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13. ABSTRACT (Maximum 200 words) Work carried out on AFOSR 90-0266 made major progress in several areas, including: 1) Development of technology for recording large numbers of single neurons (up to 64) simultaneously through microwires implanted at multiple levels of the somatosensory system in awake rats. 2) Utilization of an operant conditioning paradigm for investigating the detection and processing of sensory cues which trigger an active motor response. 3) Demonstration that neuronal responses in the SI and MI cortices to such sensory cues are increased when they are used to trigger a conditioned motor response. 4) Demonstration that this conditioning increases the prevalence of functional connections between neurons in the SI and MI cortices. 5) Used quantitative techniques to defined dynamic and distributed properties of receptive fields in the somatosensory cortex and thalamus. 6) Developed the use of multivariate statistical techniques to define population coding within ensembles of recorded neurons. 7) Continued to define neuroanatomical substrates for processing within this system.					
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FINAL TECHNICAL REPORT

AFOSR 90-0266: CORTICAL MECHANISMS OF ATTENTION

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III. LIST OF PUBLICATIONS (1990-1993)

A. Published papers (1990) supported by AFOSR 90-0266:

1. Chapin, J.K. and Lin, C.-S. (1990) The somatosensory cortex of rat. In R. Tees and B. Kolb Eds. The Neocortex of Rat Academic Press.
2. Shin, H.-C. and Chapin, J.K. (1990) Mapping the effects of motor cortex stimulation on somatosensory relay neurons in the rat thalamus: direct responses and afferent modulation. *Brain Res. Bull.* 24:257-265.
3. Shin, H.-C. and Chapin, J.K. (1990) Modulation of afferent transmission to single neurons in the ventroposterior thalamus during movement in rats. *Neurosci. Letters* 108:116-120.
4. Patel, I.M. and Chapin, J.K. (1990) Ketamine effects on somatosensory cortical single neurons in behaving rats. *Anesth. & Analg.* 70:635-644.
5. Lin, C.-S., Nicolelis, M.A.L., Schneider, J.S. and Chapin, J.K. (1990) A major direct GABAergic pathway from zona incerta to neocortex. *Science* 248:1553-1556.
6. Shin, H.-C. and Chapin, J.K. (1990) Movement-induced modulation of afferent transmission to single neurons in the ventroposterior thalamus and somatosensory cortex in rat. *Exp. Brain Res.* 81:515-522.
7. Shin, H.-C. and Chapin, J.K. (1990) Mapping the effect of SI cortex stimulation on somatosensory relay neurons in the rat thalamus: direct responses and afferent modulation. *Somatosens. & Motor Res.* 7:421-434.
8. West, M.O., Carelli, R.M., Pomerantz, M., Cohen, S.M., Gardner, J.P., Chapin, J.K., and Woodward, D.O. (1990) Single units in the dorsolateral striatum of the rat are correlated with specific locomotor limb movements. *J. Neurophys.* 64:1233-1246.

Abstracts (1990):

9. Chapin, J.K. and Shin, H.-C. (1990) Heterosynaptic and behavioral modulation of functional connections between neurons simultaneously recorded in cortex and thalamus. *Abst. in Soc. Neurosci. Mtg. 1990*
10. Utz, J.P., Nicolelis, M.A. and Chapin, J.K. (1990) Emergent properties revealed in multi-layer neuronal network models: feedforward vs. feedback inhibition. *Abst. in Soc. Neurosci. Mtg. 1990*
11. Fisher, T.M., Nicolelis, M.A.L. and Chapin, J.K. (1990) Chaotic dimensionality of cortical neuronal discharge patterns is altered by anesthetic state. *Abst. in Soc. Neurosci. Mtg. 1990*
12. Lin, C.-S., Nicolelis, M.A.L., Chapin, J.K. and Kaas, J.H. (1990) Functional characteristics of a direct GABAergic pathway from zona incerta to neocortex in rodents and primates. *Abst. in Soc. Neurosci. Mtg. 1990*
13. Nicolelis, M.A.L., Lin, C.-S. and Chapin, J.K. (1990) Neonatal whisker removal preserves a normally transient projection from the medial geniculate to the somatosensory cortex in rats. *Abst. in Soc. Anat. Mtg. 1990*

