Anesthesiology
58:38–43, 1983

The Local Metabolic Effects of Somatosensory Stimulation in the Central Nervous System of Rats Given Pentobarbital or Nitrous Oxide

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General anesthetics are used to eliminate perception of stimuli, yet there have been few studies of the cerebral metabolic effects of stimulation during anesthesia, and of these studies, the results are discrepant. The authors therefore applied the quantitative 2-[^{14}C]deoxyglucose method in a study of the effects of electrical stimulation (5 volts, 0.5 ms, 10 Hz) of a rat's saphenous nerve on glucose utilization in structures of the sensory pathway after administering pentobarbital or nitrous oxide. Under both conditions, stimulation produced a 75 to 108% increase in glucose utilization in the ipsilateral dorsal horn of the spinal cord, and a 9 to 11% increase in only a small fraction of the contralateral somatosensory cortex. No unilateral metabolic effect was seen in the dorsal column nuclei, ventroposterolateral thalamus, periaqueductal gray matter, dorsal raphe nuclei, or the reticular formation.

The results of this study show that during peripheral stimulation, little metabolic response is seen in the brain even if the animal is receiving only nitrous oxide (70%), while the dorsal horn of the cord responds dramatically under the same conditions. Moreover, anesthesia with the potent cerebral metabolic depressant pentobarbital does not substantially alter the metabolic responsiveness of the cord or brain to stimulation. Thus, although there are marked differences between the resting rate of metabolism produced by 70% nitrous oxide and pentobarbital, in terms of their effects on the metabolic response to stimulation, the agents are quite similar. (Key words: Anesthetics, gases: nitrous oxide. Anesthetics, intravenous: pentobarbital. Brain: glucose utilization; metabolism, regional; stimulation. Spinal cord: glucose utilization; metabolism, regional; stimulation.)

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Received from the Laboratory of Cerebral Metabolism, the National Institute of Mental Health, the U. S. Public Health Service, the Department of Health and Human Services, Bethesda, Maryland 20205, and the Department of Anesthesia, the University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania 19104. Accepted for publication June 22, 1982. Presented in part at the annual meeting of the American Society of Anesthesiologists, New Orleans, Louisiana, October 1981. Supported in part by Grant 5-T32-GM 07612, National Institute of General Medical Sciences, NIH. This manuscript was awarded first prize in the 1981 Resident's Research Contest.

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ANESTHETIC AGENTS are used to reduce or eliminate the perception of peripheral stimuli, although the mechanisms of this action are still not completely understood. It is clear that a complete block of sensory transmission from the periphery to the cerebral cortex is not the mechanism, as evidenced by the persistence of evoked neuronal activity[1–3] in anesthetized animals. There is, however, evidence that anesthetic agents do selectively block transmission of stimuli at some levels of the central nervous system (CNS). Barbiturates,[4] nitrous oxide (N_2O),[5] morphine (MSO_4),[6] ketamine,[7] and halothane[3] all have lamina-specific actions in the spinal cord. Similarly, sensory transmission at the level of the thalamus appears to be sensitive to anesthetic depression, while that in the dorsal column nuclei is not altered.[8]

Inasmuch as neural function and metabolism are closely coupled,[9] local metabolic alterations might be expected to be demonstrable in the CNS during peripheral stimulation of anesthetized animals. Although there have been numerous studies of the cerebral metabolic effects of anesthetic agents, nearly all such studies have been conducted in unstimulated animals. The exceptions to this rule are few, and the studies have yielded contradictory results. One study[10] reported no change in cerebral oxygen consumption (CMR_{O_2}), electroencephalogram, or cerebral blood flow during stimulation of pentobarbital- and ether-anesthetized monkeys. A second, more recent report[11] measured the same functions and reported that as much as a 10 to 20% increase in the global CMR_{O_2} of brain was produced by stimulation of dogs anesthetized with various anesthetics. Oxygen consumption in both studies was measured for whole brain and would, therefore, underestimate the metabolic rate in regions of the somatosensory system specifically activated by the stimulus. Cord metabolism during stimulation of a barbiturate-anesthetized rat has been reported to increase,[12] but the data were not quantified and brain metabolism was not measured simultaneously.

