

References

- Abelaira HM, Réus GZ, Neotti MV, Quevedo J (2014) The role of mTOR in depression and antidepressant responses. Life sciences 101:10-14.
- Acheson DT, Gresack JE, Risbrough VB (2012) Hippocampal dysfunction effects on context memory: possible etiology for posttraumatic stress disorder. Neuropharmacology 62:674-685.
- Akiki TJ, Averill CL, Abdallah CG (2017) A network-based neurobiological model of PTSD: evidence from structural and functional neuroimaging studies. Current Psychiatry Reports 19:81.
- Alexander W (2012) Pharmacotherapy for post-traumatic stress disorder in combat veterans: focus on antidepressants and atypical antipsychotic agents. Pharmacy and Therapeutics 37:32.
- Atwoli L, Stein DJ, Koenen KC, McLaughlin KA (2015) Epidemiology of posttraumatic stress disorder: prevalence, correlates and consequences. Current opinion in psychiatry 28:307.
- Bale TL, Vale WW (2004) CRF and CRF receptors: role in stress responsivity and other behaviors. Annu Rev Pharmacol Toxicol 44:525-557.
- Barden N, Reul J, Holsboer F (1995) Do antidepressants stabilize mood through actions on the hypothalamic-pituitary-adrenocortical system? Trends in neurosciences 18:6-11.
- Bartolomé A, García-Aguilar A, Asahara S-I, Kido Y, Guillén C, Pajvani UB, Benito M (2017) MTORC1 regulates both general autophagy and mitophagy induction after oxidative phosphorylation uncoupling. Molecular and cellular biology 37.
- Battle D (2013) Diagnostic and Statistical Manual of Mental Disorders (DSM). In: Codas, vol. 25, p 191.
- Berger W, Mendlowicz MV, Marques-Portella C, Kinrys G, Fontenelle LF, Marmar CR, Figueira I (2009) Pharmacologic alternatives to antidepressants in posttraumatic stress disorder: a systematic review. Progress in neuro-psychopharmacology and biological psychiatry 33:169-180.
- Birrell JM, Brown VJ (2000) Medial frontal cortex mediates perceptual attentional set shifting in the rat. Journal of Neuroscience 20:4320-4324.
- Bisetti A, Cvetkovic V, Serafin M, Bayer L, Machard D, Jones B, Mühlethaler M (2006) Excitatory action of hypocretin/orexin on neurons of the central medial amygdala. Neuroscience 142:999-1004.
- Blundell J, Kouser M, Powell CM (2008) Systemic inhibition of mammalian target of rapamycin inhibits fear memory reconsolidation. Neurobiology of learning and memory 90:28-35.
- Bohnhoff M, Miller CP, Martin WR (1964) Resistance of the mouse's intestinal tract to experimental salmonella infection: I. factors which interfere with the initiation of infection by oral inoculation. The Journal of experimental medicine 120:805-816.
- Bonaventure P, Yun S, Johnson PL, Shekhar A, Fitz SD, Shireman BT, Lebold TP, Nepomuceno D, Lord B, Wennerholm M (2015) A selective orexin-1 receptor antagonist attenuates stress-induced hyperarousal without hypnotic effects. Journal of Pharmacology and Experimental Therapeutics 352:590-601.
- Bonnavion P, Jackson AC, Carter ME, De Lecea L (2015) Antagonistic interplay between hypocretin and leptin in the lateral hypothalamus regulates stress responses. Nature communications 6:1-14.

- Brady K, Pearlstein T, Asnis GM, Baker D, Rothbaum B, Sikes CR, Farfel GM (2000) Efficacy and safety of sertraline treatment of posttraumatic stress disorder: a randomized controlled trial. Jama 283:1837-1844.
- Brigman JL, Bussey TJ, Saksida LM, Rothblat LA (2005) Discrimination of multidimensional visual stimuli by mice: intra-and extradimensional shifts. Behavioral neuroscience 119:839.
- Brown RE, Sergeeva OA, Eriksson KS, Haas HL (2002) Convergent excitation of dorsal raphe serotonin neurons by multiple arousal systems (orexin/hypocretin, histamine and noradrenaline). Journal of Neuroscience 22:8850-8859.
- Burlet S, Tyler CJ, Leonard CS (2002) Direct and indirect excitation of laterodorsal tegmental neurons by hypocretin/orexin peptides: implications for wakefulness and narcolepsy. Journal of Neuroscience 22:2862-2872.
- Chase EA, Tait DS, Brown VJ (2012) Lesions of the orbital prefrontal cortex impair the formation of attentional set in rats. European Journal of Neuroscience 36:2368-2375.
- Chen H, Chan DC (2009) Mitochondrial dynamics–fusion, fission, movement, and mitophagy–in neurodegenerative diseases. Human molecular genetics 18:R169-R176.
- Corradi J, Bouzat C (2016) Understanding the bases of function and modulation of α7 nicotinic receptors: implications for drug discovery. Molecular pharmacology 90:288-299.
- Daskalakis NP, Lehrner A, Yehuda R (2013) Endocrine aspects of post-traumatic stress disorder and implications for diagnosis and treatment. Endocrinology and Metabolism Clinics 42:503-513.
- Date Y, Mondal MS, Matsukura S, Ueta Y, Yamashita H, Kaiya H, Kangawa K, Nakazato M (2000) Distribution of orexin/hypocretin in the rat median eminence and pituitary. Molecular brain research 76:1-6.
- Davis LL, Suris A, Lambert MT, Heimberg C, Petty F (1997) Post-traumatic stress disorder and serotonin: new directions for research and treatment. Journal of Psychiatry and Neuroscience 22:318.
- de la Monte SM, Wands JR (2006) Molecular indices of oxidative stress and mitochondrial dysfunction occur early and often progress with severity of Alzheimer's disease. Journal of Alzheimer's disease 9:167-181.
- Debiec J, Bush DE, LeDoux JE (2011) Noradrenergic enhancement of reconsolidation in the amygdala impairs extinction of conditioned fear in rats—a possible mechanism for the persistence of traumatic memories in PTSD. Depress Anxiety 28:186-193.
- Diana M (2011) The dopamine hypothesis of drug addiction and its potential therapeutic value. Frontiers in psychiatry 2:64.
- Dickens C, Jayson M, Sutton C, Creed F (2000) The relationship between pain and depression in a trial using paroxetine in sufferers of chronic low back pain. Psychosomatics 41:490-499.
- Drouin J, Sun YL, Tremblay S, Lavender P, Schmidt TJ, de Lean A, Nemer M (1992) Homodimer formation is rate-limiting for high affinity DNA binding by glucocorticoid receptor. Molecular Endocrinology 6:1299-1309.
- Dubey AK, Handu SS, Mediratta PK (2015) Suvorexant: the first orexin receptor antagonist to treat insomnia. Journal of pharmacology & pharmacotherapeutics 6:118.
- Durairaja A, Fendt M (2020) Orexin deficiency modulates cognitive flexibility in a sex-dependent manner. Genes, Brain and Behavior e12707.