B. Published papers and abstracts (1991) supported by AFOSR 90- 0266:

14. Nicolelis, M.A.L., Lin, C.-S., and Chapin, J.K. (1991) Early postnatal development of thalamocortical and corticocortical connections in rat. *Somatosens. & Motor Res.* 8:
15. Nicolelis, M.A.L., Chapin, J.K. and Lin, C.-S. (1991) Thalamic plasticity induced by early whisker removal in rats. *Brain Res.* 561:344-349.
16. Nicolelis, M.A.L., Chapin, J.K., and Lin, C.-S. (1991) Neonatal whisker removal in rats stabilizes a transient projection from the auditory thalamus to the primary somatosensory cortex. *Brain Res.* 567:133-139.

Abstracts (1991):

17. Kosobud, A.E., Shin, H.-C., and Chapin, J.K. (1991) The effect of ethanol on sensory processing in rat somatosensory (S1) cortex and VPL thalamus during locomotion. *Abst. in Ann. Mtg. Res. Soc. Alc.*
18. Lin, R.C.-S., Nicolelis, M.A.L., McLean, J., and Chapin, J.K. (1991) The topographic organization of the rat zona incerta. *Abst. in Soc. Neurosci.* 119.5
19. Chapin, J.K. and Mariano, R.T. (1991) Multineuronal responses in the SI and MI cortex during learning of a stimulus cued motor task. *Abst. in Soc. Neurosci.* 248.17
20. Utz, J.P., Waterhouse, B.D., and Chapin, J.K. (1991) Effects of circuit oscillations and norepinephrine-like modulation in a neuronal network model of the somatosensory system. *Abst. in Soc. Neurosci.* 248.18
21. Fisher, T., Gupta, A., Nicolelis, M.A.L., and Chapin, J.K. (1991) Modeling the circuit characteristics which may underlie oscillatory properties of thalamocortical networks. *Abst. in Soc. Neurosci.* 248.19
22. Nicolelis, M., Lin, C.-S., and Chapin, J.K. (1991) Applying multi-single unit recording techniques to the study of plasticity at multiple levels of the rat trigeminal pathway. *Abst. in Soc. Neurosci.* 248.20
23. Jaslow, R., Nicolelis, M.A.L., Lin, R.C.-S., Chapin, J.K. and Waterhouse, B.D. (1991) Projections from the nucleus paragigantocellularis in the ventrolateral medulla to the neocortex: A double labeling study in the rat. *Abst. in Soc. Neurosci.* 413.3
24. Kosobud, A.E. and Chapin, J.K. (1991) Single unit activity in prefrontal cortex and mediodorsal thalamus in the rat: Behavioral correspondance and effects of ethanol. 631.16

C. Published papers (1992) supported by AFOSR 90-0266:

25. Nicolelis, M.A.L., Chapin, J.K., and Lin, C.-S. (1992) Somatotopic maps within the zona incerta relay parallel GABAergic somatosensory pathways to the neocortex, superior colliculus, and brainstem. *Brain Res.* 577:134-141.
26. Chapin, J.K. (1992) Ethanol effects on cortical circuits during sensory and motor processing. In R.R. Watson, ed. Alcohol and Neurobiology: Brain Development and Hormone Regulation, CRC Press, Boca Raton, FL.