In view of the controversy regarding the metabolic consequences of peripheral stimulation during anesthesia, we chose to examine the question with the 2-[^{14}C]deoxyglucose [2-[^{14}C]DG] technique for measuring local cerebral glucose utilization (LCGU),[13] which has

0003-3022/83/0100/0038 $01.10

proved useful for mapping various sensory pathways in unanesthetized animals. The study was designed to measure the effects of peripheral stimulation on glucose utilization in several regions of the CNS known to be involved in the transmission of somatosensory information. Because resting metabolic rate might affect information transfer between neurons, studies were undertaken in animals given either pentobarbital (PB), a potent cerebral metabolic depressant,[13] or N_2O, an agent that produces little or no reduction in cerebral metabolism.[14] Our results indicate that little increase in brain glucose utilization occurs during stimulation, even in the animals receiving only N_2O. In the spinal cord, however, anesthesia with an agent which profoundly reduces cerebral metabolic rate does not prevent a substantial metabolic response to stimulation.

Methods

The studies were performed using adult, male Sprague-Dawley rats that were allowed free access to food and water until the time of the experiment. Animals were anesthetized with 1% halothane and 70% N_2O for surgical preparation. This period was limited to approximately 20 min, just long enough to perform a tracheostomy and insert catheters into one femoral artery and vein. Thereafter, animals were paralyzed with gallamine (4 mg intravenously and supplemented) and artificially ventilated (Harvard Rodent Respirator, Harvard Apparatus Co., Boston, Massachusetts); the halothane was then discontinued and the anesthetic for that study substituted. Six rats received 70% N_2O and 30% oxygen (O_2); in six additional rats N_2O was terminated and the animals were maintained on room air and PB (15 mg/kg intravenously, supplemented as necessary). The N_2O/O_2 was administered from a blender (Bird Corp., Palm Springs, California) calibrated before each experiment with a paramagnetic O_2 analyzer (Beckman, Model D2, Beckman, Fullerton, California) over a range of O_2:N_2O ratios of 1:0 to 3:7.

The saphenous nerve on the side opposite the femoral catheters was carefully dissected free of surrounding tissue and bathed in mineral oil to prevent dessication. The side chosen for stimulation was varied randomly. In order to reduce noxious input from the incisions, all wound edges were infiltrated with 0.5% bupivicaine. Rectal temperature, arterial blood pressure, blood gases, and *p*H (Instrumentation Laboratories, Lexington, Massachusetts) were monitored. At least one hour and 15 min after discontinuation of halothane, electrical stimulation (bipolar electrodes, 10 Hz, 0.5 ms, and 5 volts) of the saphenous nerve was begun and was followed two minutes later by a bolus injection

TABLE 1. Physiologic Parameters

	Barbiturate (6)	Nitrous Oxide (6)
Mean arterial blood pressure (mmHg)	118 ± 4	136 ± 4*
Rectal temperature (°C)	36.4 ± 0.4	36.6 ± 0.02
*p*H	7.41 ± 0.01	7.38 ± 0.01
P_{O_2} (mmHg)	91 ± 5	114 ± 5*
P_{CO_2} (mmHg)	40 ± 1	42 ± 1

* $P < 0.01$.
Data are means ± standard errors in the number of animals indicated.
The units for each variable are shown in parentheses.

of 125 μCi/kg of 2-[^{14}C]DG (New England Nuclear, Boston, Massachusetts). Experiments were continued for 45 min during which timed arterial blood samples were taken for plasma glucose (Beckman Glucose Analyzer, Fullerton, California) and for 2-[^{14}C]DG determinations (Beckman Scintillation Counter, IL-255, Fullerton, California). Animals were killed with an overdose of PB, and both the lumbar spinal cord and brain were removed and frozen in isopentane (−50° C) and processed as described previously.[13] Sections, 20 μm thick, of both spinal cord and brain were taken serially in the areas anticipated to be involved (less frequently in other areas) and were exposed, along with a set of previously calibrated [^{14}C]methylmethacrylate standards (Amersham, Arlington Heights, Illinois), on Kodak MRI film (Kodak, Rochester, New York).

