Responses of Thalamic Neurons to Input From the Male Genitalia

CHARLES H. HUBSCHER1 AND RICHARD D. JOHNSON2

1Department of Anatomical Sciences and Neurobiology University of Louisville, Louisville, Kentucky 40292; and
2Department of Physiological Sciences, University of Florida Brain Institute, University of Florida, Gainesville, Florida 32610-0144

Submitted 19 April 2002; accepted in final form 27 August 2002

Hubscher, Charles H., and Richard D. Johnson. Responses of thalamic neurons to input from the male genitalia. J Neurophysiol 89: 2–11, 2003; 10.1152/jn.00294.2002. There have been relatively few electrophysiological studies, in any species, describing the supraspinal processing of inputs from the male genital tract. The thalamus was the focus of the present study. In 11 urethan-anesthetized male rats, subregions of the thalamus were surveyed for neuronal responses to the search stimulus, bilateral electrical stimulation of the dorsal nerve of the penis (DNP). A total of 133 DNP-responsive neurons were found and further tested for degree of somatovisceral convergence from other peripheral structures. Histological reconstruction of the recording sites revealed that the penile-responsive neurons were distributed among various thalamic subregions. These thalamic subregions included the medial-dorsal nucleus and ventral and lateral thalamic subregions (majority of neurons responsive to both tactile and pinch stimulation of the penis) as well as intralaminar, posterior and reticular subregions (majority responsive to pinch only). Taken together, the data demonstrate the existence of thalamic neurons with inputs from the male genitalia with widespread somatovisceral convergence. These neurons likely contribute to the neural circuitries underlying various aspects of penile sensation associated with reproductive and nociceptive events.

INTRODUCTION

Our knowledge of the central processing of inputs from the male genitalia is quite limited. Peripherally, the electrophysiology and morphology of primary afferent receptors innervating the genitalia has been characterized for both male (Johnson 1988; Johnson and Halata 1991; Johnson and Murray 1992) and female (Berkley and Hubscher 1995b) rats. These and other studies have shown that the receptors and physiological response patterns (and human percepts) of this sensory system are unlike those found in typical skin or viscera. The external genitalia are classified as mucocutaneous tissue, possessing morphological characteristics of skin and viscera. In males, the glans penis contains an unusually high number of free nerve endings innervated by A-delta fibers (Halata and Munger 1986; Johnson and Halata 1991), particularly around the external urethral orifice. In the rat, primary dorsal nerve of the penis (DNP) afferents have their cell bodies in L6/S1 dorsal root ganglia and many of their central processes terminate bilaterally (McKenna and Nadelhaft 1986; Nunez et al. 1986) on interneurons (Johnson 1989).

The spinal pathways and higher CNS regions involved in processing DNP input have been the focus of our recent electrophysiological investigations. Medullary reticular formation (MRF) neurons, involved in regulating coordinated perineal muscle contractions that mediate sexual reflexes (de Groat and Booth 1993; Marson and McKenna 1990), respond to low- and high-threshold levels of penile stimulation (Hubscher and Johnson 1996) via spinal projections within the dorsal columns and dorsal lateral funiculus, respectively, at the T8 spinal level (Hubscher and Johnson 1999b). The MRF is known to process (Bower 1976; Gebhart 1982; Hubscher and Johnson 1996, 1999a; Peschanski and Besson 1984) and transmit nociceptive inputs rostrally to many thalamic subregions of the rat (Jones and Yang 1985; Peschanski and Besson 1984), particularly in “nonspecific” nuclei. Therefore the objective of the present study was to survey portions of thalamus for low- and high-threshold penile inputs.

