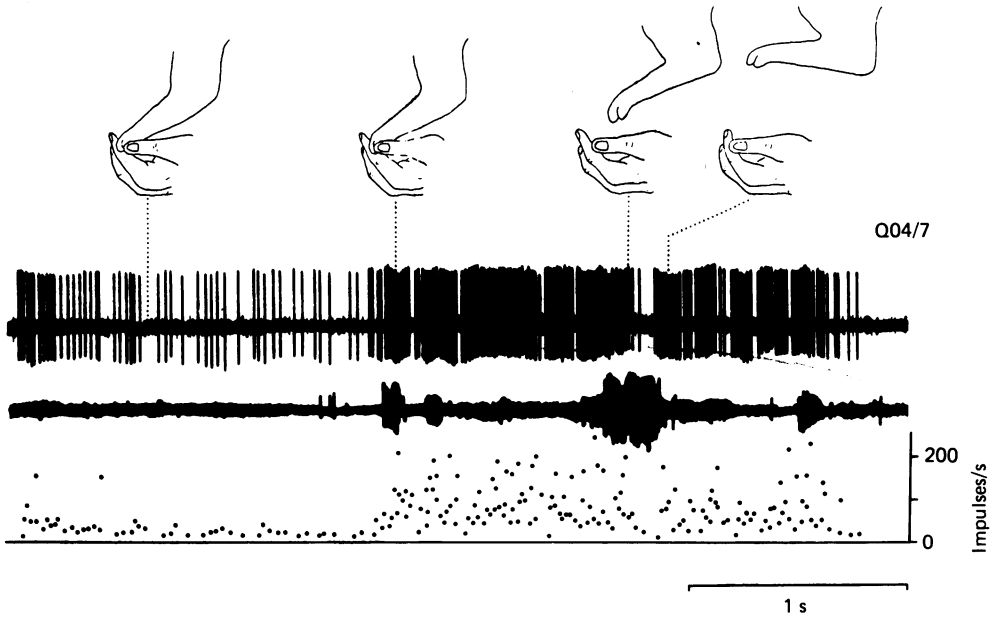

Fig. 9. Discharge of s.n.r. neurone during obstructed self-generated flexion movement, followed by powerful flexion to overcome the impediment. Same experiment as in Fig. 8.

experimenter. When the cat withdrew the limb, some e.m.g. developed along with activity of the nigral unit. The experimenter then let the paw go and the cat fully flexed its limb. In successive trials, despite some variability, these self-generated flexion movements were regularly preceded and accompanied by increased activity of the s.n.r. neurone.

Whenever such self-generated movements were firmly obstructed by the experimenter, this was regularly associated with powerful activation of this type of s.n.r. neurone. Such a discharge pattern is shown in Fig. 9. The experimenter firmly held the animal's forepaw during attempted flexion. Towards the end of the record, the cat overcame the obstruction and made a brisk, powerful flexion movement. During such trials, the nigral unit discharged well in excess of 200 impulses/s. A comparable discharge pattern was observed during imposed movements involving substantial resistance by the animal.

DISCUSSION

Identification of s.n.r. neurones

In the present experiments 96 of 109 s.n.r. neurones were classified as presumed non-dopaminergic neurones on the basis of their stereotaxic location and the differences in their patterns of firing from dopaminergic neurones of the nigro-striatal projection (Bunney *et al.* 1973; Guyenet & Aghajanian, 1978; Steinfels *et al.* 1981; Trulson, Preussler & Howell, 1981). The small number of dopaminergic pars compacta (s.n.c.) neurones (13 out of 109) was not surprising, since the lateral part of s.n. is known to be largely composed of non-dopaminergic neurones which project to thalamus, tectum and reticular formation (Hopkins & Niessen, 1976; Rinvik, Grofova & Ottersen, 1976; Kultas-Ilinsky, Ilinsky, Massopust, Young & Smith, 1978; Usunoff, Hassler, Romansky, Usunova & Wagner, 1976).

Since the s.n.r. of the cat contains output neurones, interneurones and fibres '*en passant*' (Afifi, Bahuth & Jabbur, 1970; Rinvik, 1972; Juraska, Wilson & Groves, 1977), the possibility that our sample included records from the latter two populations should be considered. Three factors argue that recordings were preferentially, if not exclusively, made from output neurones: (i) unitary recording is inevitably biased towards large neurones which have been shown to be output neurones (Danner & Pfister, 1982); (ii) with the technique employed (tip of electrodes 25 μm diameter) it was virtually impossible to record from fibres as indicated by the lack of unitary recordings from seven electrodes which happened to be wrongly placed in the medial lemniscus or the cerebral peduncle; (iii) with similar electrodes, recordings from fibres < 10 μm diameter in dorsal roots of the conscious, freely moving animal have never been obtained (Prochazka & Wand, 1981). As the diameters of *ca.* 98% of lemniscal and cortico-spinal tract fibres are in this range (Dilly, Wall & Webster, 1968; Wiesendanger, 1969), this further argues against our recordings as having been from '*en passant*' fibres.

