

**ROLE OF NEUROTRANSMITTERS OTHER THAN GLUTAMATE IN THE ANTIDEPRESSANT ACTION OF KETAMINE**

Opioid System Pretreatment with naltrexone, a mu opioid receptor antagonist (with mild kappa and delta receptor blocking properties), was reported to block the antidepressant effect of ketamine in patients with TRD (20). In summary, while there are data suggesting the involvement of opioid receptor signaling, it alone does not appear sufficient to produce rapid antidepressant effects (85). The OPRM1 single-nucleotide polymorphism rs 1799971 (A118G), which results in a missense mutation (Asn44Asp), reduces stability and expression of mu opioid receptors (88, 89). This finding sparked speculation that the mu opioid receptor is the target for the antidepressant effects of ketamine, and ketamine does have high binding affinity for mu receptors (84).