References

Aghajanian GK (1972) Chemical-feedback regulation of serotonin-containing neurons in brain. Ann N Y Acad Sci 193:86-94.

Albert DJ, Mah CJ (1973) Passive avoidance deficit with septal lesions: disturbance of response inhibition or response acquisition? Physiol Behav 11:205-213.

Albert DJ, Madryga FJ (1980) An examination of the functionally effective spread of 4 microliters of slowly infused lidocaine. Behav Neural Biol 29:378-384.

Alex KD, Pehek EA (2007) Pharmacologic mechanisms of serotonergic regulation of dopamine neurotransmission. Pharmacol Ther 113:296-320.

Alexander GE, DeLong MR, Strick PL (1986) Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annu Rev Neurosci 9:357-381.

Allen PP, Cleare AJ, Lee F, Fusar-Poli P, Tunstall N, Fu CH, Brammer MJ, McGuire PK (2006) Effect of acute tryptophan depletion on pre-frontal engagement. Psychopharmacology (Berl) 187:486-497.

Amat J, Baratta MV, Paul E, Bland ST, Watkins LR, Maier SF (2005) Medial prefrontal cortex determines how stressor controllability affects behavior and dorsal raphe nucleus. Nat Neurosci 8:365-371.

Anderson IM, McKie S, Elliott R, Williams SR, Deakin JF (2008) Assessing human 5-HT function in vivo with pharmacoMRI. Neuropharmacology 55:1029-1037.

Ardis TC, Cahir M, Elliott JJ, Bell R, Reynolds GP, Cooper SJ (2009) Effect of acute tryptophan depletion on noradrenaline and dopamine in the rat brain. J Psychopharmacol 23:51-55.

Ashley DV, Curzon G (1981) Effects of long-term low dietary tryptophan intake on determinants of 5-hydroxytryptamine metabolism in the brains of young rats. J Neurochem 37:1385-1393.

Auerbach SB, Hjorth S (1995) Effect of chronic administration of the selective serotonin (5-HT) uptake inhibitor citalopram on extracellular 5-HT and apparent autoreceptor sensitivity in rat forebrain in vivo. Naunyn Schmiedebergs Arch Pharmacol 352:597-606.

Badawy AA (2005) Acute tryptophan or tyrosine depletion test: time for reappraisal? J Psychopharmacol 19:429-430; author reply 431.

Balleine BW (2005) Neural bases of food-seeking: affect, arousal and reward in corticostriatolimbic circuits. Physiol Behav 86:717-730.

Balleine BW, Dickinson A (1998) Goal-directed instrumental action: contingency and incentive learning and their cortical substrates. Neuropharmacology 37:407-419.

Bari A, Theobald DE, Caprioli D, Mar AC, Aidoo-Micah A, Dalley JW, Robbins TW (2010) Serotonin modulates sensitivity to reward and negative feedback in a probabilistic reversal learning task in rats. Neuropsychopharmacology 35:1290-1301.

Barnes NM, Sharp T (1999) A review of central 5-HT receptors and their function. Neuropharmacology 38:1083-1152.

Baumgarten HG, Bjorklund A (1976) Neurotoxic indoleamines and monoamine neurons. Annu Rev Pharmacol Toxicol 16:101-111.

Bechara A, Damasio H, Damasio AR (2000) Emotion, decision making and the orbitofrontal cortex. Cereb Cortex 10:295-307.

Bel N, Artigas F (1996) Reduction of serotonergic function in rat brain by tryptophan depletion: effects in control and fluvoxamine-treated rats. J Neurochem 67:669-676.

Bell C, Abrams J, Nutt D (2001) Tryptophan depletion and its implications for psychiatry. Br J Psychiatry 178:399-405.

Beninger RJ, Phillips AG (1979) Possible involvement of serotonin in extinction. Pharmacol Biochem Behav 10:37-41.

Benveniste H (1989) Brain microdialysis. J Neurochem 52:1667-1679.

Berg KA, Harvey JA, Spampinato U, Clarke WP (2008) Physiological and therapeutic relevance of constitutive activity of 5-HT_{2A} and 5-HT_{2C} receptors for the treatment of depression. Prog Brain Res 172:287-305.

Biggio G, Fadda F, Fanni P, Tagliamonte A, Gessa GL (1974) Rapid depletion of serum tryptophan, brain tryptophan, serotonin and 5-hydroxyindoleacetic acid by a tryptophan-free diet. Life Sci 14:1321-1329.