- Fani N, Kitayama N, Ashraf A, Reed L, Afzal N, Jawed F, Bremner JD (2009) Neuropsychological functioning in patients with posttraumatic stress disorder following short-term paroxetine treatment. Psychopharmacology bulletin 42:53.
- Feng P, Vurbic D, Wu Z, Hu Y, Strohl K (2008) Changes in brain orexin levels in a rat model of depression induced by neonatal administration of clomipramine. Journal of Psychopharmacology 22:784-791.
- Fifield K, Hebert M, Angel R, Adamec R, Blundell J (2013) Inhibition of mTOR kinase via rapamycin blocks persistent predator stress-induced hyperarousal. Behavioural brain research 256:457-463.
- Flippo KH, Strack S (2017) Mitochondrial dynamics in neuronal injury, development and plasticity. Journal of cell science 130:671-681.
- Flores Á, Saravia R, Maldonado R, Berrendero F (2015) Orexins and fear: implications for the treatment of anxiety disorders. Trends in neurosciences 38:550-559.
- Flores Á, Valls-Comamala V, Costa G, Saravia R, Maldonado R, Berrendero F (2014) The hypocretin/orexin system mediates the extinction of fear memories. Neuropsychopharmacology 39:2732.
- Fragkaki I, Roelofs K, Stins J, Jongedijk RA, Hagenaars MA (2017) Reduced Freezing in Posttraumatic Stress Disorder Patients while Watching Affective Pictures. Frontiers in Psychiatry 8:39.
- Frank JB, Kosten TR, Giller EL, Dan E (1988) A randomized clinical trial of phenelzine and imipramine for posttraumatic stress disorder. The American journal of psychiatry.
- Friedman MJ, Resick PA, Bryant RA, Brewin CR (2011) Considering PTSD for DSM-5. Depression and anxiety 28:750-769.
- Frommberger U, Stieglitz R-D, Nyberg E, Richter H, Novelli-Fischer U, Angenendt J, Zaninelli R, Berger M (2004) Comparison between paroxetine and behaviour therapy in patients with posttraumatic stress disorder (PTSD): a pilot study. International Journal of Psychiatry in Clinical Practice 8:19-23.
- Garabadu D, Ahmad A, Krishnamurthy S (2015) Risperidone attenuates modified stress—re-stress paradigm-induced mitochondrial dysfunction and apoptosis in rats exhibiting post-traumatic stress disorder-like symptoms. Journal of Molecular Neuroscience 56:299-312.
- Garner JP, Thogerson CM, Würbel H, Murray JD, Mench JA (2006) Animal neuropsychology: validation of the Intra-Dimensional Extra-Dimensional set shifting task for mice. Behavioural brain research 173:53-61.
- George SA, Rodriguez-Santiago M, Riley J, Abelson JL, Floresco SB, Liberzon I (2015) Alterations in cognitive flexibility in a rat model of post-traumatic stress disorder. Behavioural brain research 286:256-264.
- Gonzalez P, Martinez KG (2014) The role of stress and fear on the development of psychopathology. The Psychiatric clinics of North America 37:535.
- Gormanns P, Mueller NS, Ditzen C, Wolf S, Holsboer F, Turck CW (2011) Phenometranscriptome correlation unravels anxiety and depression related pathways. Journal of psychiatric research 45:973-979.
- Gotter AL, Winrow CJ, Brunner J, Garson SL, Fox SV, Binns J, Harrell CM, Cui D, Yee KL, Stiteler M (2013) The duration of sleep promoting efficacy by dual orexin receptor antagonists is dependent upon receptor occupancy threshold. BMC neuroscience 14:90.
- Grafe LA, Bhatnagar S (2018) Orexins and stress. Frontiers in neuroendocrinology 51:132-145.