Abstracts (1992):

27. Utz, J.P. and Chapin, J.K. (1992) A large scale computer model of the rat thalamocortical somatosensory system: sensory processing and spatiotemporal oscillations. Abstr. in Mtg. Soc. Neurosci. 1992
28. Fisher, T.M., Nicolelis, M.A.L. and Chapin, J.K. (1992) Sensory and oscillatory properties of simultaneously recorded multi- single units in the thalamic reticular nucleus of the rat. Abstr. in Mtg. Soc. Neurosci. 1992
29. Hashemiyoony, R. and Chapin, J.K. (1992) Oscillatory properties of neurons in a newly defined region of the pretectal area. Abstr. in Mtg. Soc. Neurosci. 1992
30. Bacala, L., Nicolelis, M.A.L. and Chapin, J.K. (1992) Multivariate statistical techniques allow characterization of distributed population codes in simultaneously recorded neuronal ensembles. Abstr. in Mtg. Soc. Neurosci. 1992

D. Published papers (1993) supported by AFOSR 90-0266:

31. Nicolelis, M.A.L., Lin, C.-S., Woodward, D.J. and Chapin, J.K. (1993) Distributed processing of somatic information by networks of thalamic cells induces time-dependent shifts of their receptive fields. *Proc. Natl. Acad. Sci.* 90:2212-2216.
32. Nicolelis, M.A.L., Lin, C.-S., Woodward, D.J. and Chapin, J.K. (1993) Peripheral block of ascending cutaneous information induces immediate spatio-temporal changes in thalamic networks. *Nature* 361:533-536.
33. Shin, H.-C., Park, H.J., and Chapin, J.K. (1993) Differential phasic modulation of short and long latency afferent sensory transmission to single neurons in the ventroposterolateral thalamus in behaving rats. *Neurosci. Res.* 17:117-125.

Abstracts:

34. Chapin, J.K., Woodward, D.J., Bloedel, J.R., Fetz, E.E. and Nicolelis, M.A.L. (1993) Decoding the population code in neuronal networks: new approaches using concurrent multi-channel recordings. *Abst. of Workshop organized by PI at Winter Conference on Brain Research, January, 1993.*

Manuscripts in Preparation:

35. Chapin, J.K. and Mariano, R.T. Distributed sensory and motor information processing in the SI and MI cortex during learning of a stimulus cued motor task.
36. Chapin, J.K. and Nicolelis, M.A.L. Multiple dimensions of information processing in the somatosensory thalamus and cortex defined by principal components analysis.

IV. TECHNICAL REPORT:

General areas of progress: Work carried out on AFOSR 90-0266 made major progress in several areas, including:

- 1) Development of technology for recording large numbers of single neurons (up to 64) simultaneously through microwires implanted at multiple levels of the somatosensory system in awake rats.
- 2) Utilization of an operant conditioning paradigm for investigating the detection and processing of sensory cues which trigger an active motor response.
- 3) Demonstration that neuronal responses in the SI and MI cortices to such sensory cues are increased when they are used to trigger a conditioned motor response.
- 4) Demonstration that this conditioning increases the prevalence of functional connections between neurons in the SI and MI cortices.
- 5) Used quantitative techniques to define dynamic and distributed properties of receptive fields in the somatosensory cortex and thalamus.
- 6) Developed the use of multivariate statistical techniques to define population coding within ensembles of recorded neurons.
- 7) Continued to define neuroanatomical substrates for processing within this system.

(For continuity, the research reported below is grouped according to subject, citing publications in the above list by number.)

A. Behavioral modulation of sensory processing at different levels of the somatosensory system.

Pub. 3: Modulation of afferent transmission to single neurons in the ventroposterior thalamus during movement in rats. This paper describes studies on movement related sensory gating in the VPL thalamic forepaw area of rats. While previous experiments in the SI cortex [8-10] had demonstrated an overall 71% suppression of paw stimulus induced input from the paw during treadmill locomotion, in the thalamus only a 30% reduction was found.

Pubs. 6 and 33: Movement-induced modulation of afferent transmission to single neurons in the ventroposterior thalamus and somatosensory cortex in rat. This paper utilized simultaneous single unit recordings in the forepaw areas of the SI cortex and VPL thalamus to determine the differences in movement related suppression of short vs. longer latency responses to forepaw stimulation. Our available evidence suggests that the short latency responses arise exclusively through the dorsal column nuclei, whereas the longer latency responses may be transmitted in part through extralemniscal systems. It was found that at the cortical level, both the short and long latency responses were strongly suppressed during movement, while at the thalamic level, only the long latency responses were strongly suppressed.