Compared with somatosensory pathways from limbs, studies of pathways from pelvic and visceral regions to thalamus have been limited. No electrophysiological studies to date, in any species, describe thalamic input from the male genital tract. In the present study, we hypothesized that DNP input would be found in regions of the thalamus where other pelvic and visceral inputs have already been demonstrated. For example, in females, individual neurons in and around the ventrobasal complex (VB) of the thalamus have been shown to respond to stimulation (noxious and nonnoxious range) of one or more portions of the reproductive tract (uterus, cervix, and vagina) in addition to small cutaneous regions (Berkley et al. 1993a). In contrast, neurons in the intralaminar thalamic complex have been shown to be driven by widespread cutaneous pinch and noxious reproductive organ stimuli (Berkley et al. 1995). Possible sources of reproductive organ input to thalamus in female rats include the MRF (Horney and Rose 1976; Hubscher and Johnson 2001) and/or solitary nucleus (Hubscher and Berkley 1994, 1995) to the intralaminar nuclei, and spinal cord (Berkley et al. 1993b; Wall et al. 1993) and/or dorsal column nuclei (Berkley and Hubscher 1995a) to VB. Other pelvic/visceral inputs that have already been demonstrated to medial and lateral thalamus in rats and other species include the bladder, colon, esophagus, intestines, and cardiovascular structures (Al-Chaer et al. 1996; Berkley et al. 1993a; Bruggemann et al. 1993, 1994a; Chandler et al. 1992; Chernigovskiy and Onis-
The temperature was maintained at 37°C through an esophageal thermistor. Only single neurons well-isolated from surrounding activity were recorded extracellularly, and the spikes were stored on video tape. Conventional electrophysiological instrumentation was used. Electrical and mechanical stimulation ofafferents in the dorsal nerve of the penis. Because many thalamic neurons process convergent ascending somatovisceral sensory inputs, electrical stimulation of the pelvic nerve (PN), distension of the distal colon, and mechanical stimulation of the skin over the whole body (stroke/pressure/pinch) were also tested. Preliminary data have been reported in abstract form (Hubscher and Johnson 1998).

**METHODS**

Eleven male Wistar rats at approximately 90–120 days of age were used in these experiments. Each rat was anesthetized with urethan (1.2 g/kg ip) and supplements of 5% urethan were given as needed (intravenous infusion) to maintain an even level of anesthesia; i.e., just at the point that the corneal reflex is lost. The common carotid artery, jugular vein, and trachea were intubated for the purposes of blood pressure monitoring, intravenous infusion route, and end-expired pCO2 monitoring, respectively (Johnson and Murray 1992). Body temperature was maintained at 37°C through an esophageal thermistor and circulating water heating pad and body coils.

The PN, DNP, and the motor branch of the pudendal nerve were exposed bilaterally beginning with a dorsal midline incision as previously described (Hubscher and Johnson 1996). The head was clamped in a stereotaxic holder, with skull flat. An opening was made over the cortex on the left side by first drilling a small hole into the skull and then expanding the opening with bone rongeurs. The exposure coordinates were 1.5 mm through 4.5 mm caudal to bregma and 4.5 mm from mid-line laterally.

The hindquarters were pivoted with hip pins and the tail tied in an upward direction to allow the penis, ventral abdomen, and perineum to be exposed for surface stimulation. Specially fabricated bipolar silicone-cuff microelectrodes were then placed around both DNPs and both viscerocutaneous branches of the PN (Fig. 1) (Hubscher and Johnson 1996). Recording electrodes were placed bilaterally around each motor branch of the pudendal nerve. The pudendal reflex threshold, assurance of cathodal nerve stimulation, and the segmental synaptic integrity of DNP and PN afferents on pudendal reflex circuitry were continually monitored by recording polysynaptic reflex discharges in left and right pudendal motor axons (Johnson 1995; Johnson and Hubscher 1998).

Glass-coated platinum-plated tungsten microelectrodes (Merrill and Ainsworth 1972) were then advanced stereotaxically into the left thalamus with a stepping microdrive using previously described protocols (Berkley et al. 1993b; Hubscher and Berkley 1994; Hubscher and Johnson 1996). To maximize the number of neurons recorded per experiment, two microelectrodes were lowered simultaneously in the same anterior/posterior plane (see Fig. 1). Two identical sets of recording equipment (preamplifier, audio monitor, analog delay, oscilloscope, PCM adapter, VCR channel) allowed for simultaneous recording from both thalamic microelectrodes. The microelectrodes for most tracks were set at 2,000 μm apart, i.e., one through the medial thalamus and one through the lateral thalamus. Due to the size of the thalamus, the search in the present study was limited to the rostral-to-caudal extent of the ventroposterolateral nucleus [i.e., −2.1 to −4.3 mm caudal to bregma (Paxinos and Watson 1997)]. The depth range for all tracks began at 4,000 μm below the cortex surface and traversed to a depth of 7,500 μm; i.e., from just above to just below the thalamus (Paxinos and Watson 1997). Single identified neurons were recorded extracellularly, and the spikes were stored on video tape. Conventional electrophysiological instrumentation was used. Only single neurons well-isolated from surrounding activity were reported in abstract form (Hubscher and Johnson 1998).