- Grafe LA, Cornfeld A, Luz S, Valentino R, Bhatnagar S (2017) Orexins mediate sex differences in the stress response and in cognitive flexibility. Biological psychiatry 81:683-692.
- Halonen JD, Zoladz PR, Park CR, Diamond DM (2016) Behavioral and neurobiological assessments of predator-based fear conditioning and extinction. Journal of Behavioral and Brain Science 6:337.
- Hannibal KE, Bishop MD (2014) Chronic stress, cortisol dysfunction, and pain: a psychoneuroendocrine rationale for stress management in pain rehabilitation. Physical therapy 94:1816-1825.
- Harvey BH, Brand L, Jeeva Z, Stein DJ (2006) Cortical/hippocampal monoamines, HPA-axis changes and aversive behavior following stress and restress in an animal model of post-traumatic stress disorder. Physiology & behavior 87:881-890.
- Hasselmo ME, Wyble BP, Wallenstein GV (1996) Encoding and retrieval of episodic memories: role of cholinergic and GABAergic modulation in the hippocampus. Hippocampus 6:693-708.
- Haydar SN, Dunlop J (2010) Neuronal nicotinic acetylcholine receptors-targets for the development of drugs to treat cognitive impairment associated with schizophrenia and Alzheimer's disease. Current topics in medicinal chemistry 10:144-152.
- Heim C, Nemeroff CB (2001) The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. Biological psychiatry 49:1023-1039.
- Herrmann N, Chau SA, Kircanski I, Lanctot KL (2011) Current and emerging drug treatment options for Alzheimer's disease. Drugs 71:2031-2065.
- Holmes A, Singewald N (2013) Individual differences in recovery from traumatic fear. Trends in neurosciences 36:23-31.
- Ida T, Nakahara K, Murakami T, Hanada R, Nakazato M, Murakami N (2000) Possible involvement of orexin in the stress reaction in rats. Biochemical and biophysical research communications 270:318-323.
- Jeffereys M (2012) Clinician's guide to medications for PTSD. United States Department of Veterans Affairs website.
- Jin C, Qi R, Yin Y, Hu X, Duan L, Xu Q, Zhang Z, Zhong Y, Feng B, Xiang H (2014) Abnormalities in whole-brain functional connectivity observed in treatment-naive post-traumatic stress disorder patients following an earthquake. Psychological medicine 44:1927-1936.
- Johnson PL, Molosh A, Fitz SD, Truitt WA, Shekhar A (2012) Orexin, stress, and anxiety/panic states. In: Progress in brain research, vol. 198, pp 133-161: Elsevier.
- Kakinuma Y, Akiyama T, Sato T (2009) Cholinoceptive and cholinergic properties of cardiomyocytes involving an amplification mechanism for vagal efferent effects in sparsely innervated ventricular myocardium. The FEBS journal 276:5111-5125.
- Karanges E, Li KM, Motbey C, Callaghan PD, Katsifis A, McGregor IS (2011) Differential behavioural and neurochemical outcomes from chronic paroxetine treatment in adolescent and adult rats: a model of adverse antidepressant effects in human adolescents? International Journal of Neuropsychopharmacology 14:491-504.
- Kasckow J, Baker D, Geracioti Jr T (2001) Corticotropin-releasing hormone in depression and post-traumatic stress disorder. Peptides 22:845-851.
- Keith J, Velezmoro R, O'Brien C (2015) Correlates of cognitive flexibility in veterans seeking treatment for posttraumatic stress disorder. The Journal of nervous and mental disease 203:287-293.

- Kelmendi B, Adams TG, Yarnell S, Southwick S, Abdallah CG, Krystal JH (2016) PTSD: from neurobiology to pharmacological treatments. European journal of psychotraumatology 7:31858.
- Kilpatrick DG, Resnick HS, Milanak ME, Miller MW, Keyes KM, Friedman MJ (2013) National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. Journal of traumatic stress 26:537-547.
- Kim H-J, Park HJ, Hong MS, Song JY, Park H-K, Jo DJ, Park SW, HwanYun D, Park H-K, Yang J-S (2010) Effect by acupuncture on hypothalamic expression of maternally separated rats: proteomic approach. Neurological research 32:69-73.
- Kirouac GJ, Parsons MP, Li S (2005) Orexin (hypocretin) innervation of the paraventricular nucleus of the thalamus. Brain research 1059:179-188.
- Kishi T, Sakuma K, Okuya M, Ninomiya K, Oya K, Kubo M, Matsui Y, Nomura I, Okuyama Y, Matsunaga S (2019) Suvorexant for insomnia in patients with psychiatric disorder: A 1-week, open-label study. Neuropsychopharmacology reports 39:252-255.
- Klann E, Antion MD, Banko JL, Hou L (2004) Synaptic plasticity and translation initiation. Learning & Memory 11:365-372.
- Klenowski PM, Shariff MR, Belmer A, Fogarty MJ, Mu EW, Bellingham MC, Bartlett SE (2016) Prolonged consumption of sucrose in a binge-like manner, alters the morphology of medium spiny neurons in the nucleus accumbens shell. Frontiers in behavioral neuroscience 10:54.
- Koenen K, Ratanatharathorn A, Ng L, McLaughlin K, Bromet E, Stein D, Karam E, Ruscio AM, Benjet C, Scott K (2017) Posttraumatic stress disorder in the world mental health surveys. Psychological medicine 47:2260-2274.
- Koenigs M, Grafman J (2009) Posttraumatic stress disorder: the role of medial prefrontal cortex and amygdala. The Neuroscientist 15:540-548.
- Koenigs M, Huey ED, Raymont V, Cheon B, Solomon J, Wassermann EM, Grafman J (2008) Focal brain damage protects against post-traumatic stress disorder in combat veterans. Nature neuroscience 11:232-237.
- Kohda K, Harada K, Kato K, Hoshino A, Motohashi J, Yamaji T, Morinobu S, Matsuoka N, Kato N (2007) Glucocorticoid receptor activation is involved in producing abnormal phenotypes of single-prolonged stress rats: a putative post-traumatic stress disorder model. Neuroscience 148:22-33.
- Kok S, Roelfsema F, Overeem S, Lammers G, Strijers R, Frolich M, Meinders A, Pijl H (2002) Dynamics of the pituitary-adrenal ensemble in hypocretin-deficient narcoleptic humans: blunted basal adrenocorticotropin release and evidence for normal time-keeping by the master pacemaker. The Journal of Clinical Endocrinology & Metabolism 87:5085-5091.
- Kolisnyk B, Guzman MS, Raulic S, Fan J, Magalhaes AC, Feng G, Gros R, Prado VF, Prado MA (2013) ChAT–ChR2–EYFP mice have enhanced motor endurance but show deficits in attention and several additional cognitive domains. Journal of Neuroscience 33:10427-10438.
- Korotkova TM, Sergeeva OA, Eriksson KS, Haas HL, Brown RE (2003) Excitation of ventral tegmental area dopaminergic and nondopaminergic neurons by orexins/hypocretins. Journal of Neuroscience 23:7-11.
- Krishnamurthy S, Garabadu D, Joy KP (2013) Risperidone ameliorates post-traumatic stress disorder-like symptoms in modified stress re-stress model. Neuropharmacology 75:62-77.