Pub. 19 and 34: Multineuronal responses in the SI and MI cortex during learning of a stimulus cued motor cortex. To define the neuronal network mechanisms by which the cortex processes sensory stimuli to trigger motor responses we trained rats in a task in which they were required to hold their forepaw on a bar and to move the bar immediately after a vibratory cue. Ensembles of neurons were recorded simultaneously through microwire electrodes chronically implanted in the MI cortical forelimb area, and in the SI cortical forepaw-forelimb area, including the granular zone (GZ, homologous with area 3b) and the caudally adjacent perigranular zone (PGZ, homologous with areas 1-2). The GZ neurons had cutaneous receptive fields (RFs) on the forepaw, and PGZ neurons had deep/proprioceptive RFs in the forelimb. In one rat, 22 microwires were implanted, of which 16 recorded discriminable neurons. 100Hz vibratory stimuli produced responses in both GZ and PGZ neurons during rest, but only in GZ neurons during and just before forelimb movement. 50Hz stimuli produced strong excitatory responses in the GZ at 10 msec latency, and weak excitatory or inhibitory responses in the PGZ at 15-20 msec latency. These responses, especially those in the GZs, were markedly increased during trials in which the animal properly moved its forelimb in response to the sensory cue. Initially, the MI neurons had no RFs, and did not respond to the 50Hz cue (though one did respond to 100Hz). However, after the animal learned the task, the MI neurons did respond to the cue, at 20-30 msec latency. Cross-correlating the activity of the simultaneously recorded neurons revealed serial functional connections between neurons within the GZ and PGZ, but not between the PGZ and MI, which nevertheless are known to be neuroanatomically connected. However, after learning the task such serial connections between the PGZ and the MI began to be observed, suggesting a learning related enhancement of the pathway for transmission of cue related sensory information to the MI cortex.

B. Use of spike-triggered cross-correlations to measure serial connections between simultaneously recorded neurons in awake, behaving rats.

Pub. 9: Heterosynaptic and behavioral modulation of functional connections between neurons simultaneously recorded in cortex and thalamus. Spike-triggered cross-correlations between pairs of simultaneously recorded neurons can be used to characterize and measure serial (putatively monosynaptic) transmission between those neurons. Such "serial" connections are distinguished from the more nonspecific "common input" correlations by their extremely discrete, short latency (1-4 msec), and short duration (1-3 msec) responses in

post-spike histograms. Several types of serial connections have been recorded so far, including local cortico-cortical, thalamocortical, corticothalamic, and cuneothalamic. See Exp. Design: Aim II for more details.

C. Neuroanatomical and neurophysiological studies of paths for somatosensory information flow to, and within the SI cortex of rat.

Pub. 1: The somatosensory cortex of rat. In R. Tees and B. Kolb Eds. *The Neocortex of Rat*. This chapter presents an extensive survey of the current state of our knowledge of the neuroanatomy and electrophysiology of the rat somatosensory cortex. Particular emphasis is placed on the subject of this grant, ie. behavioral control of sensory transmission through the neurons in this area. This is supported by previously published and also new unpublished research data from this laboratory.

Pub. 14: Development of corticocortical connections in the rat. This paper reports results of fluorescent retrograde tracer injections in the SI cortex of developing and adult rats. These findings extend our previous findings, identifying three distinct sources of local cortico-cortical connections in the rat SI. These include projections emanating from layers III, V, and VIb. The ipsilateral projections come from distinct layers of cells in layer Va and Vb, with callosal projection neurons interdigitated between.