Responses to skin stimulation

The sensory input generated by light tactile stimulation of the hairy and glabrous skin presumably derives predominantly from activation of sensitive mechanoreceptors in skin and subcutaneous tissue (for references see Burgess & Perl, 1973) and probably low-threshold muscle receptors (Prochazka *et al.* 1979; Prochazka & Wand, 1980).

S.n.r. neurones responding to skin stimulation invariably increased their discharge rates. Most investigators testing the responses of s.n.r. neurones to peripheral stimulation in the anaesthetized rat (Hommer & Bunney, 1980) and cat (Féger *et al.* 1978; Harper *et al.* 1979) have reported increases in discharge, although a small fraction of the recorded neurones did show reductions in firing (Hommer & Bunney, 1980; Yoshida, 1981). The stimulation procedure employed in these cases, however, was high-threshold electrical stimulation of peripheral nerve trunks which most likely also included activation of group III and possibly C fibres. Noxious stimuli (Barasi, 1979) generally depressed firing of nigral neurones.

The latency and form of the responses of s.n.r. neurones to natural peripheral stimulation generally resembled those previously described for electrical stimulation

in the anaesthetized cat (Féger *et al.* 1978) and rat (Hommer & Bunney, 1980), although the response amplitudes tended to be generally smaller and of shorter duration in the anaesthetized preparation. Comparable results were obtained, whenever the chronic cats used in the present study were anaesthetized during recording sessions by I.V. application of various anaesthetics (M. Schwarz & P. Wand, unpublished results).

The pathway by which input from the somatosensory periphery may reach the s.n.r. is not known. The striatum is the main source of monosynaptic afferent input to the s.n. (Dray, 1980) and therefore, the thalamo-striato-nigral projection would have seemed the most likely candidate for relaying these inputs. However, two findings argue against this view: (i) the latencies of peripherally evoked s.n.r. responses were in the majority of cases shorter than the latencies of striatal responses evoked by similar types of stimulation (Albe-Fessard, Rocha-Miranda & Oswaldo-Cruz, 1960; Féger *et al.* 1978; Harper *et al.* 1979); (ii) nigral responses to somatic peripheral stimulation persisted even if structures rostral to the s.n. were removed (Féger *et al.* 1978; Yoshida, 1981). The striato-nigral projection, however, seems to be essential for the peripherally evoked responses of dopaminergic s.n.c. neurones (Hommer & Bunney, 1980; Tsai, Nakamura & Iwama, 1980). Input from the somatosensory periphery alternatively might be relayed to s.n.r. neurones through the cerebello-nigral or raphe-nigral projections (for references see Dray, 1980).

Visual, acoustic and vestibular stimulation

None of the recorded s.n.r. neurones responded either to flashing lights or clicks. In this respect the presumed non-dopaminergic s.n.r. neurones investigated in this study contrast with the dopaminergic s.n.c. neurones in which long-term visual and acoustic stimulation changed background firing activity and altered dopaminergic transmission (Nieuollon, Cheramy & Glowinsky, 1977; Chiodo *et al.* 1980; Steinfels, Heym, Strecker & Jacobs, 1983). In the anaesthetized cat (Yoshida, 1981) light flashes likewise did not modulate s.n.r. unit firing.

In our experiments, the presentation of moving visual stimuli frequently led to net excitation of s.n.r. neurones. This type of response occurred in cells with low background discharge. Some s.n.r. neurones with a steady rapid discharge rate (> 30 impulses/s; Fig. 4*B*) showed decreases in rate related to moving visual stimuli, thus resembling largely the dominant pattern of s.n.r. neuronal discharge in the conscious monkey in relation to visually guided saccadic eye movements (Hikosaka & Wurtz, 1980). The anatomical connexions and temporal relation of cell discharge to saccades led these authors to suggest that some cells in s.n.r. are involved in the initiation and execution of visually guided saccadic eye movements.

In the anaesthetized cat stimulation from both labyrinths had no effect on neurones of s.n.r. (Yoshida, 1981). In the present study, with the restricted methods which can be employed in the conscious cat, there was no really convincing evidence for vestibular input to s.n.r. neurones.

Stimulation of deep structures, passive manipulation of joints and active movements

Due to the relative strength of tap stimuli and the large angular displacement necessary to elicit s.n.r. neuronal responses to mechanical stimulation of deep

structures around single joints, it seems unlikely that the main input derived from low-threshold muscle mechanoreceptors (spindle endings and Golgi tendon organs), but rather from joint mechanoreceptors probably of the Ruffini type (Burgess & Clark, 1969). Regardless of the origin of sensory input, these s.n.r. neurones responded similarly during imposed movements and self-generated movements, whenever the relevant receptors were stimulated. In contrast, the activity of dopaminergic s.n.c. neurones is remarkably unperturbable in the face of ordinary sensory stimulation and is unaltered during movement (Steinfels *et al.* 1981, 1983; Trulson *et al.* 1981).