- Krishnamurthy S, Garabadu D, Reddy NR, Joy KP (2011) Risperidone in ultra low dose protects against stress in the rodent cold restraint model by modulating stress pathways. Neurochemical research 36:1750-1758.
- Krystal JH, Neumeister A (2009) Noradrenergic and serotonergic mechanisms in the neurobiology of posttraumatic stress disorder and resilience. Brain research 1293:13-23.
- Kukkonen JP (2013) Physiology of the orexinergic/hypocretinergic system: a revisit in 2012. American Journal of Physiology-Cell Physiology 304:C2-C32.
- Kumar P, Kumar A (2009) Possible role of sertraline against 3-nitropropionic acid induced behavioral, oxidative stress and mitochondrial dysfunctions in rat brain. Progress in Neuro-Psychopharmacology and Biological Psychiatry 33:100-108.
- Lapiz-Bluhm MDS, Bondi CO, Doyen J, Rodriguez G, Bédard-Arana T, Morilak DA (2008) Behavioural assays to model cognitive and affective dimensions of depression and anxiety in rats. Journal of neuroendocrinology 20:1115-1137.
- Lassiter K, Greene E, Piekarski A, Faulkner OB, Hargis BM, Bottje W, Dridi S (2015) Orexin system is expressed in avian muscle cells and regulates mitochondrial dynamics. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology 308:R173-R187.
- Lee KM, Coehlo MA, Solton NR, Szumlinski KK (2017) Negative affect and excessive alcohol intake incubate during protracted withdrawal from binge-drinking in adolescent, but not adult, mice. Frontiers in psychology 8:1128.
- Lerner C, Bitto A, Pulliam D, Nacarelli T, Konigsberg M, Van Remmen H, Torres C, Sell C (2013) Reduced mammalian target of rapamycin activity facilitates mitochondrial retrograde signaling and increases life span in normal human fibroblasts. Aging cell 12:966-977.
- Li J, Hu Z, de Lecea L (2014a) The hypocretins/orexins: integrators of multiple physiological functions. British journal of pharmacology 171:332-350.
- Li J, Kim SG, Blenis J (2014b) Rapamycin: one drug, many effects. Cell metabolism 19:373-379.
- Li M, Meng Y, Chu B, Shen Y, Liu X, Ding M, Song C, Cao X, Wang P, Xu L (2020) Orexin-A aggravates cytotoxicity and mitochondrial impairment in SH-SY5Y cells transfected with APPswe via p38 MAPK pathway. Annals of Translational Medicine 8.
- Li Y, Han F, Shi Y (2013) Increased neuronal apoptosis in medial prefrontal cortex is accompanied with changes of Bcl-2 and Bax in a rat model of post-traumatic stress disorder. Journal of Molecular Neuroscience 51:127-137.
- Li Y, Tang Q, Wang P, Qin J, Wu H, Lin J, Huang Z (2017) Dynamic changes of mitochondrial fusion and fission in brain injury after cardiac arrest in rats. BioMed research international 2017.
- Liberzon I, Krstov M, Young EA (1997) Stress-restress: effects on ACTH and fast feedback. Psychoneuroendocrinology 22:443-453.
- Liberzon I, Lopez J, Flagel S, Vazquez D, Young E (1999) Differential regulation of hippocampal glucocorticoid receptors mRNA and fast feedback: relevance to post-traumatic stress disorder. Journal of neuroendocrinology.
- Lindauer RJ, Olff M, van Meijel EP, Carlier IV, Gersons BP (2006) Cortisol, learning, memory, and attention in relation to smaller hippocampal volume in police officers with posttraumatic stress disorder. Biological psychiatry 59:171-177.
- Liu Y, Zhao Y, Guo L (2016) Effects of orexin A on glucose metabolism in human hepatocellular carcinoma in vitro via PI3K/Akt/mTOR-dependent and-independent mechanism. Molecular and cellular endocrinology 420:208-216.