The autoradiographs generated were analyzed with the aid of a computerized image-processing system[15] which allowed high resolution densitometric analysis of the autoradiographs. The dorsal horn of the spinal cord was divided into two parts and measured either as "superficial" (dorsal one-third) or "deep" (ventral two-thirds). The ventral horn of the spinal gray matter also was measured. In the somatosensory cortex, two measurements, one involving an area with a visually apparent increase in optical density and the other an averaged value for a much larger area of somatosensory cortex, were made. In the remaining structures the LCGU represents the average either for the whole structure or a large portion of it. Optical density measurements for a given structure were made in a minimum of six brain or cord sections in anatomically comparable areas ipsilateral and contralateral to the stimulating electrode. Local glucose utilization was calculated from the optical density measurements, plasma glucose and 2-[^{14}C]DG concentrations, and knowledge of various constants according to the operational equation of the method.[13] Statistical analysis of side-to-side differences within groups was carried out with a paired *t* test, while sta-

TABLE 2. Local Cerebral Glucose Utilization during Unilateral Saphenous Nerve Stimulation ($\mu mol \cdot 100\ g^{-1} \cdot min^{-1}$)

	Barbiturate (6)	Nitrous Oxide (6)
Spinal cord		
Dorsal horn		
Superficial		
I	73 ± 6†	70 ± 6†
C	35 ± 2	40 ± 3
Intermediate		
I	52 ± 3†	59 ± 3†
C	43 ± 3*	53 ± 3
Ventral Horn		
I	48 ± 4	56 ± 3
C	46 ± 3*	56 ± 3
Dorsal column nuclei		
Cuneate nucleus		
I	50 ± 3	62 ± 5
C	48 ± 4*	62 ± 6
Gracilis nucleus		
I	45 ± 3	63 ± 6
C	42 ± 3§	61 ± 3
Thalamus		
Ventroposterolateral		
I	48 ± 3§	93 ± 8
C	47 ± 3	93 ± 7
Somatosensory cortex		
Average		
I	57 ± 3§	76 ± 4
C	58 ± 4	78 ± 4
Hindlimb proj. area		
I	57 ± 3	78 ± 4
C	63 ± 4†	85 ± 4†
Brainstem		
Periaqueductal g.		
I	43 ± 3§	62 ± 4
C	43 ± 3	62 ± 4
Dorsal raphe		
I	48 ± 3§	73 ± 5
C	48 ± 3	72 ± 5
Reticular form		
I	43 ± 2§	63 ± 4
C	44 ± 2	64 ± 4

I = ipsilateral relative to the stimulating electrode; C = contralateral relative to the stimulating electrode.

† $P < 0.01$. These values refer to side-to-side comparisons with paired *t* test.

* $P < 0.05$; § $P < 0.01$ for comparisons between groups. Grouped comparisons were made in order to assess the effect of the drug alone on metabolic rate; therefore, grouped statistics were calculated only for the side of each structure not affected by the stimulus. For example, since peripheral stimulation should affect the contralateral thalamus and cortex, only data from the ipsilateral side were subjected to grouped statistics.

Data are means ± standard errors obtained in number of animals in parentheses, except for the spinal cord and the dorsal column nuclei in both groups, where only five animals were measured.

tistical comparisons between groups were made with a Student's *t* test for group comparisons.

Results

The few differences in physiologic variables between groups (table 1) were expected. Blood pressure was higher in the N_2O group, probably reflecting the minimal CNS and cardiovascular depression with this agent. The higher arterial P_{O_2} in the N_2O animals was due to the higher fraction of inspired O_2 (0.30 *vs.* 0.21 in the barbiturate group) which this group received.

