Studies have shown that N-methyl-D-aspartate (NMDA) receptors play a critical role in pain processing at different levels of the central nervous system. In this study, we used female adult Wistar rats to examine the effects of antagonizing the NR2B subunit of the NMDA receptor in phasic and tonic pain processes. All the rats underwent stereotaxic surgery for cortical cannula implantation and after at least one week of recovery, rats performed behavioral tests. For evaluating the effects of drugs on motor coordination rats were tested in the rotarod apparatus. Moreover, rats were evaluated in the paw withdrawal latency (PWL) to a noxious thermal stimulus. Furthermore, rats were tested in the formalin pain test. Rats that received the NR2B antagonist Ro 25-6981 before and after formalin injection showed significantly reduced pain responses in the formalin test, as compared with female control rats (p<0.05). In contrast, no differences among groups were found in the phasic pain test (Hargreaves) and the rotarod test. Taken together, these results suggest that cortical antagonism of the NR2B subunit of NMDA receptors is able to reduce inflammatory pain levels not only before, but after the formalin injection in females at different phases of the estrous cycle.