- López J, Imperial S, Valderrama R, Navarro S (1993) An improved Bradford protein assay for collagen proteins. Clinica chimica acta 220:91-100.
- Lu A, Steiner M, Whittle N, Vogl A, Walser S, Ableitner M, Refojo D, Ekker M, Rubenstein J, Stalla G (2008) Conditional mouse mutants highlight mechanisms of corticotropin-releasing hormone effects on stress-coping behavior. Molecular psychiatry 13:1028-1042.
- MacAskill AF, Rinholm JE, Twelvetrees AE, Arancibia-Carcamo IL, Muir J, Fransson A, Aspenstrom P, Attwell D, Kittler JT (2009) Miro1 is a calcium sensor for glutamate receptor-dependent localization of mitochondria at synapses. Neuron 61:541-555.
- Manson SM, Beals J, Klein SA, Croy CD, Team A-s (2005) Social epidemiology of trauma among 2 American Indian reservation populations. American journal of public health 95:851-859.
- Marshall RD, Beebe KL, Oldham M, Zaninelli R (2001) Efficacy and safety of paroxetine treatment for chronic PTSD: a fixed-dose, placebo-controlled study. American Journal of Psychiatry 158:1982-1988.
- Martyn AC, De Jaeger X, Magalhães AC, Kesarwani R, Gonçalves DF, Raulic S, Guzman MS, Jackson MF, Izquierdo I, MacDonald JF (2012) Elimination of the vesicular acetylcholine transporter in the forebrain causes hyperactivity and deficits in spatial memory and long-term potentiation. Proceedings of the National Academy of Sciences 109:17651-17656.
- McEwen BS, Chattarji S, Diamond DM, Jay TM, Reagan LP, Svenningsson P, Fuchs E (2010) The neurobiological properties of tianeptine (Stablon): from monoamine hypothesis to glutamatergic modulation. Molecular psychiatry 15:237-249.
- Merlo-Pich E, Melotto S (2014) Orexin 1 receptor antagonists in compulsive behaviour and anxiety: possible therapeutic use. Frontiers in neuroscience 8:26.
- Mikics E, Baranyi J, Haller J (2008) Rats exposed to traumatic stress bury unfamiliar objects—a novel measure of hyper-vigilance in PTSD models? Physiol Behav 94:341-348.
- Milad MR, Pitman RK, Ellis CB, Gold AL, Shin LM, Lasko NB, Zeidan MA, Handwerger K, Orr SP, Rauch SL (2009) Neurobiological basis of failure to recall extinction memory in posttraumatic stress disorder. Biological psychiatry 66:1075-1082.
- Mitsushima D, Yamada K, Takase K, Funabashi T, Kimura F (2006) Sex differences in the basolateral amygdala: the extracellular levels of serotonin and dopamine, and their responses to restraint stress in rats. European Journal of Neuroscience 24:3245-3254.
- Mnie-Filali O, Abrial E, Lambás-Señas L, Haddjeri N (2013) Long-term adaptive changes induced by antidepressants: From conventional to novel therapies. Mood Disorders 145.
- Morita M, Prudent J, Basu K, Goyon V, Katsumura S, Hulea L, Pearl D, Siddiqui N, Strack S, McGuirk S (2017) mTOR controls mitochondrial dynamics and cell survival via MTFP1. Molecular cell 67:922-935. e925.
- Mousum SA, Ahmed S, Gawali B, Kwatra M, Ahmed A, Lahkar M (2018) Nyctanthes arbor-tristis leaf extract ameliorates hyperlipidemia-and hyperglycemia-associated nephrotoxicity by improving anti-oxidant and anti-inflammatory status in high-fat diet–streptozotocin-induced diabetic rats. Inflammopharmacology 26:1415-1428.
- Mukherjee S, Sen S, Biswas A, Barman TK, Tripathi SK (2015) Impact on behavioral changes due to chronic use of sertraline in Wistar albino rats. Indian journal of pharmacology 47:657.

