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We appreciate Cunha and Dias for their scholastic review of our recent work (Cunha and Dias, 2009). We have a few comments based on some of the issues they discuss. First, we agree with their thoughts on which neurotransmitters or mediators may evoke earlier microglial activation and a delayed and prolonged astrocytic activation and how microglia interact with astrocyte in the RVM after trigeminal nerve injury. Further study should be performed to address these issues. Second, it has been known that fluorocitrate is only relatively selective as an astrocytic inhibitor. In our study (Wei et al., 2008), we showed that intra-RVM microinjection of fluorocitrate blocked the nerve injury-induced increase of the astrocytic marker GFAP but not the microglial marker CD11b, supporting the conclusion that fluorocitrate, at the dose we used, selectively inhibited astrocytic function. However, we did not examine whether the microglial inhibitor, minocycline, had an effect on astrocytic activation. Third, as Cunha and Dias suggest, we would be delighted to know if activated microglia release BDNF in the RVM after nerve injury. Our previous study has shown that upregulation of BDNF in the RVM contributes to descending facilitation during development of persistent pain (Guo et al., 2006). Moreover, truncated TrkB receptors were expressed in astrocytes and BDNF evoked calcium signals in glia (Rose et al., 2003). These findings suggest that periaqueductal gray-derived BDNF could mediate RVM glial activation after tissue and nerve injury. Finally, our experiments show that intrathecal pretreatment with the 5-HT3 receptor antagonist Y-25130 completely blocked the intra-RVM injection of IL-1β-induced descending facilitation (unpublished observations), supporting the reviewers' suggestion that spinal 5-HT3 receptor should be involved in descending facilitation induced by glial-derived cytokines. In addition to an enhancement of descending facilitation, it

would be very interesting to further explore whether pro-inflammatory cytokines alter the inhibitory component of descending modulation.

References

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