

## OPEN PEER REVIEW REPORT 1

**Name of journal:** Neural Regeneration Research

**Manuscript NO:** NRR-D-21-00208

**Title:** The power of “touch” and early enriched sensory stimulation: effects on brain development, neuroregeneration, neurodegeneration in rodents and human infants

**Reviewer’s Name:** Luz Elena Durán-Carabali

**Reviewer’s country:** Brazil

### COMMENTS TO AUTHORS

The present opinion discussed the effect of neonatal handling and environmental enrichment protocols in the developing brain, in order to suggest non-pharmacological strategies as protective alternative in vulnerable subjects.

Although the behavioral function and cellular response are of great importance, in attempt to establish functional prognostic and to evaluate future therapeutic approaches, the manuscript has some point should be discussed:

In third paragraph of the section "the power of "touch": from NH treatment in rodents to massage therapy of preterm human infants", the authors well described the effects of massage therapy, however, is not clearly stated the EE effect. Could the authors include this information?

The authors do not extend their discussion or make any conclusions about the sex-specific responses to enriched sensory stimulation, considering the vulnerability of male subjects to brain insult and in view of the need to outline future protocols that included sexual dimorphism in the assessment parameters, this should be taken into account. Moreover, some conclusion considering age-related effect and the onset of the stimulation will be important.

In the paragraph in which the clinical relevance of EE and translatability of this approach is mentioned, It would also be good if you could extend how EE protocols would be used for human neonates, in addition to others already in use treatment options

This reviewer urges to mention what might further improve outcomes and stop using EE alone as translational intervention. Though experimental effects are easy to achieve given the multifactorial nature of enrichment, it remains unclear how the deprived conditions or less realistic baseline that serve as control groups model the human condition..

Minor:

I suggest changing the title "human infants" by preterm infants.

Please check the sentence on the pg. 3, lines 2 -4, in order to clearly describe that massage therapy was performed in preterm infant and pup rats while EE exposure was only performed in rats.