- Nakamura M, Nagamine T (2017) Neuroendocrine, autonomic, and metabolic responses to an orexin antagonist, suvorexant, in psychiatric patients with insomnia. Innovations in clinical neuroscience 14:30.
- Nikiforuk A, Kos T, Potasiewicz A, Popik P (2015) Positive allosteric modulation of alpha 7 nicotinic acetylcholine receptors enhances recognition memory and cognitive flexibility in rats. European Neuropsychopharmacology 25:1300-1313.
- Nutt D (1986) Benzodiazepine dependence in the clinic: reason for anxiety? Trends in Pharmacological Sciences 7:457-460.
- Ojha R, Sahu AN, Muruganandam A, Singh GK, Krishnamurthy S (2010) Asparagus recemosus enhances memory and protects against amnesia in rodent models. Brain and cognition 74:1-9.
- Old SL, Johnson MA (1989) Methods of microphotometric assay of succinate dehydrogenase and cytochromec oxidase activities for use on human skeletal muscle. The Histochemical journal 21:545-555.
- Önder E, Tural Ü, Aker T (2006) A comparative study of fluoxetine, moclobemide, and tianeptine in the treatment of posttraumatic stress disorder following an earthquake. European psychiatry 21:174-179.
- Parsons RG, Gafford GM, Helmstetter FJ (2006) Translational control via the mammalian target of rapamycin pathway is critical for the formation and stability of long-term fear memory in amygdala neurons. Journal of Neuroscience 26:12977-12983.
- Pattanashetti LA, Taranalli AD, Parvatrao V, Malabade RH, Kumar D (2017) Evaluation of neuroprotective effect of quercetin with donepezil in scopolamine-induced amnesia in rats. Indian journal of pharmacology 49:60.
- Paxinos G, Ashwell KW (2018) Atlas of the developing rat nervous system: Academic Press.
- Perez-Ternero C, Werner CM, Nickel AG, Herrera MD, Motilva M-J, Böhm M, de Sotomayor MA, Laufs U (2017) Ferulic acid, a bioactive component of rice bran, improves oxidative stress and mitochondrial biogenesis and dynamics in mice and in human mononuclear cells. The Journal of Nutritional Biochemistry 48:51-61.
- Piantadosi PT, Holmes A, Roberts BM, Bailey AM (2015) Orexin receptor activity in the basal forebrain alters performance on an olfactory discrimination task. Brain research 1594:215-222.
- Pietrzak RH, Goldstein RB, Southwick SM, Grant BF (2011) Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. Journal of anxiety disorders 25:456-465.
- Pooley AE, Benjamin RC, Sreedhar S, Eagle AL, Robison AJ, Mazei-Robison MS, Breedlove SM, Jordan CL (2018) Sex differences in the traumatic stress response: PTSD symptoms in women recapitulated in female rats. Biology of sex differences 9:31.
- Prado CE, Watt S, Crowe SF (2018) A meta-analysis of the effects of antidepressants on cognitive functioning in depressed and non-depressed samples. Neuropsychology review 28:32-72.
- Prado VF, Janickova H, Al-Onaizi MA, Prado MA (2017) Cholinergic circuits in cognitive flexibility. Neuroscience 345:130-141.
- Prajapati SK, Dangi DS, Krishnamurthy S (2019a) Repeated caffeine administration aggravates post-traumatic stress disorder-like symptoms in rats. Physiology & behavior 211:112666.

- Prajapati SK, Krishnamurthy S (2020a) Non-selective orexin-receptor antagonist attenuates stress-re-stress-induced core PTSD-like symptoms in rats: behavioural and neurochemical analyses. Behavioural Brain Research 113015.
- Prajapati SK, Krishnamurthy S (2021) Development and treatment of cognitive inflexibility in sub-chronic stress—re-stress (SRS) model of PTSD. Pharmacological Reports.
- Prajapati SK, Singh N, Garabadu D, Krishnamurthy S (2019c) A novel stress re-stress model: Modification of re-stressor cue induces long-lasting post-traumatic stress disorder-like symptoms in rats. International Journal of Neuroscience 1-21.
- Qin S, Hermans EJ, van Marle HJ, Luo J, Fernández G (2009) Acute psychological stress reduces working memory-related activity in the dorsolateral prefrontal cortex. Biological psychiatry 66:25-32.
- Quirk GJ, Mueller D (2008) Neural mechanisms of extinction learning and retrieval. Neuropsychopharmacology 33:56-72.
- Ragozzino ME, Jih J, Tzavos A (2002) Involvement of the dorsomedial striatum in behavioral flexibility: role of muscarinic cholinergic receptors. Brain research 953:205-214.
- Ramaswamy S, Driscoll D, Smith LM, Bhatia SC, Petty F (2016) Failed efficacy of ziprasidone in the treatment of post-traumatic stress disorder. Contemporary clinical trials communications 2:1-5.
- Rampin C, Cespuglio R, Chastrette N, Jouvet M (1991) Immobilisation stress induces a paradoxical sleep rebound in rat. Neuroscience letters 126:113-118.
- Reddy NR, Krishnamurthy S (2018) Repeated olanzapine treatment mitigates PTSD like symptoms in rats with changes in cell signaling factors. Brain research bulletin.
- Richardson A, Galvan V, Lin A-L, Oddo S (2015) How longevity research can lead to therapies for Alzheimer's disease: The rapamycin story. Experimental gerontology 68:51-58.
- S Tait D, Alexander Chase E, J Brown V (2014) Attentional set-shifting in rodents: a review of behavioural methods and pharmacological results. Current pharmaceutical design 20:5046-5059.
- Saeed SA, Bruce TJ (1998) Panic disorder: effective treatment options. American family physician 57:2405.
- Saito YC, Tsujino N, Abe M, Yamazaki M, Sakimura K, Sakurai T (2018) Serotonergic input to orexin neurons plays a role in maintaining wakefulness and REM sleep architecture. Frontiers in Neuroscience 12:892.
- Sakurai T, Amemiya A, Ishii M, Matsuzaki I, Chemelli RM, Tanaka H, Williams SC, Richardson JA, Kozlowski GP, Wilson S (1998) Orexins and orexin receptors: a family of hypothalamic neuropeptides and G protein-coupled receptors that regulate feeding behavior. Cell 92:573-585.
- Salehabadi S, Abrari K, Salmani ME, Nasiri M, Lashkarbolouki T (2020) Investigating the role of the amygdala orexin receptor 1 in memory acquisition and extinction in a rat model of PTSD. Behavioural Brain Research 384:112455.
- Salomon RM, Ripley B, Kennedy JS, Johnson B, Schmidt D, Zeitzer JM, Nishino S, Mignot E (2003) Diurnal variation of cerebrospinal fluid hypocretin-1 (Orexin-A) levels in control and depressed subjects. Biological psychiatry 54:96-104.
- Samaiya PK, Narayan G, Kumar A, Krishnamurthy S (2017) Tempol (4 hydroxy-tempo) inhibits anoxia-induced progression of mitochondrial dysfunction and associated neurobehavioral impairment in neonatal rats. Journal of the neurological sciences 375:58-67.