Birrell JM, Brown VJ (2000) Medial frontal cortex mediates perceptual attentional set shifting in the rat. J Neurosci 20:4320-4324.

Block AE, Dhanji H, Thompson-Tardif SF, Floresco SB (2007) Thalamic-prefrontal cortical-ventral striatal circuitry mediates dissociable components of strategy set shifting. Cereb Cortex 17:1625-1636.

Boehnke SE, Rasmusson DD (2001) Time course and effective spread of lidocaine and tetrodotoxin delivered via microdialysis: an electrophysiological study in cerebral cortex. J Neurosci Methods 105:133-141.

Boeijinga PH, Mulder AB, Pennartz CM, Manshanden I, Lopes da Silva FH (1993) Responses of the nucleus accumbens following fornix/fimbria stimulation in the rat. Identification and long-term potentiation of mono- and polysynaptic pathways. Neuroscience 53:1049-1058.

Bohn I, Giertler C, Hauber W (2003) Orbital prefrontal cortex and guidance of instrumental behaviour in rats under reversal conditions. Behav Brain Res 143:49-56.

Booij L, van der Does W, Benkelfat C, Bremner JD, Cowen PJ, Fava M, Gillin C, Leyton M, Moore P, Smith KA, van der Kloot WA (2002) Predictors of mood response to acute tryptophan depletion. A reanalysis. Neuropsychopharmacology 27:852-861.

Booij L, van der Does AJ, Riedel WJ (2003) Monoamine depletion in psychiatric and healthy populations: review. Mol Psychiatry 8:951-973.

Boulougouris V, Dalley JW, Robbins TW (2007) Effects of orbitofrontal, infralimbic and prelimbic cortical lesions on serial spatial reversal learning in the rat. Behav Brain Res 179:219-228.

Boulougouris V, Glennon JC, Robbins TW (2008) Dissociable effects of selective 5-HT_{2A} and 5-HT_{2C} receptor antagonists on serial spatial reversal learning in rats. Neuropsychopharmacology 33:2007-2019.

Boulougouris V, Robbins TW (2010) Enhancement of spatial reversal learning by 5-HT_{2C} receptor antagonism is neuroanatomically specific. J Neurosci 30:930-938.

Bouret S, Sara SJ (2005) Network reset: a simplified overarching theory of locus coeruleus noradrenaline function. Trends Neurosci 28:574-582.

Brazhnik E, Borgnis R, Muller RU, Fox SE (2004) The effects on place cells of local scopolamine dialysis are mimicked by a mixture of two specific muscarinic antagonists. J Neurosci 24:9313-9323.

Bremner JD, Innis RB, Salomon RM, Staib LH, Ng CK, Miller HL, Bronen RA, Krystal JH, Duncan J, Rich D, Price LH, Malison R, Dey H, Soufer R, Charney DS (1997) Positron emission tomography measurement of cerebral metabolic correlates of tryptophan depletion-induced depressive relapse. Arch Gen Psychiatry 54:364-374.

Brioni JD, Nagahara AH, McGaugh JL (1989) Involvement of the amygdala GABAergic system in the modulation of memory storage. Brain Res 487:105-112.

Bussey TJ, Muir JL, Everitt BJ, Robbins TW (1997) Triple dissociation of anterior cingulate, posterior cingulate, and medial frontal cortices on visual discrimination tasks using a touchscreen testing procedure for the rat. Behav Neurosci 111:920-936.

Butters N, Butter C, Rosen J, Stein D (1973) Behavioral effects of sequential and one-stage ablations of orbital prefrontal cortex in the monkey. Exp Neurol 39:204-214.

Cahir M, Ardis T, Reynolds GP, Cooper SJ (2007) Acute and chronic tryptophan depletion differentially regulate central 5-HT_{1A} and 5-HT_{2A} receptor binding in the rat. Psychopharmacology (Berl) 190:497-506.

Cardinal RN, Pennicott DR, Sugathapala CL, Robbins TW, Everitt BJ (2001) Impulsive choice induced in rats by lesions of the nucleus accumbens core. Science 292:2499-2501.

Carlsson A, Lindqvist M (1978) Effects of antidepressant agents on the synthesis of brain monoamines. J Neural Transm 43:73-91.

Carpenter LL, Anderson GM, Pelton GH, Gudin JA, Kirwin PD, Price LH, Heninger GR, McDougle CJ (1998) Tryptophan depletion during continuous CSF sampling in healthy human subjects. Neuropsychopharmacology 19:26-35.

