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LETTER TO THE EDITOR

Is mTOR involved in the mechanisms of the fast-acting antidepressant effects of AMPA receptor agonists?

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We read with great interest the article "The involvement of AMPA-ERK1/2-BDNF pathway in the mechanism of new antidepressant action of prokinetic meranzin hydrate", in which the authors concluded that AMPA receptors were involved in the mechanism of the antidepressant effects of prokinetic meranzin hydrate (Xie et al. 2012). We appreciate the author's excellent perspectives and want to raise a hypothesis regarding the mechanisms of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor agonists exerting fast-acting antidepressant effects.

A series of studies have demonstrated that AMPA receptor agonist such as LY392098 show fast-acting antidepressant effects in the rodent animal models (Li et al. 2001). Moreover, Maeng et al. (2008) have observed that pretreatment with AMPA receptor antagonist NBQX can significantly reduce the ketamine's antidepressant effects. The ketamine-induced increase in glutamate release preferentially favors AMPA receptors over NMDA receptors because the latter have been occupied by ketamine, therefore the net antidepressant effect of ketamine is increased by glutamatergic throughput (Machado-Vieira et al. 2009). Collectively, these studies have indicated that AMPA receptors are essential for ketamine to exert its antidepressant effects (Duman and Voleti 2012). Recently, an innovative study conducted by Li et al. (2010) showing that mammalian target of rapamycin (mTOR) activation in prefrontal cortex is involved in the ketamine exerting fast-acting antidepressant effects. Thus, we hypothesized that AMPA receptor agonists exerting their antidepressant effects are potentially via up-regulating Akt and ultimately activating mTOR. Future studies are needed to verify the hypothesis and enrich this field knowledge.

Conflict of interest We declare no potential conflicts of interest.

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