Measurements of metabolic rate were made bilaterally for eleven structures (table 2). Excluding the superficial dorsal horn of the cord, the metabolic rate in most structures examined was, as anticipated, 20 to 50% lower in the barbiturate-anesthetized animals (table 2). During both N_2O analgesia and PB anesthesia, increases in regional glucose utilization were evident in the ipsilateral spinal cord and the contralateral sensory cortex (table 2). Peripheral stimulation produced unilateral increases in LCGU in the superficial and deep zones of the dorsal horn of the cord, with the superficial portion manifesting the largest (75–108%) evoked increase in LCGU of all structures examined. In addition, both groups demonstrated a 9 to 11% increase in metabolic activity in a small, well-delineated area of the somatosensory cortex contralateral to the stimulating electrode (fig. 1*B*). When LCGU in somatosensory cortex as a whole was measured, the measurement was weighted toward areas of cortex unaffected by stimulation and, therefore, no significant unilateral effect could be demonstrated (table 2). Metabolic rate in the spinal cord ventral horn, dorsal column nuclei (cuneatus and gracilis), ventroposterolateral thalamus, periaqueductal gray matter, the dorsal raphe nuclei, and the reticular formation also was examined, and no unilateral effects of stimulation are evident (table 2). Finally, stimulation-induced per cent increases in LCGU of spinal cord and cortex were slightly higher in animals anesthetized with PB despite the lower baseline LCGU in this group (table 2).

Discussion

The present study examined the metabolic effects in the somatosensory pathway of unilateral electrical stimulation of the saphenous nerve in rats given PB or N_2O. Most of the structures examined mediate sensory transmission in either the spinothalamic tract or the dorsal column-lemniscothalamic system. Both pathways are trisynaptic; the first synapses occur ipsilateral to the stimulus in either the dorsal horn of the cord or the nucleus gracilis (for hindlimb), while the second and third order synapses occur in the contralateral ventroposterolateral (VPL) thalamus and sensory cortex, respectively.[1] The results of the study indicate that stimulus-evoked increases in metabolic activity occur in some, but surprisingly not all, of the structures in the sensory pathway. The most dramatic increases (75–108%) in LCGU during stimulation occur in the superficial portion of the dorsal horn; less substantial increases (11–21%) are

present in the deep region of the dorsal horn (table 2). The primary sensory cortex was the only other part of the sensory pathway examined to show a small (9–11%) stimulus-evoked metabolic change (table 2) which was, in addition, limited anatomically (fig. 1*B*). Neither the dorsal column nuclei nor the VPL thalamus demonstrated unilateral metabolic effects (table 2). Perhaps most interesting is the finding that the magnitude of the evoked increase in metabolism in the cord and cortex was similar in both groups despite a 20 to 50% lower LCGU in the PB anesthetized rats (table 2).

Only two previous studies[10,11] have examined the stimulation-induced modification of cerebral metabolism during anesthesia. Meyer *et al.*[10] stimulated a femoral nerve in two PB- and ether-anesthetized monkeys, and reported no change in CMR_{O_2}. Evaluation of the report is difficult, however, inasmuch as their anesthetic conditions are described poorly and stimulation parameters are not given. In contrast, Kuramoto *et al.*[11] reported a 10–20% increase in CMR_{O_2} of brain produced by bilateral sciatic nerve stimulation (6 volts, 0.1 ms, 100 Hz) in halothane, methoxyflurane, and N_2O plus MSO_4 anesthetized dogs. A threshold effect was seen with the volatile agents since increasing the anesthetic dose to exceed the minimum alveolar concentration prevented the metabolic change.[11] The increase in CMR_{O_2} during anesthesia with as much as 1.5 mg/kg of MSO_4 alone, however, was not reduced by the addition of 60% N_2O.[11] The authors point out that the increased CMR_{O_2} peaks soon after stimulation is begun but, nevertheless, record a mean increase of 11 to 17% over the five minutes of the measurement.[11] It is evident that such an increase in CMR_{O_2} of the whole brain would greatly underestimate the increase in the few structures specifically activated by stimulation. Thus, our finding of a 9–11% increase in LCGU occurring in such a small area of cortex that it was not detected in a measurement of somatosensory cortex as a whole (table 2) stands in sharp contrast to the report of Kuramoto *et al.*[11] Although methodologic differences between the studies are apparent, they unfortunately do not satisfactorily account for such large differences in results.

