Response to reviewer 1.

We are glad to hear from Reviewer 1 that our submitted review is a well-written piece of work, focused on interesting issues in the field and that you consider it acceptable for publication in the World Journal of Neurology.

Response to reviewer 2.

We have gladly read the comments prepared by Reviewer 2 on our work. All suggestions have been incorporated into the final version of the manuscript. We are certain that, with these modifications, the paper has improved. The manuscript has been proofread by a native speaker.

Minor comments.

Comment 1. Lots of literatures are relative old, some new literatures can be reviewed.

Response: As recommended we have included some new references about oculomotor and respiratory system development. See, for example, in the reference list, Fogarty et al., 2013; Purvis and Butera, 2005; Berger, 2011; Funk et al., 2011; Bouryi and Lewis, 2003; Gottmann et al., 2009; Fung and Chase, 2015, etc…)

However, we consider it necessary to keep some of the old literature cited in order to fully describe a framework of 25 years of research. No superfluous literature can be observed in the final version of the manuscript.

Comment 2. What is the relationship of these 2 groups of MN can be discussed, like literature Sleep. 2015 Jan 1;38(1):139-46.

Response: Regarding the Discussion section ("Time windows in the context of development of the respiratory and oculomotor systems"), and as recommended, a new paragraph has been added in order to describe the functional relationship between the two populations of motoneurons in the study. We have also included the suggested reference (Fung and Chase, 2015) in the reference list.

An extract from the new paragraph incorporated in the Discussion section is shown below:

> The modulation of these K+ channels causes genioglossus inhibition due to postsynaptic inhibition of GG MNs in rapid eye movement sleep [151-152], which in turn produces periods of upper airway motor suppression, atonia of the genioglossal muscle, hypoventilation and obstructive apneas. Patency of the upper airway (i.e, tone of the genioglossus muscle) is essential to maintain ventilatory processes during wakefulness as well as nonrapid eye movement (NREM) and rapid eye movement (REM) sleep [152]. (Page 21, paragraph 1, line 12).

Comment 3. As the authors stated that epigenetic/genetic factors (page 4 line 5-7) and transcription factors (page 6 bottom and page 7 top) may shape the neuronal phenotypes, but there is no any discussion about these factors and their roles in the time window of development.

Response. As recommended, the Discussion section ("Time windows in the context of development of the respiratory and oculomotor systems") incorporates more explanations on the contribution of epigenetic/genetic factors during motoneurons development. We have included new paragraphs.

An extract from the new text incorporated in the Discussion section is shown below:

> The brain-derived neurotrophic factor, when acting via its high-affinity receptor TrkB, has intensively been studied in brainstem neurons during development because of its growth-promoting and trophic effects, including those involved in respiratory control and normal breathing [30,139-140]. It is known that the loss of particular trophic signaling alters the development of different subpopulations of motoneurons in heterogeneous way [32]. Thus, the absence of cardiotrophin-1[141-142] or IGF-1 causes significant reduction in the number of brainstem motoneurons [143]. (Page 19, paragraph 2, line 8).

Still, one further extract:

> This imbalance is characterized by a decrease in the amplitude and frequency of excitatory postsynaptic current and an increase in the amplitude and frequency of inhibitory postsynaptic currents [63] as a result of a transient reduced expression of brain-derived neurotrophic factor and TrKB expression [30]. Concurrently with the abrupt fall in brain-derived neurotrophic factor at P12-13, the expression of excitatory neurochemicals (glutamate and NMDA receptor subunit 1) is drastically reduced, whereas that of inhibitory neurochemicals (GABAA, GABAB receptors and glycine receptors) is significantly enhanced in hypoglossal MNs and in other respiratory-related nuclei [149]. (Page 20, paragraph 2, line 25).

Comment 4. Page 11 line 6 from bottom, what are other contributors for the IR decrease? and did glutamate play effect?.

Response: We have included new information about the contribution of neurotransmitters for the input resistance decrease, as suggested by the reviewer, in the section entitled "A decrease in time constant and input resistance characterizes development".

In the text, the following is now stated:

> In OCM MNs, it seems that GABA, but not glutamate, may contribute to membrane resistance in juvenile rats [23-24]. On the other hand, noradrenergic and serotoninergic modulation in hypoglossal MNs has also been associated with significant changes in neuronal input resistance [97-98]. (Page 12, paragraph 3. Line 27).

Comment 5. Any proposal for the time window change?

Response: The reviewer's question is very interesting for us. We think that the changes in the temporal windows in each motoneuron population is related to their functionality and the

maturation of the network where they participate. This question has been tackled in an entire section (see temporary windows section, pages 19 paragraph 2).