Castañe A, Theobald DE, Robbins TW (2010) Selective lesions of the dorsomedial striatum impair serial spatial reversal learning in rats. Behav Brain Res 210:74-83.

Chamberlain SR, Muller U, Blackwell AD, Clark L, Robbins TW, Sahakian BJ (2006) Neurochemical modulation of response inhibition and probabilistic learning in humans. Science 311:861-863.

Chudasama Y, Robbins TW (2003) Dissociable contributions of the orbitofrontal and infralimbic cortex to pavlovian autoshaping and discrimination reversal learning: further evidence for the functional heterogeneity of the rodent frontal cortex. J Neurosci 23:8771-8780.

Chudasama Y, Robbins TW (2006) Functions of frontostriatal systems in cognition: comparative neuropsychopharmacological studies in rats, monkeys and humans. Biol Psychol 73:19-38.

Clarke HF, Dalley JW, Crofts HS, Robbins TW, Roberts AC (2004) Cognitive inflexibility after prefrontal serotonin depletion. Science 304:878-880.

Clarke HF, Walker SC, Crofts HS, Dalley JW, Robbins TW, Roberts AC (2005) Prefrontal serotonin depletion affects reversal learning but not attentional set shifting. J Neurosci 25:532-538.

Clarke HF, Walker SC, Dalley JW, Robbins TW, Roberts AC (2007) Cognitive inflexibility after prefrontal serotonin depletion is behaviorally and neurochemically specific. Cereb Cortex 17:18-27.

Clarke HF, Robbins TW, Roberts AC (2008) Lesions of the medial striatum in monkeys produce perseverative impairments during reversal learning similar to those produced by lesions of the orbitofrontal cortex. J Neurosci 28:10972-10982.

Cools R, Clark L, Owen AM, Robbins TW (2002) Defining the neural mechanisms of probabilistic reversal learning using event-related functional magnetic resonance imaging. J Neurosci 22:4563-4567.

Cools R, Robinson OJ, Sahakian B (2008a) Acute tryptophan depletion in healthy volunteers enhances punishment prediction but does not affect reward prediction. Neuropsychopharmacology 33:2291-2299.

Cools R, Roberts AC, Robbins TW (2008b) Serotoninergic regulation of emotional and behavioural control processes. Trends Cogn Sci 12:31-40.

Cools R, Frank MJ, Gibbs SE, Miyakawa A, Jagust W, D'Esposito M (2009) Striatal dopamine predicts outcome-specific reversal learning and its sensitivity to dopaminergic drug administration. J Neurosci 29:1538-1543.

Coutureau E, Killcross S (2003) Inactivation of the infralimbic prefrontal cortex reinstates goal-directed responding in overtrained rats. Behav Brain Res 146:167-174.

Crespi F (1990) In vivo voltammetry with micro-biosensors for analysis of neurotransmitter release and metabolism. J Neurosci Methods 34:53-65.

Crockett MJ, Clark L, Robbins TW (2009) Reconciling the role of serotonin in behavioral inhibition and aversion: acute tryptophan depletion abolishes punishment-induced inhibition in humans. J Neurosci 29:11993-11999.

Crofts HS, Dalley JW, Collins P, Van Denderen JC, Everitt BJ, Robbins TW, Roberts AC (2001) Differential effects of 6-OHDA lesions of the frontal cortex and caudate nucleus on the ability to acquire an attentional set. Cereb Cortex 11:1015-1026.

D'Souza DN, Zhang Y, Garcia F, Battaglia G, Van de Kar LD (2004) Fluoxetine-induced changes in body weight and 5-HT_{1A} receptor-mediated hormone secretion in rats on a tryptophan-deficient diet. Am J Physiol Regul Integr Comp Physiol 286:R390-397.

Daberkow DP, Riedy MD, Kesner RP, Keefe KA (2008) Effect of methamphetamine neurotoxicity on learning-induced Arc mRNA expression in identified striatal efferent neurons. Neurotox Res 14:307-315.

Dalley JW, Theobald DE, Eagle DM, Passetti F, Robbins TW (2002) Deficits in impulse control associated with tonically-elevated serotonergic function in rat prefrontal cortex. Neuropsychopharmacology 26:716-728.

Dalley JW, Cardinal RN, Robbins TW (2004) Prefrontal executive and cognitive functions in rodents: neural and neurochemical substrates. Neurosci Biobehav Rev 28:771-784.

