

GUIDELINES FOR THE USE OF NEUROMUSCULAR BLOCKING DRUGS IN ANESTHETIZED ANIMALS

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Purpose

Systemic paralysis is most commonly utilized in neuroscience research. These experiments require that the animal be paralyzed with a neuromuscular blocking agent (NMBD) to minimize or prevent self-generated movement, such as movement of the ocular muscles during visual experiments. However, the use of these agents eliminates many of the typical indicators of anesthetic depth. This document provides guidance to laboratory personnel so that the use of these agents in laboratory animals is carefully and properly managed.

Procedures

NMBDs may only be used in conjunction with and following induction of general anesthesia. NMBDs provide no anesthesia or analgesia and interfere with standard indicators of anesthetic depth so their use will only be approved under the following conditions:

1. The use of neuromuscular blocking drugs (paralytics or NMBDs) in animals will only be approved in specific situations for which investigators can document the scientific necessity of their use. Use of NMBDs therefore must be described and justified in the AUP and then approved by the Animal Care and Use Committee (ACUC).
2. Prior to using NMBDs in mammals, investigators must demonstrate to an Office of Laboratory Animal Care (OLAC) veterinarian that the anesthetic technique is sufficient to prevent pain and distress associated with the experimental procedure in the absence of the NMBD.
3. All surgical or otherwise potentially painful procedures must be performed under adequate anesthesia prior to NMBD administration. After the surgical or painful portion of the procedure is complete, the animal must be maintained without NMBDs at a fixed anesthetic level until physiologically stable. At least 15 minutes of stable, effective anesthesia is required prior to NMBD administration. Longer anesthetic stabilization periods may be required for some protocols. During this time, negative stimuli, such as “toe pinch” tests, must occur at least once every 15 minutes to assess adequacy of anesthesia. There must be no muscular response (withdrawal reflex) or increase in heart or respiratory rate in response to this stimulus.
4. Controlled ventilation must be initiated prior to administration of the neuromuscular blocking drug. Once NMBDs have been administered, the anesthetic level must not be decreased except as described below.
5. The adequacy of anesthesia must be assessed and documented. In mammals, this should be accomplished by means of a noxious stimulus, such as a “toe pinch”, throughout the period during which NMBDs are administered. An increase in heart rate

of 20% or greater within 1 minute of the toe pinch will be taken as a significant positive response, indicating that the depth of anesthesia is insufficient. The frequency of noxious stimulus (e.g., toe pinch) testing after NMBDs have been administered depends on the nature of the recording procedure being performed. In most cases, this should be performed at least once every 15 minutes. For longer procedures, longer intervals between noxious stimuli may be approved by the Animal Care and Use Committee (ACUC) in consultation with the OLAC's Attending Veterinarian.

6. Parameters, such as core temperature, heart rate, EEG, and end-tidal CO₂, must be monitored continuously and documented periodically to ensure that physiologic homeostasis is maintained during the periods of paralysis. Documentation must be performed at least every 15 minutes during the surgical portion of the procedure but may be extended to every 30 minutes during more stable periods after NMBDs have been administered (e.g., during periods of neurophysiological recordings). If animals will be paralyzed for long periods of time (e.g., greater than 4 hours), provision must be made for periodic voiding of the urinary bladder, if applicable.
7. If animals are anesthetized for prolonged procedures, anesthetic levels may need to be decreased to allow successful neurophysiological recordings to continue. In such cases, NMBD administration must be discontinued, such that normal muscle and physiologic responses allow assessment anesthetic depth prior to re-induction of paralysis
8. Details of all drugs administered and actions taken (e.g., "toe pinch" testing) during the procedure must be documented on the animal's monitoring record. Notations must include the time, date (if appropriate) and the name (or initials) of the individual making the comment.
9. In some cases, the ACUC will require that a copy of the animal's records, including the monitoring record, be returned to the Director of the Office of the Animal Care and Use (OACU) within 7 days of completion of the procedure. An OLAC veterinarian may then review said records and retain the documentation. If any concerns arise, OLAC or the OACU will notify the ACUC Chair, who will determine if further action is needed.

References

- Committee on Guidelines for the Use of Animals in Neuroscience and Behavioral Research. National Research Council. (2003). *Guidelines for the Care and Use of mammals in Neuroscience and Behavioral Research*. National Academy Press: Washington, D.C.
- Drummond, J.C. (1996). Use of neuromuscular blocking drugs in scientific investigations involving animal subjects. *Anesthesiology*, 85(4), 697-9.