Whereas no previous studies have quantified the local metabolic response to stimulation during anesthesia, neurophysiologic studies have been concerned with regional anesthetic effects for some time. Studies of spontaneous and evoked neuronal firing of spinal cord cells during anesthesia, for example, have demonstrated lamina-specific effects of several agents.[3–7] Anesthetics affect supraspinal structures selectively as well. Angel,[8] using microelectrode techniques for the measurement of evoked potentials, reported that the dorsal column nuclei retain their ability to transmit impulses even at near-lethal levels of anesthesia. Unlike the effect in the

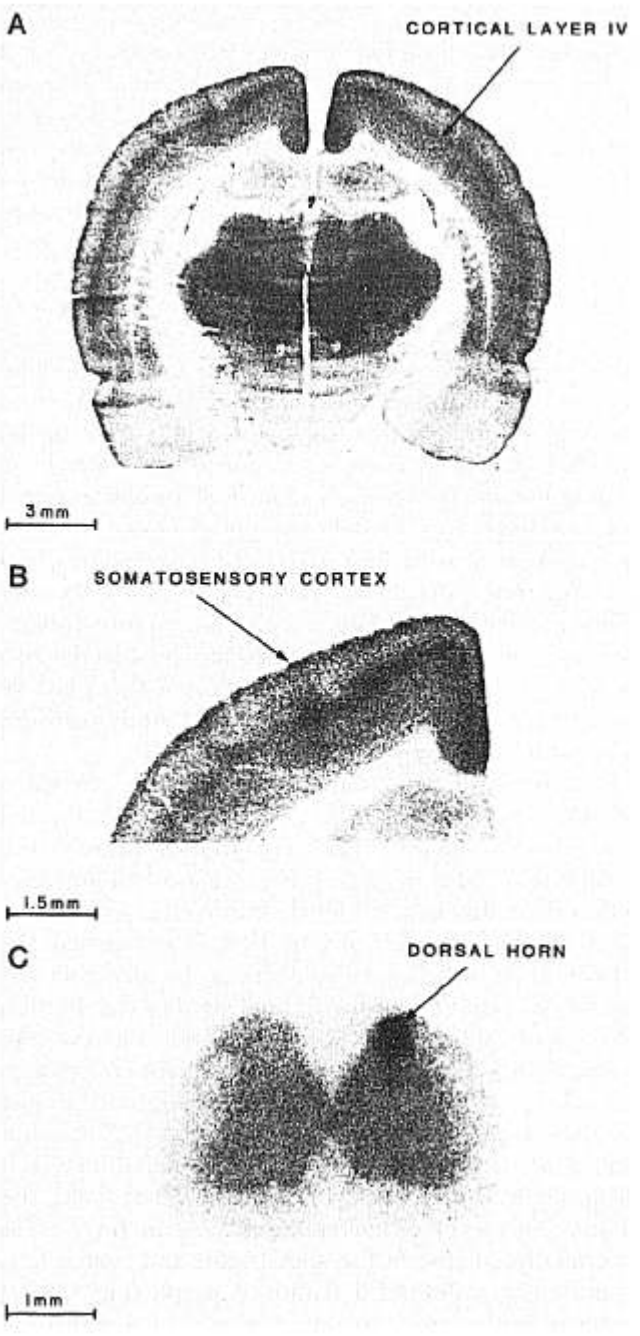

FIG. 1. Autoradiographic sections from the brain (*A*), left somatosensory cortex of A (*B*), and lumbar spinal cord (*C*) of a rat receiving N_2O in which the right saphenous nerve was stimulated electrically. A striking increase in optical density is evident in the right dorsal horn (*C*). A smaller, columnar increase in optical density is evident in the left somatosensory cortex (*B*). The fact that the cord effect is seen on the right and the cortical effect on the left merely reflects the decussated nature of this pathway. The somatopic distribution of the cortical evoked-metabolic effect corresponds to the hindlimb area of the sensory cortex (see text), and is seen most prominently in cortical layer IV (left cortex of A, B). Layer IV itself normally is seen throughout the cortex as a dark line of metabolic activity (*A*). Autoradiographs from the pentobarbital-anesthetized animals are qualitatively similar to these and, therefore, have not been included.