**FIG. 1.** Diagram illustrating the experimental setup for bilateral nerve stimulation (S) and recording (R) from segmental sites and bilateral recording sites in thalamus (see details in METHODS). Schematic sketch of the L6 spinal cord shows the hypothetical segmental inputs from the dorsal nerve of the penis (DNP) and pelvic nerve (PN) and the pudendal motoneuron cell bodies in the dorsolateral (DL) and dorsomedial (DM) nuclei. AV, anteroventral; CL, centrolateral; CM, centromedial; LDDM, lateraldorsal, dorsomedial; LDVL, lateraldorsal, ventrolateral; PC, paracentral; PV, paraventricular; Rt, reticular; VL, ventrolateral; VM, ventromedial; VPL, ventral posterolateral; VPM, ventral postero medial; Sub, submedius. Thalamic diagram modified from Paxinos and Watson (1997).
counted in the sample. Single neuron isolation was established and maintained by monitoring the action potential on an oscilloscope with a spike-triggered analog delay module. Careful records of the stereotaxic location of each neuron were kept (track location and depth). These locations were confirmed and/or adjusted with postmortem histological reconstructions.

The peripheral search stimulus consisted of bilateral electrical stimulation of the DNP (trains of 14 pulses at 70 pps, 100-ms train duration, 1 train/s). Stimulus pulse strength was set at approximately five times pudendal reflex threshold (i.e., 30-50 μA, 0.1-ms duration). These stimuli activate myelinated DNP nerve fibers in the Aβ and Aδ range (Johnson and Murray 1992). Following the isolation of a single neuron, the action potential was continually monitored on an oscilloscope as previously described (Hubschers and Johnson 1996). In addition, when the lateral electrode was positioned in the vicinity of VB, brushing of the skin over the contralateral body was also tested as an indicator of approximate location (as pertaining to previous maps of others) (e.g., Emmers 1964). However, during the course of the study (5th animal of the 11), a neuron was found that responded to stimulation of a small contralateral field on the face and this response was altered with DNP stimulation (even though the neuron itself did not directly respond to DNP stimulation or mechanical stimulation of the penis). Thus for the remaining animals in the study, all the neurons responsive to the contralateral brush stimulus were further tested for convergent effects (cutaneous and pelvic/visceral).

All neurons excited or inhibited by electrical stimulation of the DNP were tested further. To determine the responsiveness to DNP and PN afferent inputs, an electrical stimulation array device was employed. In response to solitary stimulation of afferent fibers in each of the four cuffed nerves, the degree of facilitation or inhibition of the thalamic neuron was determined including the latency of the response. In addition, the bilateral response was determined using single and tandem afferent stimuli. If the thalamic neuron exhibited spontaneous activity, the receptive field (see following text) was scrutinized for evidence of both inhibitory and excitatory zones. A response to stimulation of a peripheral structure/nervous system not noted if the number of spikes fired approximately two times (excitation) or one half (inhibition) of background levels based on digital oscilloscope records. Repetitive stimuli were often required to activate a neuron from a given nerve or receptive field (“wind-up”). If present, spontaneous firing rates were measured from oscilloscope records (mean firing rate over 3-11 stimulus periods) prior to the sequence of testing. The spontaneous firing pattern was classified as regular (tonic discharge with consistent interspike interval) or intermittent (short phasic bursts separated by short quiescent periods).