Pub. 2: Mapping the effects of motor cortex stimulation on somatosensory relay neurons in the rat thalamus: Direct responses and afferent modulation. The MI stimulation had a small but measurable modulatory effect on sensory transmission through the VPL thalamus. The strongest modulation was expressed on neurons located in the periphery of the VPL. Overall, these findings support the idea that the MI's strongest modulatory effects on the lemniscal pathway are at the SI cortical level.

Pub. 7: Mapping the effect of SI cortex stimulation on somatosensory relay neurons in the rat thalamus: direct responses and afferent modulation. Stimulation of the SI cortex produced facilitory followed by inhibitory effects on VPL neurons, both in direct responses and in transmission of afferent transmission through these nuclei. The initial excitatory effects were quite spatially circumscribed, whereas the subsequent inhibitory effects were more broadly felt. These findings are consistent with a model including direct, topographically specific, and excitatory effects of SI corticothalamic efferents on neurons in the VPL and in the thalamic reticular nucleus (RT). The RT neurons could provide most of the subsequent inhibitory responses. Thus, the SI cortex could shape and control its sensory input from the VPL through these corticothalamic systems.

Pubs. 31 and 32: Dynamic and distributed properties of many- neuronal ensembles in the ventral posterior medial (VPM) thalamus of awake rats. The traditional view that the map of the face in the ventral posterior medial (VPM) thalamus is static and highly discrete was derived largely from qualitative studies which reported only small, robust, and non-overlapping receptive fields (RFs). Here, by using more quantitative techniques, we have provided evidence for an alternative hypothesis: that the RFs in the VPM are large and overlapping, and tend to shift as a function of post-stimulus time. These results were obtained through simultaneous recordings of up to 23 single neurons across the whisker representation in the VPM of rats. Under both awake and anesthetized conditions these neurons responded robustly at short (4-6 ms) and/or long (15-25ms) latencies to discrete vibromechanical stimulation of single facial whiskers. Computer graphics were used to construct 3D plots depicting the magnitudes of neuronal responses to stimulation of each of several whiskers, as a function of post-stimulus time. These

"spatiotemporal RFs" demonstrated that: 1- the RFs of many VPM neurons are quite large, covering up to 20 whiskers, and 2- the spatial locations of these RFs may shift dramatically over the first 35 ms of post-stimulus time, especially from the caudalmost to the rostralmost whiskers on the face. These results suggest that the VPM contains a dynamic and distributed representation of the face, in which stimulus information is coded in both spatial and temporal domains. These receptive field properties were subsequently shown to be subject to immediate plasticity after injection of lidocaine in the face. This constitutes further evidence for the dynamic nature of sensory representations in the somatosensory thalamocortical system.

D. Development of many-neuron recording technology:

Pubs. 6,9,19,22,24,28,30-34: Much of our effort in this grant has been devoted to development of techniques for simultaneously recording and discriminating up to 64 single neurons in awake rats. These have been used in many of our recent publications (listed above). In this technique neurons are recorded through arrays of 50 μ microwire electrodes implanted in multiple areas of the brain. In the major work described in pubs. 19 and 34, for example, the forepaw area of the somatosensory (SI) cortex and ventral posterior (VP) thalamus in rats performing a somatosensory discrimination task. To study the effect of behavioral significance on the sensory responsiveness of neurons in this system we have implemented a relatively simple behavioral paradigm: rats are operantly conditioned to make an appropriate forelimb movement immediately upon detecting a vibratory or electrical stimulus delivered to the forepaw or whisker area. We have observed modulation of neuronal responsiveness to this sensory cue over both short and long time courses: 1- From trial-to-trial, SI cortical neuronal responsiveness to the cue was greater when the animal made the appropriate motor response *rapidly enough to obtain a reward*. This may indicate spontaneous variation in the attentional state or motor set of the animal. 2- Over weeks of training in this task, increased responsiveness to the sensory cue was observed among neurons in both MI and SI cortices. Furthermore, the incidence of functional connections between these areas increased. This may indicate a functional reorganization of the cortex caused by the training.