**Table 3:** This table outlines studies that have assessed the antidepressant-like effects of ketamine in commonly used behavioral tests. Molecular alterations of relevance to ketamine’s molecular mechanism of action are also reported.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Species** | **Behaviour** | **Molecular Alteration** | | | **References** |
|  | | **mPFC** | **Hippocampus** | **NAc** |  |
| **SD Rats** | ↓Latency to feed in the NSF 24 h post-injection (5 & 10 mg/kg) | ↑mTOR phosphory-lation in males & females | ↓eEF2 phosphorylation in males (5 mg/kg) | N/A | [[57](https://www.ncbi.nlm.nih.gov/pubmed/23337256)] |
|  | ↑Sucrose consumption of males 48 h post-injection in SPT |  |  |  |  |
|  | ↓immobility in FST in males & females 30 min post-injection |  |  |  |  |
| **C57BL6/J** | ↓FST immobility time in males & free cycling females (3 mg/kg) | p-CaMKIIα & p-MAPK  ↔in all groups | p-CaMKIIα  ↔in D1 females  ↑in males (3 mg/kg)  ↑in Pro females (1.5 & 3 mg/kg) | N/A | [[59](https://www.ncbi.nlm.nih.gov/pubmed/29175352)] |
|  | ↓immobility time in D1 females treated with PPT or DPN but not P4 (1.5 mg/kg) | p-GluR1 & BDNF  ↔in D1 females  ↑in males & Pro Females (3 mg/kg) | p-GluR1  ↔D1 females  ↑in males & Pro females (3 mg/kg) |  |  |
|  | ↓immobility time in males and D1 females (3 mg/kg) | p-Akt  ↔in D1 females  ↑in males at 3 mg/kg ↑in Pro females (1.5 & 3 mg/kg) | BDNF  ↔in Pro females  ↑in males & D1 females (3 mg/kg) |  |  |
|  | ↓immobility time in Pro females (1.5 & 3 mg/kg) | p-GSK-3β  ↔in D1 females  ↑in males & Pro females (1.5 & 3 mg/kg) | p-MAPK  ↑in males & Pro females (3 mg/kg)  ↑in D1 females (1.5 & 3 mg/kg) |  |  |
|  |  | mTOR  ↔in Pro females  ↑in males & D1 females (3 mg/kg) | p-Akt↔in D1 females  ↑in males (3 mg/kg)  ↑in Pro females (1.5 & 3 mg/kg) |  |  |
|  |  |  | p-GSK-3β  ↑in males (1.5 & 3 mg/kg)  ↑in D1 & Pro females (3 mg/kg) |  |  |
| **C57BL6/J** | Females were more sensitive in the FST than males (Females responded to lower dose (3 mg/kg) and the higher doses whiles males responded to higher doses (5 & 10 mg/kg)) | ↑aspartate levels in females  ↓5-HIAA/5HT ratio in females | ↓glutamate conc. in males  ↓5-HIAA/5HT in females | N/A | [[58](https://www.ncbi.nlm.nih.gov/pubmed/25595985)] |
| ICR | ↓immobility time in FST in both sexes (10 mg/kg acute administration) | ↔beclin-1 & p62 (5 & 10 mg/kg chronic administration) | N/A | N/A | [[75](https://www.ncbi.nlm.nih.gov/pubmed/27686025)] |
|  | ↔in immobility time in FST, locomotor activity in the OFT, in both sexes (5 & 10 mg/kg chronic administration) |  |  |  |  |
| **SD Rats** | Ketamine at 10, 20 & 40 mg/kg caused  ↑locomotor activity  ↔grooming in both sexes of preadolescent rats | N/A | N/A | N/A | [[92](https://www.ncbi.nlm.nih.gov/pubmed/28589265)] |
|  | Ketamine at 20 or 40 mg/kg caused female adolescent rats to exhibit more locomotor activity than males  ↔grooming |  |  |  |  |
|  | ↔ conditioned activity after Ketamine administration in both sexes of the preadolescent rats |  |  |  |  |