Hand-held probes were used to map out the characteristics of receptive fields on the penis and surrounding preputial, scrotal, anal, and perineal skin areas in addition to visceral (urethral and colorectal) regions. Stimuli were also presented on each side of the entire body to determine if there were convergent inputs from areas outside the pudendal and pelvic nerve territories. The stimuli and the hand-held probes were as follows: brush, camel’s hair brush; firm touch and pinch [gentle, moderate and strong: (Hubscbers and Johnson 1999a)], small forceps; stretch, small forceps or fine glass rod; pressure, serrated forceps; visceral, glass probe to urethra/colorectal mucosa. In addition, a 1-cm-long latex balloon was used for distension of the descending colon (Berkeley et al. 1993b). Gentle stimuli, generating a low-threshold (LT) neuronal response, included brushing, firm touch, stretching, probing (visceral), and pressure. Intense stimuli, generating high-threshold (HT) neuronal responses, included pinching and distention (visceral).

At the end of the experiment, the animal was killed with an anesthetic overdose and perfused transcardially with 0.9% saline followed by 10% formalin. The block of brain stem tissue containing the recording sites was removed and stored in a 10% formalin/30% sucrose solution. Microelectrode tracks were visualized in 50-μm vibratome sections stained with cresyl violet. The microelectrode tracks and recording sites were reconstructed under light and dark field illumination (Paxinos and Watson 1997) as previously described (Berkeley et al. 1993b; Johnson and Hubscber 1998).

RESULTS

A total of 48 electrode tracks in 11 rats encompassed the search region within the thalamus (see shaded areas in Fig. 2). In all but five of these tracks, neurons were found that responded to the search stimulus, bilateral electrical stimulation of the DNP (n = 133). A histological reconstruction of the location of these DNP-responsive neurons is presented in Fig. 2. Thalamic subregions surveyed include the following: intralaminar (centromedial, centrolateral), lateral (dorsal, posterior), medial (dorsal: central, lateral, and medial), ventral (anterior, medial, lateral, posteromedial, posterolateral), posterior, submedius, and reticular nuclei.

Properties of DNP-responsive neurons

Most of the 133 neurons responding to bilateral electrical DNP stimulation were excitatory (n = 122; 92%). Half of the thalamic neurons with excitatory responses to DNP stimulation (61 of 122) had no resting discharges. The remaining 72 thalamic neurons (61 excitatory, 11 inhibitory) had resting discharges with patterns that were either regular (19%) or intermittent (81%). The 14 neurons with a regular resting discharge had a firing rate of 24 ± 5 (SE) spikes/s. Eleven of these neurons were inhibited by stimulation of the DNP (and its convergent receptive field territories), and the majority were located in the reticular thalamic region. Those neurons (n = 58) with an intermittent resting discharge had a bursting pattern that was either high frequency (15; 21% of total intermittent) or low frequency (43; 60% of total intermittent). Those with a high-frequency intermittent burst of activity were most often found in the ventral and lateral subthalamic regions. In contrast, neurons with a low-frequency intermittent pattern were found throughout all of the thalamic subregions surveyed. These neurons had a mean firing rate of 4 ± 0.4 spikes/s.

Response characteristics to stimulation of the DNP/penis

All of the DNP-responsive neurons tested responded to both ipsilateral and contralateral DNP stimulation and the bilateral responses were often additive. Neuronal response latencies to DNP stimulation varied from 112 to 572 ms, with a mean ± SE latency of 336 ± 13 ms. The neuronal responses to noxious mechanical stimulation of the penis were rarely time-locked to the stimulus. On occasion, afterdischarges, usually upward of several seconds, lasted up to several minutes.