Damasio AR (1996) The somatic marker hypothesis and the possible functions of the prefrontal cortex. Philos Trans R Soc Lond B Biol Sci 351:1413-1420.

Davies SJ, Hood SD, Argyropoulos SV, Morris K, Bell C, Witchel HJ, Jackson PR, Nutt DJ, Potokar JP (2006) Depleting serotonin enhances both cardiovascular and psychological stress reactivity in recovered patients with anxiety disorders. J Clin Psychopharmacol 26:414-418.

Daw ND, Kakade S, Dayan P (2002) Opponent interactions between serotonin and dopamine. Neural Netw 15:603-616.

Dayan P, Huys QJ (2009) Serotonin in affective control. Annu Rev Neurosci 32:95-126.

de Bruin JPC, Sanchez-Santed F, Heinsbroek RP, Donker A, Postmes P (1994) A behavioural analysis of rats with damage to the medial prefrontal cortex using the Morris water maze: evidence for behavioural flexibility, but not for impaired spatial navigation. Brain Res 652:323-333.

de Bruin JPC, Feenstra MGP, Broersen LM, van Leeuwen M, Arens C, de Vries S, Joosten RNJMA (2000) Role of the prefrontal cortex of the rat in learning and decision making: effects of transient inactivation. Prog Brain Res 126:103-113.

de Wit S, Kosaki Y, Balleine BW, Dickinson A (2006) Dorsomedial prefrontal cortex resolves response conflict in rats. J Neurosci 26:5224-5229.

Delgado PL (2006) Monoamine depletion studies: implications for antidepressant discontinuation syndrome. J Clin Psychiatry 67 Suppl 4:22-26.

Delgado PL, Charney DS, Price LH, Landis H, Heninger GR (1989) Neuroendocrine and behavioral effects of dietary tryptophan restriction in healthy subjects. Life Sci 45:2323-2332.

Delgado PL, Charney DS, Price LH, Aghajanian GK, Landis H, Heninger GR (1990) Serotonin function and the mechanism of antidepressant action. Reversal of antidepressant-induced remission by rapid depletion of plasma tryptophan. Arch Gen Psychiatry 47:411-418.

Di Giovanni G, Di Matteo V, Pierucci M, Esposito E (2008) Serotonin-dopamine interaction: electrophysiological evidence. Prog Brain Res 172:45-71.

Di Matteo V, Di Giovanni G, Pierucci M, Esposito E (2008) Serotonin control of central dopaminergic function: focus on in vivo microdialysis studies. Prog Brain Res 172:7-44.

Di Pietro NC, Seamans JK (2007) Dopamine and serotonin interactions in the prefrontal cortex: insights on antipsychotic drugs and their mechanism of action. Pharmacopsychiatry 40 Suppl 1:S27-33.

Dias R, Robbins TW, Roberts AC (1996) Dissociation in prefrontal cortex of affective and attentional shifts. Nature 380:69-72.

Divac I (1971) Frontal lobe system and spatial reversal in the rat. Neuropsychologia 9:175-183.

Divac I, Rosvold HE, Szwarcbart MK (1967) Behavioral effects of selective ablation of the caudate nucleus. J Comp Physiol Psychol 63:184-190.

Dudkin KN, Kruchinin VK, Chueva IV (1996) Neurophysiological correlates of improvements in cognitive characteristics in monkeys during modification of NMDA-ergic structures of the prefrontal cortex. Neurosci Behav Physiol 26:545-551.

Edeline JM, Hars B, Hennevin E, Cotillon N (2002) Muscimol diffusion after intracerebral microinjections: a reevaluation based on electrophysiological and autoradiographic quantifications. Neurobiol Learn Mem 78:100-124.

Ellenbogen MA, Young SN, Dean P, Palmour RM, Benkelfat C (1996) Mood response to acute tryptophan depletion in healthy volunteers: sex differences and temporal stability. Neuropsychopharmacology 15:465-474.

Esposito E, Di Matteo V, Di Giovanni G (2008) Serotonin-dopamine interaction: an overview. Prog Brain Res 172:3-6.

Evers EAT, Cools R, Clark L, van der Veen FM, Jolles J, Sahakian BJ, Robbins TW (2005) Serotonergic modulation of prefrontal cortex during negative feedback in probabilistic reversal learning. Neuropsychopharmacology 30:1138-1147.