dorsal column nuclei, however, anesthetics directly depress sensory transmission in the VPL thalamus,[8] and apparently because of this, evoked neuronal firing in cortex also is reduced.[1,2,8] Unfortunately, interpretation of metabolic data is less straightforward. Increases in LCGU can be attributed to either excitatory or inhibitory neuronal events; in the latter case, however, subsequent relay areas in the anatomic pathway would manifest a reduced rate of metabolism. The cord metabolic response, which is qualitatively similar to that reported by Kennedy *et al.*,[12] may, therefore, reflect the metabolic sum of activity in primary afferents and modulatory or inhibitory systems (*e.g.*, substantia gelatinosa, descending brainstem pathways) which synapse in the spinal cord. The reasons for a limited brain metabolic response in the face of such profound changes in spinal cord are less clear. The data are consistent with reduced propagation of stimulus-evoked activity to supraspinal somatosensory structures, perhaps secondary to inhibition of afferents in the cord or to the established ability of some general anesthetics to reduce the effectiveness of excitatory neurochemical transmission.[16] It must be emphasized, however, that the present study provides no data to directly support this hypothesis.

The anatomic definition of the cord laminae in which stimulus-evoked metabolic changes occur is limited somewhat by methodologic constraints, namely, the small size of the rat spinal cord and the 100-μm resolution limitation of [^{14}C] labeled 2-deoxyglucose. Insofar as the cortical effect of stimulation is concerned, the anatomically well-delineated increase in metabolic activity is consistent with the limited sensory distribution of the saphenous nerve and the small somatotopic representation of the hindlimb in rat somatosensory cortex.[17] Moreover, since thalamocortical afferents project directly to stellate cells in cortical layer IV,[1] it is not surprising that the metabolic effect of stimulation is seen primarily in this layer (fig. 1). On the other hand, the absence of increased metabolic activity in relay areas intermediate between the spinal cord and cortex (*i.e.*, in nucleus gracilis and thalamus) is perplexing. Of the possible explanations for the absence of a unilateral change in evoked metabolic activity in these structures the most likely relates to difficulty in identifying and measuring only the specific area of interest within each somatotopically organized structure.[1,17] Thus, there were no distinguishing autoradiographic characteristics of the hindlimb area in either the small nucleus gracilis or the comparatively large VPL thalamus and, therefore, the entire area was measured. Such a measurement is, of course, weighted towards areas unaffected by stimulation and could account for the failure to detect a small metabolic change. Nevertheless, it can be concluded that stimulation failed to substantially increase metabolism in either of these structures.

Finally, although stimulation activated the same structures in both groups (table 2), quantitative analysis reveals a small difference between agents. Thus, stimulation produced a consistently greater per cent effect in the barbiturate group in spite of the lower baseline LCGU (table 2). One might have expected that the 20 to 50% lower metabolic rate in the PB animals would translate into a similar reduction in metabolic reponsiveness to a stimulus. That this is not the case would suggest that prevention of a metabolic response to stimulation is not a simple function of baseline metabolism. The pharmacologic profile of the agent itself, or the dose employed, may be critical in this regard if, as Kuramoto *et al.*[11] report, some agents are capable of blocking a stimulation-induced metabolic response. Further studies will be necessary in order to clarify this point.

In summary, the significance of the present study is twofold. First, the study shows a quantitatively different evoked metabolic response in brain and spinal cord. That is, in the presence of N_2O or PB, peripheral stimulation produces little metabolic response in the brain even though the dorsal horn of the cord responds dramatically. Secondly, the evoked metabolic response is not attenuated by anesthesia with an agent (PB) which profoundly reduces cerebral metabolism. The fact that the spinal cord alone is subject to substantial stimulus-evoked increases in metabolism emphasizes the need for additional studies of the metabolic response of this portion of the CNS to anesthesia and surgery.