Of the 133 DNP-responsive neurons, all had receptive fields on the penis. Of these, 84 were low threshold; i.e., the neuron responded to gentle stroking of the glans (see example in Figs. 3 and 4), although it is important to note that the stimulation was applied under conditions of penile detumescence rather than tumescence, the latter condition having been shown to increase DNP afferent firing frequency (Johnson 1988). The location of the neurons to LT penile stimulation were found in the medial-dorsal, ventral, and lateral thalamic nuclei. Of the 84 neurons, 23 required wind-up (5 trains on average, given at a rate of one train per second—see METHODS) with bDNP.
FIG. 2. Summary of the location of single neurons in the thalamus responsive to bilateral stimulation of the DNP (●, ○, □; n = 133) and neurons responsive to stimulation of small unilateral cutaneous receptive fields but not DNP (○; n = 26). ○, search regions. Distances in mm are relative to bregma. LPLR, lateral posterior, laterorostral; LPMR, lateral posterior, mediorostral; MDC, mediodorsal, central; MDL, mediodorsal, lateral; MDM, mediodorsal, medial; Po, posterior; SubD, submedius, dorsal; SubV, submedius, ventral; VA, ventral anterior; VPPC, ventral posterior, parvicellular. Thalamic diagrams modified from Paxinos and Watson (1997).
stimulation to respond and 13 of these neurons were located in the lateral-dorsal subnuclei (see Fig. 2). The remaining 49 of the 133 DNP-responsive neurons responded to pinching of the penis, mostly to the external urethral orifice ("cup") and/or glans region. Of the 39 neurons located in the intralaminar, posterior and reticular nuclei, 33 (85%) were of this type. Interestingly, the few neurons isolated in the reticular nucleus were inhibited by stimulation of the penis and the DNP as was found in the intermediate reticular nucleus of the MRF (Hubscher and Johnson 1996). A summary and comparison of response characteristics by location is provided in Fig. 5.

Convergent somatovisceral inputs on DNP-responsive thalamic neurons

One hundred and twenty-nine of the DNP-responsive neurons (97%) were additionally responsive to bilateral electrical stimulation of PN. All of these neurons responded to both ipsi- and contralateral PN stimulation, and the majority were excitatory (92%). All of these neurons responded to mechanical stimulation of one or more cutaneous territories innervated by the PN (e.g., dorsal perineum, anus). Just one of the visceral territories innervated by the PN was tested; i.e., distension of the descending colon. Overall, only 10 of the PN-responsive neurons responded to colon stimulation. An example is provided in Fig. 4. These neurons accounted for 18% of the neurons in the four thalamic subnuclei in which they were found: the medial-dorsal central, ventrolateral, lateral-dorsal/posterior, and submedius thalamic nuclei.

The same neurons, and the four not responsive to PN stimulation, were also responsive to touching and/or pinching (bilateral) of areas outside the DNP/PN-innervated territories (see examples in Figs. 3 and 4). Many of these thalamic neurons had convergent receptive fields as seen previously in our MRF recordings (Hubscher and Johnson 1996); e.g., responses to pinching of the ears and toes (both forepaw and hindpaw—often around the joints). Other neurons had whole body convergent cutaneous fields (35% of the total DNP-responsive neurons). Whereas the majority of responses from cutaneous territories were to high-threshold levels of stimulation (pinch), a number of neurons were found that responded to low-threshold (stroking/gentle pressure) stimulation of the dorsal trunk and face (see Figs. 3–5). Most of these were located in the lateral and medial-dorsal thalamic subnuclei (see Figs. 2 and 5).

Ventralbasal complex neurons. In addition to the 133 DNP-responsive thalamic neurons, 26 neurons were found to respond to brushing of a small contralateral skin region (Fig. 2, ). These neurons did not respond to DNP stimulation. For one of these neurons, a split receptive field was identified (see Fig. 6); this does not conform to the traditional views of VB
response properties. In addition, during the course of experimentation, the responses of two of the neurons located in the ventroposteromedial (VPM) part of VB (see at −3.6 mm level in Fig. 2) was altered with stimulation of the DNP (counted toward the 133 total DNP-responsive neurons). The responses of one of these neurons is provided in Fig. 7. Pinching the toes of either hindfoot also modulated the responses to facial stimulation (i.e., the convergence on these neurons was not limited to the pelvic region).

**DISCUSSION**

The present study documents for the first time, using electrophysiological techniques, the existence of inputs from the genitalia to thalamus in the male rat. The sampling of various subregions in this initial survey of single neurons within the thalamus demonstrates that electrical stimulation of the DNP activates neurons contained within widespread thalamic regions in anesthetized rats. The results further demonstrate that DNP-responsive thalamic neurons receive convergent inputs from large, bilateral somatic territories as well as from pelvic-visceral territories, which adds to well established data, in a number of species, of widespread somatosensory inputs onto several subregions of the thalamus. Variations in neuronal response properties (excitation vs. inhibition; low vs. high threshold; DNP alone vs. DNP + PN) and location (intralaminar, ventral, posterior, etc.) suggest that these neurons may...
serve several different functions within the realm of male reproductive mechanisms and sensation.