Evers EAT, van der Veen FM, Jolles J, Deutz NE, Schmitt JA (2006) Acute tryptophan depletion improves performance and modulates the BOLD response during a Stroop task in healthy females. Neuroimage 32:248-255.

Evers EAT, van der Veen FM, Fekkes D, Jolles J (2007) Serotonin and cognitive flexibility: neuroimaging studies into the effect of acute tryptophan depletion in healthy volunteers. Curr Med Chem 14:2989-2995.

Fadda F (2000) Tryptophan-Free Diets: A Physiological Tool to Study Brain Serotonin Function. News Physiol Sci 15:260-264.

Fadda F, Cocco S, Stancampiano R (2000a) A physiological method to selectively decrease brain serotonin release. Brain Res Brain Res Protoc 5:219-222.

Fadda F, Cocco S, Rossetti ZL, Melis G, Stancampiano R (2000b) A tryptophan-free diet markedly reduces frontocortical 5-HT release, but fails to modify ethanol preference in alcohol-preferring (sP) and non-preferring (sNP) rats. Behav Brain Res 108:127-132.

Fagan AM, Olton DS (1987) Spatial learning set acquisition in rats. Q J Exp Psychol B 39:65-75.

Feenstra MG, Botterblom MH (1996) Rapid sampling of extracellular dopamine in the rat prefrontal cortex during food consumption, handling and exposure to novelty. Brain Res 742:17-24.

Feenstra MG, Botterblom MH, Mastenbroek S (2000) Dopamine and noradrenaline efflux in the prefrontal cortex in the light and dark period: effects of novelty and handling and comparison to the nucleus accumbens. Neuroscience 100:741-748.

Feierstein CE, Quirk MC, Uchida N, Sosulski DL, Mainen ZF (2006) Representation of spatial goals in rat orbitofrontal cortex. Neuron 51:495-507.

Ferry AT, Lu XC, Price JL (2000) Effects of excitotoxic lesions in the ventral striatopallidal--thalamocortical pathway on odor reversal learning: inability to extinguish an incorrect response. Exp Brain Res 131:320-335.

Finger EC, Marsh AA, Buzas B, Kamel N, Rhodes R, Vythilingham M, Pine DS, Goldman D, Blair JR (2007) The impact of tryptophan depletion and 5-HTTLPR genotype on passive avoidance and response reversal instrumental learning tasks. Neuropsychopharmacology 32:206-215.

Fiorillo CD, Tobler PN, Schultz W (2003) Discrete coding of reward probability and uncertainty by dopamine neurons. Science 299:1898-1902.

Floresco SB, Zhang Y, Enomoto T (2009) Neural circuits subserving behavioral flexibility and their relevance to schizophrenia. Behav Brain Res 204:396-409.

Franklin M, Craven RD, Dowling B, Campling G, Elliott JM, Cowen PJ (1999) Effect of a long-term low tryptophan diet on the prolactin responses to the 5-HT_{1A} and 5-HT_{2C} agonists, 8-OH-DPAT and mCPP in the male rat. J Psychopharmacol 13:58-63.

Frazer A, Hensler JG (1999) Serotonin. Basic neurochemistry; molecular, cellular and medical aspects, 6th edn.:264-292.

Fusar-Poli P, Allen P, Cortesi M (2007) Can acute tryptophan depletion modulate brain function in absence of behavioural effects? Med Hypotheses 68:722.

Fuster JM (1997) The prefrontal cortex: anatomy, physiology, and neuropsychology of the frontal lobe, 3rd edn. New York: Raven Press.

Fuster JM (2001) The prefrontal cortex--an update: time is of the essence. Neuron 30:319-333.

Fuxe K, Ogren SO, Agnati LF, Andersson K, Eneroth P (1982) Effects of subchronic antidepressant drug treatment on central serotonergic mechanisms in the male rat. Adv Biochem Psychopharmacol 31:91-107.

Gartside SE, Cowen PJ, Sharp T (1992a) Effect of amino acid loads on hippocampal 5-HT release in vivo evoked by electrical stimulation of the dorsal raphe nucleus and d-fenfluramine administration. Brit J Pharmacol 107:448P.

Gartside SE, Cowen PJ, Sharp T (1992b) Evidence that the large neutral amino acid L-valine decreases electrically-evoked release of 5-HT in rat hippocampus in vivo. Psychopharmacology (Berl) 109:251-253.

Gerstein GL, Kiang NY (1960) An approach to the quantitative analysis of electrophysiological data from single neurons. Biophys J 1:15-28.