| **SD Rats** | 2.5 mg/kg  ↑in sucrose preference in OVX females + E2 + P4 | N/A | Protein levels of BDNF  ↑in OVX female + E2 + P4 | N/A | [[91](https://www.ncbi.nlm.nih.gov/pubmed/26888470)] |
|  | ↔in sucrose preference in OVX females + E2 |  | ↔in OVX females + E2  ↔in OVX females + P4 |  |  |
|  | ↔in sucrose preference in OVX females + P4 |  | ↔ in intact males + P4  ↓in intact males + E2 |  |  |
|  | ↑in sucrose preference in intact males + P4 |  | ↑in intact males + E2 + P4  ↔ in intact males + P4 |  |  |
|  | ↔in sucrose preference in intact males + E2 |  | protein levels of Akt & - p-Akt  ↔in all groups |  |  |
|  | ↔in sucrose preference in females + testosterone |  | protein levels of p-ERK  ↑in OVX females + E2  ↔ in all other groups |  |  |
|  | ↔in sucrose preference in gonadectomized males + testosterone |  | protein levels of CaMKIIα & p-CaMKIIα ↓OVX females + E2 of CaMKIIα  ↑in intact males + E2  ↑in intact males + E2 + P4 |  |  |
| **SD Rats** | ↔Conditioned placed preference in both sexes | 5 mg/kg  ↑spine density in the NAcSh in males | N/A | N/A | [[62](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5520991/)] |
|  |  | ↑spine density in NAcSh & NAcC in females |  |  |  |
|  |  | ↑∆fosB, CaMKIIα, GluA1 and BDNF in males |  |  |  |
|  |  | ↔∆fosB, CaMKIIα and BDNF in females  ↑GluA1 in females |  |  |  |
| **C57BL6/J** | ↑time spent in the center in OFT in males  ↓time spent in the center in the OFT in females | ↔glutamate & aspartate in levels in males  ↑5-HIAA/5HT ratio in males | N/A | N/A | [[60](https://www.ncbi.nlm.nih.gov/pubmed/27343934)] |
|  |  | ↑Synapsin I & SNARE levels in males  ↓glutamate & aspartate levels in females |  |  |  |
|  |  | ↔5-HIAA/5HT ratio in females |  |  |  |
|  |  | ↔ Synapsin I & SNARE levels in females |  |  |  |
| **SD Rats** | 5 & 10 mg/kg chronic administration  ↑time in males in the drug-paired chamber (10 mg/kg) | N/A | N/A | ↑∆fosB expression in both sexes but it was higher in females than in males | [[63](https://www.ncbi.nlm.nih.gov/pubmed/29055748)] |
|  | ↓time in females in the drug-paired chamber (5 mg/kg) |  |  |  |  |
|  | ↑in running in locomotor activity in both sexes but the females ran more than the males |  |  |  |  |

FST: Forced swim test; NSF: Novelty suppressed feeding; SPT: Sucrose preference test; OFT: Open field test; mPFC: Medial prefrontal cortex; NAcSh: Nucleus accumbens shell; NAcC: Nucleus accumbens core; eEF2: Eukaryotic elongation factor 2; D1: Diestrus 1; Pro: Proestrous; E2: Estradiol; P4: Progesterone; OVX: Ovariectomized; PPT: 4,4’,4’’-(4-Propyl-[1H]-pyrazole-1,3,5-triyl) trisphenol; DPN: Diarylpropionitrile; mTOR: Mechanistic target of rapamycin; CaMKIIα: Calcium calmodulin kinase II alpha; GluA1: Glutamate ionotropic receptor AMPA type subunit 1; MAPK: Mitogen-activated protein kinase; BDNF: Brain derived neurotrophic factor; GSK-3: Glycogen synthase kinase 3; 5-HIAA: 5hydroxyindoleacetic acid; 5-HT: 5-hydroxytryptamine; SNARE: Soluble NSF attachment protein receptor; ↑: Increasing; ↓: Decreasing; ↔: Propositional.