Little information is available on the relative distribution of input from the somatosensory periphery. Our findings are similar to those of Yoshida (1981) in the anaesthetized cat, where the distribution was clearly biased towards input from the skin. In the conscious monkey (DeLong & Georgopoulos, 1979), the responses of most of the recorded s.n.r. neurones were related to active and passive movements or associated with manipulation of deep structures (muscles, tendons, joints), while responses from superficial structures (skin, hair) were only rarely observed.

A small fraction of s.n.r. neurones showed, at best, weak responses to stimulation of superficial and deep structures, but regularly increased their discharge rate prior to and during active movements. This finding emphasizes the likely 'motor' function of s.n.r. neurones (DeLong & Georgopoulos, 1979), which constitute one output station of basal ganglia (Dray, 1980). Behavioural studies have indeed shown that nigral output neurones projecting to thalamus, reticular formation and tectum (Hopkins & Niessen, 1976; Rinvik *et al.* 1976; Kultas-Ilinsky *et al.* 1978), are associated with motor mechanisms (Di Chiara *et al.* 1977; Garcia-Munoz *et al.* 1977; Kilpatrick & Starr, 1981; Cools *et al.* 1983).

Functional considerations

The facts that (i) non-dopaminergic s.n.r. neurones did not respond to typical arousal stimuli (light flashes, clicks), (ii) very weak natural stimuli were highly effective in changing neuronal activity and (iii) latencies were short and stable, suggest that these neurones respond to 'specific' stimuli rather than being activated by an 'unspecific arousal' reaction. In this respect they clearly differ from dopaminergic s.n.c. neurones (Nieoullon *et al.* 1977; Barasai, 1979; Tulloch & Arbuthnott, 1979; Chiodo *et al.* 1980; Tsai *et al.* 1980; Steinfels *et al.* 1983). On the other hand, a certain degree of specificity at the level of s.n.r. is apparently lost, since there is a considerable convergence of inputs from different sensory modalities and different parts of the body, and no somatotopic organization could be found in the present experiments. It therefore seems unlikely that the s.n.r. is involved in simple reflex loops controlling variables such as force or length of particular muscle groups.

More probably, s.n.r. neurones may participate in the gating and sequencing of motor programmes. Several lines of evidence support such a concept. First, careful electrical stimulation of s.n.r. never elicited muscle contractions or overt limb movements (Winkelmüller, 1972). Rather, changes were found in the level of excitability in α-motoneurones (Stern & Ward, 1962; York, 1972), and the firing levels of γ-motoneurones (Wagner & Kalmring, 1968) and spinal interneurones, i.e. Renshaw cells and Ia inhibitory interneurones (Benecke, Hagenah, Henatsch & Schmidt, 1975). Secondly, in both monkey (DeLong & Georgopoulos, 1979) and cat

(present results) the firing of some s.n.r. neurones was regularly temporally related to self-generated movements, whilst other s.n.r. neurones responded to convergent somatosensory input, the relative proportions differing between the two species. Thirdly, in the present experiments the 'motor' fraction of s.n.r. neurones, even if small, regularly exhibited its most prominent increase in discharge rate, whenever an imposed movement was resisted by the cat or a self-generated movement by the animal was obstructed by the experimenter, i.e. whenever the animal changed its motor strategy to try to overcome an external impediment. Recording of low-threshold muscle mechanoreceptors in intact cats has revealed that in this latter condition the previous dominant moderate static fusimotor action on muscle spindle endings was removed and replaced by tonic dynamic fusimotor action (Prochazka & Wand, 1981). In the anaesthetized preparation, it has been demonstrated that functional activation of s.n.r. neurones, by block with picrotoxin of GABA-mediated inhibition, could actually depress static fusimotor action, at least on hind limb flexor muscle spindle primary endings (Wand, Schwarz, Kolasiewicz & Sontag, 1981).

Taken together, these findings indicate that the s.n.r. may influence spinal structures of the final 'motor output stage' (Hultborn, Lindström & Wigström, 1979), i.e. α- and γ-motoneurones, Ia inhibitory interneurones and Renshaw cells. These components of the final 'motor output stage' are argued to serve as a 'variable gain regulator' at motoneuronal level in order to obtain an optimum resolution in force generation during weak as well as strong contractions (Hultborn *et al.* 1979). Deficits in s.n. function have indeed been shown to be associated with deficits in grading of voluntary force. Hallett & Koshbin (1980) demonstrated in e.m.g. studies that the difficulty experienced by patients with Parkinsonism to move fast is due to an inability to adjust the amplitude of the first burst of skeletomotor activation initiating a fast movement.

It is suggested that neurones of the s.n.r. respresent an output station of the basal ganglia which determines the spinal 'motor set-point', in that this structure is involved in the subconscious processing of multimodal sensory and C.N.S. information, which is required to pre-set appropriate gains and biasses of spinal neurones, thus enabling the executing motor systems (cerebral cortex and spinal cord) to adequately deal with changing motor requirements.

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