- Samson WK, Taylor MM, Follwell M, Ferguson AV (2002) Orexin actions in hypothalamic paraventricular nucleus: physiological consequences and cellular correlates. Regulatory peptides 104:97-103.
- Santiago RM, Zaminelli T, Bassani TB, Boschen SL, Lima MM, Da Cunha C, Andreatini R, Vital MA (2015) The mechanism of antidepressant-like effects of piroxicam in rats. Journal of pharmacology & pharmacotherapeutics 6:7.
- Schwartz AC, Rothbaum BO (2002) Review of sertraline in post-traumatic stress disorder. Expert opinion on pharmacotherapy 3:1489-1499.
- Shapiro BL, Lam L, Feigal RJ (1982) Mitochondrial NADH dehydrogenase in cystic fibrosis: enzyme kinetics in cultured fibroblasts. American journal of human genetics 34:846.
- Sharko AC, Fadel JR, Kaigler KF, Wilson MA (2017) Activation of orexin/hypocretin neurons is associated with individual differences in cued fear extinction. Physiology & behavior 178:93-102.
- Sherin JE, Nemeroff CB (2011) Post-traumatic stress disorder: the neurobiological impact of psychological trauma. Dialogues in clinical neuroscience 13:263.
- Shi Y (2001) A structural view of mitochondria-mediated apoptosis. Nature structural biology 8:394-401.
- Shimohama S, Kihara T (2001) Nicotinic receptor—mediated protection against β-amyloid neurotoxicity. Biological psychiatry 49:233-239.
- Shin LM, Rauch SL, Pitman RK (2006) Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. Annals of the New York Academy of Sciences 1071:67-79.
- So M, Hashimoto H, Saito R, Yamamoto Y, Motojima Y, Ueno H, Sonoda S, Yoshimura M, Maruyama T, Kusuhara K (2018) Inhibition of ghrelin-induced feeding in rats by pretreatment with a novel dual orexin receptor antagonist. The Journal of Physiological Sciences 68:129-136.
- Steckler T, Sahgal A (1995) The role of serotonergic-cholinergic interactions in the mediation of cognitive behaviour. Behavioural brain research 67:165-199.
- Strawn JR, Pyne-Geithman GJ, Ekhator NN, Horn PS, Uhde TW, Shutter LA, Baker DG, Geracioti Jr TD (2010) Low cerebrospinal fluid and plasma orexin-A (hypocretin-1) concentrations in combat-related posttraumatic stress disorder. Psychoneuroendocrinology 35:1001-1007.
- Su D, Zhao Y, Wang B, Xu H, Li W, Chen J, Wang X (2011) Isoflurane-induced spatial memory impairment in mice is prevented by the acetylcholinesterase inhibitor donepezil. PLoS One 6:e27632.
- Sutcliffe JG, de Lecea L (2000) The hypocretins: excitatory neuromodulatory peptides for multiple homeostatic systems, including sleep and feeding. Journal of neuroscience research 62:161-168.
- Szymańska M, Budziszewska B, Jaworska-Feil L, Basta-Kaim A, Kubera M, Leśkiewicz M, Regulska M, Lasoń W (2009) The effect of antidepressant drugs on the HPA axis activity, glucocorticoid receptor level and FKBP51 concentration in prenatally stressed rats. Psychoneuroendocrinology 34:822-832.
- Tait DS, Bowman EM, Neuwirth LS, Brown VJ (2018) Assessment of intradimensional/extradimensional attentional set-shifting in rats. Neuroscience & Biobehavioral Reviews 89:72-84.
- Takada-Takatori Y, Kume T, Ohgi Y, Fujii T, Niidome T, Sugimoto H, Akaike A (2008) Mechanisms of α7-nicotinic receptor up-regulation and sensitization to donepezil induced by chronic donepezil treatment. European journal of pharmacology 590:150-156.