The authors thank Ruth Bower for her expert editorial assistance and J. D. Brown for his excellent photography.

References

1. Angel A: Processing of sensory information. Prog Neurobiol 9:1–122, 1977
2. Angel A: Theories of the mechanism of action of general anesthetic agents. Anesthesiology. International Congress Series 399. Edited by Hülsz E, San-Chez Hernandez JA, Vasconcelos G, Lunn JN. Amsterdam-Oxford, Excerpta Medica, 1977, pp 67–76
3. Akiyoshi N, Collins JG, Kitahata LM, Kikuchi H, Homma E, Thalhammer JG: Effects of halothane on spinal neuronal responses to graded noxious heat stimulation in the cat. ANESTHESIOLOGY 53:475–480, 1980
4. Kitahata LM, Ghazi-Saidi K, Yamashita M, Kosaka Y, Bonikos C, Taub A: The depressant effect of halothane and sodium thiopental on the spontaneous and evoked activity of dorsal horn cells: Lamina specificity, time course and dose dependence. J Pharmacol Exp Ther 195:515–521, 1975
5. de Jong RH, Robles R, Morikawa K: Actions of halothane and nitrous oxide on dorsal horn neurons ("the spinal gate"). ANESTHESIOLOGY 31:205–212, 1969

6. Kitahata LM, Collins JG: Spinal action of narcotic analgesics. ANESTHESIOLOGY 54:153–163, 1981
7. Kitahata LM, Taub A, Kosaka Y: Lamina-specific suppression of dorsal horn unit activity by ketamine hydrochloride. ANESTHESIOLOGY 38:4–11, 1973
8. Angel A: Modulation of information transmission in the dorsal column-lemniscothalamic pathway by anesthetic agents. Anesthesiology. International Congress Series 399. Edited by Hülsz E, San-Chez Hernandez JA, Vasconcelos G, Lunn JN. Amsterdam-Oxford, Excerpta Medica, 1977, pp 82–89
9. Sokoloff L: Relation between physiological function and energy metabolism in the central nervous system. J Neurochem 29:13–26, 1977
10. Meyer JS, Nomura F, Sakamoto K, Kondo A: Effect of stimulation of the brain-stem reticular formation on cerebral blood flow and oxygen consumption. Electroencephalogr Clin Neurophysiol 26:125–132, 1969
11. Kuramoto T, Oshita S, Takeshita H, Ishikawa T: Modification of the relationship between cerebral metabolism, blood flow, and electroencephalogram by stimulation during anesthesia in the dog. ANESTHESIOLOGY 51:211–217, 1979
12. Kennedy C, Des Rosiers MH, Jehle JW, Reivich M, Sharp F, Sokoloff L: Mapping of functional neural pathways by autoradiographic survey of local metabolic rate with [^{14}C]deoxyglucose. Science 187:850–853, 175
13. Sokoloff L, Reivich M, Kennedy C, et al: The [^{14}C]deoxyglucose method for the measurement of local cerebral glucose utilization: Theory, procedure, and normal values in the conscious and anesthetized albino rat. J Neurochem 28:897–916, 1977
14. Ingvar M, Abdul-Rahman A, Siesjö B: Local cerebral glucose consumption in the artificially ventilated rat: Influence of nitrous oxide analgesia and of phenobarbital anesthesia. Acta Physiol Scand 109:177–185, 1980
15. Goochee C, Rasband W, Sokoloff L: Computerized densitometry and color coding of [^{14}C]deoxyglucose autoradiographs. Ann Neurol 7:359–370, 1980
16. Koblin DD, Eger EI, II: Theories of narcosis. N Engl J Med 301:1222–1224, 1979
17. Welker C: Microelectrode delineation of fine grain somatotopic organization of SmI cerebral neocortex in albino rat. Brain Res 26:259–275, 1971