DNP-RESPONSIVE NEURONS. Many neurons throughout thalamus responded to stimulation of DNP. The number of neurons per electrode track may be an underestimate of DNP input to this region because the search stimulus only activated Aβ and Aδ DNP afferents. The DNP also contains a large population of C fibers (Johnson and Halata 1991).

All of the neuronal responses to stimulation of the DNP in the thalamus, like in the MRF, could be elicited by bilateral stimulation. These findings are consistent with behavioral data where bilaterally complete, but not partial, sectioning of the DNP results in the loss of ejaculatory function (Sachs and Meisel 1988). The majority of neurons responsive to DNP stimulation had no background activity, which was also found for DNP-responsive MRF neurons. However, the response latencies for the DNP-responsive thalamic neurons were on average three times longer than those found in MRF, suggesting that at least some of these inputs to thalamus from the penis may be conveyed rostrally via a spino-reticulo-thalamic pathway that has been implicated in the transmission of nociceptive information (Peschanski and Besson 1984).

Some of the DNP-responsive thalamic neurons, like those studied in the MRF, required wind-up with bilateral electrical stimulation of the DNP (on average, 7 trains) to respond. This finding suggests that in a functional context, the neurons requiring wind-up may be firing near the threshold required for the ejaculatory response, which depends on a gradual build-up of activity produced by multiple rapid intromissions (Sachs and Meisel 1988). Wind-up, a response and/or increase in response requiring repeated exposure to a stimulus, was also occasionally a prerequisite for detection of convergent cutaneous inputs. Multiple brief stimuli to the same cutaneous territory or prior stimulation of another territory with a lower response threshold were sometimes necessary to reach the response threshold and then sustain the response. Aside from the DNP stimulus, the convergent territory most often used for wind-up was the ears (i.e., typically have a lower response threshold) (Hubscber and Johnson 1996).

DNP VS. PN. Most DNP-responsive neurons responded to bilateral (and unilateral) stimulation of the PN. This high degree of convergence differs from what was found previously in the MRF (Hubscber and Johnson 1996), where only one-half of the DNP-responsive neurons responded to stimulation of the PN. This difference can be explained by the multitude of inputs to thalamus (e.g., Desbois and Villanueva 2001; Herkenham 1979; Krout and Loewy 2000; McAllister and Wells 1981; Shibata 2000), only some of which are from the MRF (e.g., Kevetter and Willis 1982; Peschanski and Besson 1984). Likewise, the MRF projects to many different areas (Jones 1995; Jones and Yang 1985), only some of which are located in the thalamus. Note that it is possible that there is a group of neurons that may respond to unilateral and/or bilateral stimulation of the PN but not the DNP (search stimulus). This possibility will be addressed in future studies.

In contrast with the DNP, which innervates the entire penis and prepuce, the viscerocutaneous branch of the PN innervates multiple visceral organs and a small perianal skin region (Lucio et al. 1994). Stimulation of PN-innervated cutaneous regions produced many thalamic neurons responding to electrical stimulation of PN. In addition, responses were also expected from PN-innervated visceral territories. In the present study, only distention of the distal descending colon was tested. Responses were found in similar thalamic subregions (see RESULTS) as reported in three previous studies (see Berkley et al. 1993b; Kawakita et al. 1997; Yang et al. 1998). In the present study, however, only 18% of the neurons in these subregions responded. This value is significantly lower than the numbers found in two of these three previous studies [79% overall (Yang et al. 1998); 80% overall (Kawakita et al. 1997)]. This difference may be due to the size and location of the stimulus itself, and/or differences in the search protocols. For example, studies examining neural responses to colorectal distention use a much larger balloon (7–8 cm long) and stimulate the rectum in addition to the distal portion of the descending colon (Al-Chaer et al. 1996; Kawakita et al. 1997; Ness and Gebhart 1987; Yang et al. 1998). In the present study, a 1-cm balloon restricted to the descending colon was used.