- Takahashi T, Morinobu S, Iwamoto Y, Yamawaki S (2006) Effect of paroxetine on enhanced contextual fear induced by single prolonged stress in rats. Psychopharmacology 189:165-173.
- Thomas E, Stein DJ (2017) Novel pharmacological treatment strategies for posttraumatic stress disorder. Expert review of clinical pharmacology 10:167-177.
- Vermetten E, Bremner JD (2002) Circuits and systems in stress. II. Applications to neurobiology and treatment in posttraumatic stress disorder. Depression and anxiety 16:14-38.
- Volke V, Soosaar A, Ko S, Bourin M, Männistö PT, Vasar E (1997) 7-Nitroindazole, a nitric oxide synthase inhibitor, has anxiolytic-like properties in exploratory models of anxiety. Psychopharmacology 131:399-405.
- Walker DL, Davis M (2002) The role of amygdala glutamate receptors in fear learning, fear-potentiated startle, and extinction. Pharmacology Biochemistry and Behavior 71:379-392.
- Walling SG, Nutt DJ, Lalies MD, Harley CW (2004) Orexin-A infusion in the locus ceruleus triggers norepinephrine (NE) release and NE-induced long-term potentiation in the dentate gyrus. Journal of Neuroscience 24:7421-7426.
- Waltz JA (2017) The neural underpinnings of cognitive flexibility and their disruption in psychotic illness. Neuroscience 345:203-217.
- Wang A, Keita ÅV, Phan V, McKay CM, Schoultz I, Lee J, Murphy MP, Fernando M, Ronaghan N, Balce D (2014a) Targeting mitochondria-derived reactive oxygen species to reduce epithelial barrier dysfunction and colitis. The American journal of pathology 184:2516-2527.
- Wang C, Wang Q, Ji B, Pan Y, Xu C, Cheng B, Bai B, Chen J (2018) The orexin/receptor system: molecular mechanism and therapeutic potential for neurological diseases. Frontiers in molecular neuroscience 11:220.
- Wang W, Liu Y, Zheng H, Wang HN, Jin X, Chen YC, Zheng LN, Luo XX, Tan QR (2008) A modified single-prolonged stress model for post-traumatic stress disorder. Neuroscience letters 441:237-241.
- Wang Z, Liu S, Kakizaki M, Hirose Y, Ishikawa Y, Funato H, Yanagisawa M, Yu Y, Liu Q (2014b) Orexin/hypocretin activates mTOR complex 1 (mTORC1) via an Erk/Akt-independent and calcium-stimulated lysosome v-ATPase pathway. Journal of Biological Chemistry 289:31950-31959.
- Winrow CJ, Gotter AL, Cox CD, Doran SM, Tannenbaum PL, Breslin MJ, Garson SL, Fox SV, Harrell CM, Stevens J (2011) Promotion of sleep by suvorexant—a novel dual orexin receptor antagonist. Journal of neurogenetics 25:52-61.
- Winrow CJ, Gotter AL, Cox CD, Tannenbaum PL, Garson SL, Doran SM, Breslin MJ, Schreier JD, Fox SV, Harrell CM (2012) Pharmacological characterization of MK-6096–a dual orexin receptor antagonist for insomnia. Neuropharmacology 62:978-987.
- Winsky-Sommerer R, Yamanaka A, Diano S, Borok E, Roberts AJ, Sakurai T, Kilduff TS, Horvath TL, de Lecea L (2004) Interaction between the corticotropin-releasing factor system and hypocretins (orexins): a novel circuit mediating stress response. Journal of Neuroscience 24:11439-11448.
- Xing G, Barry ES, Benford B, Grunberg NE, Li H, Watson WD, Sharma P (2013) Impact of repeated stress on traumatic brain injury-induced mitochondrial electron transport chain expression and behavioral responses in rats. Frontiers in neurology 4:196.

- Yamanaka A, Muraki Y, Ichiki K, Tsujino N, Kilduff TS, Goto K, Sakurai T (2006) Orexin neurons are directly and indirectly regulated by catecholamines in a complex manner. Journal of neurophysiology 96:284-298.
- Yang C, Zhang L, Hao H, Ran M, Li J, Dong H (2019) Serotonergic neurons in the dorsal raphe nucleus mediate the arousal-promoting effect of orexin during isoflurane anesthesia in male rats. Neuropeptides 75:25-33.
- Yehuda R, Antelman SM (1993) Criteria for rationally evaluating animal models of postraumatic stress disorder. Biological psychiatry 33:479-486.
- Yehuda R, Southwick SM, Krystal JH, Bremner D, Charney DS, Mason JW (1993) Enhanced suppression of cortisol following dexamethasone administration in posttraumatic stress disorder. American Journal of Psychiatry 150:83-83.
- Yehuda R, Southwick SM, Nussbaum G, Wahby VS, Giller EL, Mason JW (1990) Low urinary cortisol excretion in patients with posttraumatic stress disorder. Journal of Nervous and Mental Disease.
- Yeoh JW, Campbell EJ, James MH, Graham BA, Dayas CV (2014) Orexin antagonists for neuropsychiatric disease: progress and potential pitfalls. Frontiers in neuroscience 8:36.
- Zangar RC, Davydov DR, Verma S (2004) Mechanisms that regulate production of reactive oxygen species by cytochrome P450. Toxicology and applied pharmacology 199:316-331.
- Zemirli N, Morel E, Molino D (2018) Mitochondrial dynamics in basal and stressful conditions. International journal of molecular sciences 19:564.
- Zhang L, Li H, Hu X, Benedek D, Fullerton C, Forsten R, Naifeh J, Li X, Wu H, Benevides K (2015) Mitochondria-focused gene expression profile reveals common pathways and CPT1B dysregulation in both rodent stress model and human subjects with PTSD. Translational psychiatry 5:e580-e580.
- Zhao D, Xu X, Pan L, Zhu W, Fu X, Guo L, Lu Q, Wang J (2017) Pharmacologic activation of cholinergic alpha7 nicotinic receptors mitigates depressive-like behavior in a mouse model of chronic stress. Journal of neuroinflammation 14:234.
- Zoladz PR, Conrad CD, Fleshner M, Diamond DM (2008) Acute episodes of predator exposure in conjunction with chronic social instability as an animal model of post-traumatic stress disorder. Stress 11:259-281.

List of Publications

List of Publication from Thesis

- **1. Prajapati SK,** Krishnamurthy S. Non-selective orexin-receptor antagonist attenuates stress-re-stress-induced core PTSD-like symptoms in rats: Behavioural and neurochemical analyses. Behavioural Brain Research. 2020 Nov 16;399:113015.
- **2.** <u>Prajapati SK</u>, Krishnamurthy S. Development and treatment of cognitive inflexibility in sub-chronic stress—re-stress (SRS) model of PTSD. Pharmacological Reports.:1-6.