Last Word on Point: Counterpoint “Medullary pacemaker neurons are essential for both eupnea and gasping in mammals vs. medullary pacemaker neurons are essential for gasping, but not eupnea, in mammals”

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TO THE EDITOR: Implicit in the commentaries concerning the possible role of medullary pacemakers in the neurogenesis of eupnea and gasping is one critical and recurring question: How are in vitro rhythms related to these classical patterns of automatic ventilatory activity? Suzue (5) considered in detail this ambiguity between the in vitro rhythm and eupnea or gasping in vivo in his original description of the en bloc brain stem-spinal cord preparation in 1984. Yet this ambiguity concerning in vitro rhythms remains.

Regardless of what in vitro rhythms may represent, the concept was strongly advanced that the discharge of medullary pacemakers underlay the in vitro rhythm. Originally, a single group of pacemakers, dependent on persistent sodium current, was described in a relatively thin medullary slice preparation from neonatal rat (1–3). A second group of pacemakers, dependent on calcium conductances, was subsequently described in a relatively thick slice preparation from neonatal mouse (1, 3). To date, this second group of pacemakers has only been identified in this thick medullary slice preparation and has not been described in thin medullary slices nor have we recorded any in the in situ preparation of the rat (2).

Recently, the concept that the discharge of pacemakers might underlie respiratory rhythm generation, even in vitro rhythms, has been challenged by one laboratory that had originally advanced this concept (1). This laboratory now reports that an in vitro rhythm can be reestablished following a pharmacological blockade and elimination of the discharge of the two types of pacemaker neurons previously described in vitro.

We raise the issue that not all in vitro preparations are the same. Thus not only the thickness, but also the angle of section and level of the medulla may differ. Slices containing different portions of medulla thus may well account for the heterogeneity in data. Pharmacological problems, including lack of specificity of blockers and limited diffusion into medullary slices, might also contribute to these divergent results.

At present, we have three different mechanisms proposed for generation of in vitro respiratory rhythms: pacemakers, neuronal circuits, hybrid pacemaker circuits. Exclusive of the rhythm that the Ramirez laboratory records in anoxia and considers akin to gasping (3), all rhythmic “respiratory” activities of in vitro preparations have been considered to be the same “fundamental units” of breathing. Yet, as we recently reported, it is incorrect to assume that all rhythms that can be recorded from the isolated medulla, if not gasping, must be variants of eupnea (4).

In summary, the introduction of in vitro preparations has stimulated much excellent work into examining mechanisms of rhythm generation for respiration. However, understanding of these mechanisms will remain confused and obscure until additional work establishes which findings from in vitro preparations are applicable to the generation of unequivocally defined normal breathing. The challenge is now on to put the slice back into the whole system.

REFERENCES