## EDITORIAL VIEWS

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# *Spinal Cord as a Site of Anesthetic Action*

In clinical practice, anesthesiologists attempt to prevent consciousness, pain perception, and memory. These are functions associated with supraspinal areas of the central nervous system (CNS). Accordingly, much experimental work has been directed to assessment of anesthetic effects on supraspinal areas including cortex. Because of its presumed role in memory formation and attentiveness, a large body of recent work has focused on the hippocampus.[1] However, in both humans and experimental animals, anesthetic potency is operationally defined as MAC: the minimal anesthetic concentration required to prevent movement in 50% of test subjects in response to a noxious stimulus.[2] A state of anesthesia is therefore defined in terms of a motor response, most commonly a flexion withdrawal reflex, mediated at the spinal level. Anesthetic levels measured as MAC relate well to clinical anesthesia; at MAC, the patient is unconscious, analgesic, and amnestic. Although it is always necessary to be aware that suppression of movement may not be an infallible index of anesthesia, MAC determinations have provided an essential means of establishing anesthetic properties of novel compounds, comparing potency among anesthetics, and testing theories of anesthesia. Because of its usefulness in these respects, it is important to understand the neurophysiologic basis of MAC determinations, in order to evaluate drug pharmacology and theories of anesthesia based on this measure and to provide a broad understanding of the CNS effects of anesthetic agents in clinical use.

The article by Antognini and Schwartz[3] reports experiments designed to identify the CNS structures that govern MAC determinations. Goats were instrumented so that isoflurane could be delivered either to the entire circulation or preferentially to the cerebral circulation *via* carotid artery bypass. MAC was 1.2% when isoflurane was delivered to the whole body, and 2.9% when only the brain was exposed to the anesthetic. The results imply that anesthesia as defined by MAC is determined by CNS structures other than those supplied by the carotid arteries; these include brainstem and spinal cord and exclude cortical structures.

The converse experiment, in which only spinal cord was exposed to anesthetic, was not done. If anesthesia is due to a spinal cord action of anesthetics, the predicted outcome of such a study is that MAC would be the same in the whole animal as in the animal with only spinal cord exposed. A related set of experiments was reported previously in this journal: Rampil *et al.* determined MAC in rats before and after precollicular decerebration, a procedure that removed cortical structures. MAC was the same before and after the procedure.[4] The results of both studies are consistent with the hypothesis that anesthetic potency is determined by actions of anesthetics at the midbrain level or lower, in the spinal cord and/or brainstem, rather than by supraspinal actions. More recent studies, in which spinal cords of rats were transected without significantly altering MAC,[5] suggest that the relevant site for MAC determinations is the spinal cord.

Experimental studies on the spinal cord support this hypothesis. Much of the early work on anesthetic actions was done on spinal cord.[6] Anesthetic agents of all classes depress excitatory transmission in spinal cord at their anesthetic concentrations.[7,8] A possible basis for this has been observed in the depression of activity in dorsal horn interneurons that respond to noxious stimuli.[9] Neural activity in the spinal cord employs the same molecular machinery as the rest of the central nervous system and offers the same potential sites of anesthetic action as have been proposed in cortex, most prominently depression of glutamate excitatory transmission and enhancement of GABA inhibition.[1]

If anesthetic actions at the spinal cord level determine MAC, what can be said of spinal contributions to the triad of unconsciousness, analgesia, and amnesia by which clinical anesthesia usually is defined? The evidence is strongest for a link to analgesia, because reducing nociceptive neurotransmission in spinal cord is inherently analgesic. Reduction in the strength of nociceptive input may contribute to loss of consciousness by diminishing the strength of arousing stimuli arriving at cortical structures. Amnesia probably has the most tenuous connection to the spinal cord and is

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almost certainly due to supraspinal actions of anesthetics.

Following a period of intense interest in spinal cord actions of anesthetics, including consideration of anesthesia as a state of functional deafferentation, interest centered on cortical actions of anesthetics, in part because of the technical development of brain slice preparations. It was assumed that actions on hippocampus and neocortex were important determinants of anesthetic potency. The recent evidence adduced by Antognini and Schwartz[3] and similar evidence by Rampil *et al.*[4] and Rampil,[5] suggest that anesthetic potency measured by MAC determination is based on actions in spinal cord. The results have important implications for directions of future research. They may provide a rationale, for instance, for attempts to relate anesthetic potency to selective actions on receptor subtypes with spinal cord *versus* cortical distribution. The spinal cord has always been a useful model in which to study anesthetic action, because the results could be generalized to other CNS sites that share the same basic molecular machinery. Studies on spinal cord now assume an enhanced importance as directly relevant to understanding the basis of anesthesia.

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## References

1. Kendig JJ, MacIver MB, Roth SH: Anesthetic actions in the hippocampal formation. Ann N Y Acad Sci 625:37–53, 1991

2. Quasha AL, Eger EI, Tinker JH: Determination and applications of MAC. ANESTHESIOLOGY 53:315–334, 1980

3. Antognini JF, Schwartz K: Exaggerated anesthetic requirements in the preferentially anesthetized brain. ANESTHESIOLOGY 79:1244–1249, 1993

4. Rampil IJ, Mason P, Singh H: Anesthetic potency (MAC) is independent of forebrain structures in the rat. ANESTHESIOLOGY 78:707–712, 1993

5. Rampil IJ: Is MAC testing a spinal reflex (abstract)? ANESTHESIOLOGY 79:A422, 1993

6. Somjen G: Effects of anesthetics on spinal cord of mammals. ANESTHESIOLOGY 28:135–143, 1967

7. Savola MKT, Woodley SJ, Maze M, Kendig JJ: Isoflurane and an $\alpha_2$-adrenoceptor agonist suppress nociceptive neurotransmission in neonatal rat spinal cord. ANESTHESIOLOGY 75:489–498, 1991

8. Jewett BA, Tarasiuk A, Gibbs L, Kendig JJ: Propofol and barbiturate depression of spinal nociceptive neurotransmission. ANESTHESIOLOGY 77:1148–1154, 1992

9. Namiki A, 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



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