LETTER TO THE EDITOR

Factual Errors in Brooks and Peever's Rebuttal to Critiques

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VOLUME 31, ISSUE 11 OF SLEEP CONTAINED A CRITICAL TOPICS FORUM FOCUSED ON THE MOTOR ATONIA OF REM SLEEP. THAT FORUM COMPRISED FIVE commentaries[1-5] on a previously published paper that was co-authored by Patricia Brooks and John Peever.[6] In response to the five commentaries, Brooks and Peever wrote a rebuttal.[7] In this letter, I highlight important errors of fact in their rebuttal. Before doing so, however, I want to express my belief that it is always important, especially in science, to not only be open, but also to welcome new data as well as concepts that challenge consensus views. On the other hand, there must be positive evidence to reject an established set of data. In the present situation, to be credible, it is not sufficient for Brooks and Peever[7] to simply state that the consensus opinion that glycine is responsible for atonia during REM sleep is inaccurate. It is also not sufficient to propose that postsynaptic inhibition of motoneurons is responsible for atonia during the tonic periods of REM sleep unless they also identify the unknown biological substrate[6] which they believe mediates this postsynaptic inhibitory process.

In their rebuttal, Brooks and Peever criticized data from in vivo intracellular studies because "the dose of strychnine used (i.e., 15 mM) was orders of magnitude (i.e., 30,000 times) higher than that required to block glycine receptors in vitro (i.e., 400 nM)."[7] A key teaching point here concerns the difference between "dose" and "concentration." Dose is defined as the "quantity" of a substance that is delivered for a specific period of time, whereas "concentration" is the amount of a substance per unit volume. In our intracellular studies, a micropipette was first filled with a strychnine "concentration" of 15 mM. A current of approximately 200 nA was applied to this solution which resulted in the ejection of a final (extracellular) concentration of strychnine that was between 100 and 1000 nM (according to the formulae of Curtis (1964)[8] and Stone (1985).[9] Accordingly, the concentration of strychnine used in our intracellular studies was comparable to that employed in the in vitro studies referenced by Brooks and Peever.[6] In addition, in our intracellular studies, since current was applied for only a few minutes, the "dose" of strychnine was much less than that used by in vitro studies, wherein strychnine was perfused continuously for the duration of the experiment. Thus, the statement of Brooks and Peever[7] that the "dose" of strychnine used in our intracellular studies was 30,000 times greater than that employed by in vitro studies is not correct.

In a commentary on the original Brooks and Peever report,[6] Berger pointed out that the concentration of strychnine that Brooks and Peever employed (100 μM) was 10 times greater than the concentration (10 μM) needed to block "not only the glycine-receptor-mediated responses but almost all $GABA_A$-receptor-mediated responses."[2] In addition, Kubin noted that "Likely due to the use of too low concentrations of the antagonists, Brooks and Peever were unable to maintain tonic masseter activation during REM sleep and could only observe phasic muscle twitches."[1]

Brooks and Peever concluded that an "unknown biological substrate" must be responsible for atonia during the tonic periods of REM sleep.[6] However, Brooks and Peever did not clarify what they mean when they use the phrase "biological substrate." Is it a neurotransmitter, a hormone, a peptide or what? An alternative hypothesis, to counter or compliment long-standing evidence, must specify the hypothetical "unknown biological substrate,"[6] demonstrate that it is responsible for producing atonia during the tonic periods of REM sleep, and show that the putative substrate is not involved in mediating atonia during the phasic periods of REM sleep. Funk reviewed the results of intracellular studies and concluded that Brooks and Peever[6] had not interpreted their data "in relation to the full scope and significance of the overwhelming database showing that active postsynaptic glycinergic inhibition accounts for all changes in motoneuron properties observed with the transition to REM."[3]

DISCLOSURE STATEMENT

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