PERIPHERAL RECEPTIVE FIELDS. All neurons that responded to bDNIP and bPN electrical stimulation also responded to stimulation of their respective cutaneous and mucocutaneous targets [as discussed in the preceding text and as seen previously in MRF (Hubscber and Johnson 1996)]. Convergent input from sources outside the pudendal/pelvic territories were also found, including inputs confined to distal body parts (e.g., ears, toes of forepaw and hindpaw). Only some of the neurons received convergent inputs from the entire body. In most thalamic regions, the responses were elicited by noxious levels of mechanical stimulation (moderate to strong pinch). In the lateral (dorsal and posterior) and medial-dorsal subnuclei, some neurons were found with low-threshold cutaneous receptive fields. The findings of noxious cutaneous inputs with large, mostly excitatory and bilateral response properties/receptive field characteristics is consistent with previous electrophysiological recording studies in rat thalamus (Dostrovsky and Guilbaud 1990; Guilbaud et al. 1980; Kawakita et al. 1993; Prieto-Gomez et al. 1989). However, evidence showing neurons with small contralateral receptive fields with convergent visceral input (e.g., Al-Chaer et al. 1996; Berkley et al. 1993b; Yang et al. 1998) suggest that DNP-responsive thalamic neurons represent a distinct subpopulation of thalamic neurons. Moreover, none of the low-threshold (tactile) penile-responsive neurons in the present study lacked a cutaneous convergent territory, suggesting that the receptive field specificity typical for many thalamic cutaneous neurons may not exist for mucocutaneous penile tissue.

There were also several VB neurons tested that had response characteristics that differed from the traditional organization of this region (see Figs. 6 and 7), i.e., exhibited a split receptive field and a modulatory effect from distant regions outside the receptive field. The relatively small number observed does not reflect the actual number of these neurons that may be present because their observation in the present study was accidental and was not systematically tested. Considerations of specific circumstances for modulation of somatic receptive fields have been discussed elsewhere for a number of pelvic viscera (see Functional Considerations in Berkley et al. 1993a). Response modulation of VB neurons with DNP (i.e., penile) stimulation could exert its influence during mating, for example. However, nonspecific modulation was observed (i.e., noxious stimulation).
of various cutaneous fields exerted the same modulatory effect, suggesting that these neurons may be part of the circuitry important for more global functions, such as autonomic responses related to behavior and emotion (Allen et al. 1991; Cechetto 1987).

VARIATIONS AMONG DIFFERENT THALAMIC SUBNUCLEI. DNP-responsive neurons were found throughout the thalamus. Regional differences in response properties were observed (Figs. 2 and 5). For example, the majority of neurons tested within intralaminar and posterior nuclear regions responded to high-threshold levels of penile stimulation versus the majority of those in medial and ventral areas which responded to both low- and high-threshold levels of stimulation (Fig. 5). In contrast, most DNP-responsive neurons in lateral-dorsal divisions of thalamus required wind-up with either the DNP search stimulus or a sustained pinch to respond (usually to a distal cutaneous structure such as the ears or a single digit of the forepaw or hindpaw). In addition, most of the neurons with spontaneous activity that were inhibited by DNP stimulation were localized within the reticular nucleus of the thalamus, which is known as a generator of GABA-mediated inhibition within the thalamus (Thomson 1988). These differences in responses among the various thalamic subregions are likely due to the different functions subserved by each of these regions (see FUNCTIONAL CONSIDERATIONS).

DNP-responsive neurons found in what constitutes the “lateral” thalamus were located in the surround areas of the ventrobasal complex (VB) and not within the VB proper (see Fig. 2). These results are similar to those found for visceral inputs in the cat (Bruggemann et al. 1993, 1994b) but are different from those found for the squirrel monkey (Bruggemann et al. 1994a) where visceroreceptive neurons were found in VPL proper. These variable results may be due to species differences. However, other studies using rats have found visceroreceptive neurons (uterus, colon) in VB proper (Al-Chaer et al. 1996; Berkley et al. 1993a). These differences may be due to one or more of the following: different search protocols, different types of tissue (visceral vs. mucocutaneous), sex differences, or other methodological differences (such as depth of anesthesia [Friedberg et al. 1999]).

Two neurons with small contralateral receptive fields on the face found medially in VB (see Figs. 2 and 7), however, were not DNP-responsive but were modulated when stimulated simultaneously with DNP or pinching of the penis. This effect was not exclusive to the penis (mucocutaneous tissue) because pinching of a single digit on the hindpaw also modulated the response as well. Perhaps some of the DNP-responsive neurons in adjacent nuclei that receive convergent inputs from many parts of the body have dendritic arbors that extend into VB to exert this modulatory effect. These effects once again reflect the dynamic nature of central neurons (see previous discussions on access vs. usage in Berkley and Hubscher 1995b; Hubscher and Johnson 1999b).

THALAMIC INPUTS/OUTPUTS. Activation of neurons in the parvicellular part of the subparafascicular nucleus in caudal thalamus has been demonstrated following sexual behavior (Veening and Coolen 1998). These neurons have been shown to be interconnected (bidirectional) with the medial preoptic area, which is an essential site for the regulation of male sexual behavior (Coolen et al. 1998). The pathways through which DNP inputs reach the thalamus, however, are unknown and will be the subject of future studies. All of the thalamic regions containing DNP-responsive neurons receive inputs from multiple sources. Some possibilities may include both direct second-order projections from neurons within one of the three main ports of entry into the CNS (i.e., spinal cord, dorsal column nuclei, or solitary nuclei) as well as indirect projections via multiple synaptic relays (e.g., a spinoreticulothalamic pathway or a postsynaptic-dorsal-column-medial lemniscal pathway).

The thalamus relays information from major sensory and motor systems to cerebral cortex. The location of the outputs to cortex in the rat relative to the genitalia are unknown. Direct recordings of cortical evoked responses in man to electrical DNP stimulation (Bradley et al. 1998) demonstrated a large area of primary sensory cortex activated by stimulation of penile afferent fibers and concluded with a proposed modification of the human male sensory homunculus. Recent investigations of the representation of pelvic/visceral sensory inputs in the human brain have shown a vast network of cortical regions activated during micturition (Nour et al. 2000), anal/rectal (Lotze et al. 2001), and esophageal (Aziz et al. 2000) stimulation. A number of experimental studies in the rat have shown cortical neurons with visceral inputs, many with somato-visceral convergence (Allen et al. 1991; Follett and Dirks 1994, 1995; Ito 1998).

FUNCTIONAL CONSIDERATIONS. Neurons in several different thalamic subregions responded to inputs from the male genitalia. These regions are known to serve many different functions (e.g., Davis et al. 1995; Duncan et al. 1998; Lenz and Dougherty 1997; McAlonan et al. 2000; Portas et al. 1998; Shibata 2000; Sziklas and Petrides 1999). For example, nociceptive neurons in medial and lateral thalamus are likely involved in the processing of information related to affective/motivational and sensory discriminative aspects of pain, respectively (see references in Apkarian and Shi 1994). These functional implications for nociceptive thalamic neurons are based on sources of inputs to some of the subregions within medial and lateral thalamus [spinoreticulothalamic vs. spinore- ticulothalamic, respectively (Peschanski and Besson 1984)], response properties for many of the neurons such as receptive field size/degree of convergence [large/bilateral/complex vs. small/unilateral, respectively; see references in Willis and Coggeshall (1991)] and outputs to cortex (Willis 1995).

The variations in DNP-responsive thalamic neurons (e.g., low threshold vs. high threshold vs. wind-up dependent) support the notion that these neurons may be involved in the processing of information important for a number of functions related to penile sensation, including one or more of the following: arousal, attention, nociception, and emotion. Future attempts to determine specific features of the various DNP-responsive thalamic neurons, such as the various sources/targets of their inputs/outputs, respectively, should narrow the possible list of related functions for this widespread presence and distribution of neuronal responsiveness to DNP stimulation within the thalamus.

The authors thank V. Dugan for excellent technical assistance. Experiments were performed at the University of Florida and were supported by a fellowship to C. Hubscher from the Paralyzed Veterans of America.
and a grant from the Brain and Spinal Cord Injury Rehabilitation Trust Fund of Florida.

REFERENCES