Gessa GL, Biggio G, Fadda F, Corsini GU, Tagliamonte A (1974) Effect of the oral administration of tryptophan-free amino acid mixtures on serum tryptophan, brain tryptophan and serotonin metabolism. J Neurochem 22:869-870.

Gothard KM, Skaggs WE, Moore KM, McNaughton BL (1996) Binding of hippocampal CA1 neural activity to multiple reference frames in a landmark-based navigation task. J Neurosci 16:823-835.

Gray CM, Maldonado PE, Wilson M, McNaughton B (1995) Tetrodes markedly improve the reliability and yield of multiple single-unit isolation from multi-unit recordings in cat striate cortex. J Neurosci Methods 63:43-54.

Groenewegen HJ, Uylings H.B.M. (2010) Organisation of prefrontal-striatal connections. In: Handbook of Basal Ganglia Structure and Function: A Decade of Progress, Eds.: Steiner H, and Tseng KY, Academic press, San Diego, Ch. 20.

Haluk DM, Floresco SB (2009) Ventral striatal dopamine modulation of different forms of behavioral flexibility. Neuropsychopharmacology 34:2041-2052.

Hariri AR, Drabant EM, Weinberger DR (2006) Imaging genetics: perspectives from studies of genetically driven variation in serotonin function and corticolimbic affective processing. Biol Psychiatry 59:888-897.

Harlow HF (1949) The formation of learning sets. Psychol Rev 56:51-65.

Harmer CJ (2008) Serotonin and emotional processing: does it help explain antidepressant drug action? Neuropharmacology 55:1023-1028.

Harrison AA, Everitt BJ, Robbins TW (1997) Central 5-HT depletion enhances impulsive responding without affecting the accuracy of attentional performance: interactions with dopaminergic mechanisms. Psychopharmacology (Berl) 133:329-342.

Harrison AA, Everitt BJ, Robbins TW (1999) Central serotonin depletion impairs both the acquisition and performance of a symmetrically reinforced go/no-go conditional visual discrimination. Behav Brain Res 100:99-112.

Heslop K, Portas CM, Curzon G (1991) Effect of altered tryptophan availability on tissue and extracellular serotonin in the rat. In: 5th international Conference on In Vivo Methods, pp 259-261. Noordwijkerhout, the Netherlands.

Heyser CJ, Fienberg AA, Greengard P, Gold LH (2000) DARPP-32 knockout mice exhibit impaired reversal learning in a discriminated operant task. Brain Res 867:122-130.

Hikosaka K, Watanabe M (2000) Delay activity of orbital and lateral prefrontal neurons of the monkey varying with different rewards. Cereb Cortex 10:263-271.

Hille B (1992) Ionic Channels of Excitable Membranes: Sinauer Associates, Inc., Sunderland MA.

Höistad M, Kehr J, Andbjer B, Jansson A, Fuxe K (2000) Intracerebral infusion of H-dopamine and H-mannitol in the striatum of halothane-anaesthetized male rats. A dual-probe microdialysis study of long-distance diffusion. Eur J Neurosci 12:2505-2514.

Hok V, Save E, Lenck-Santini PP, Poucet B (2005) Coding for spatial goals in the prelimbic/infralimbic area of the rat frontal cortex. Proc Natl Acad Sci U S A 102:4602-4607.

Holmes A, Murphy DL, Crawley JN (2003) Abnormal behavioral phenotypes of serotonin transporter knockout mice: parallels with human anxiety and depression. Biol Psychiatry 54:953-959.

Hornak J, O'Doherty J, Bramham J, Rolls ET, Morris RG, Bullock PR, Polkey CE (2004) Reward-related reversal learning after surgical excisions in orbito-frontal or dorsolateral prefrontal cortex in humans. J Cogn Neurosci 16:463-478.

Ito R, Robbins TW, Pennartz CM, Everitt BJ (2008) Functional interaction between the hippocampus and nucleus accumbens shell is necessary for the acquisition of appetitive spatial context conditioning. J Neurosci 28:6950-6959.

Ivanova SF, Bures J (1990) Acquisition of conditioned taste aversion in rats is prevented by tetrodotoxin blockade of a small midbrain region centered around the parabrachial nuclei. Physiol Behav 48:543-549.

Iversen SD, Mishkin M (1970) Perseverative interference in monkeys following selective lesions of the inferior prefrontal convexity. Exp Brain Res 11:376-386.

Izquierdo A, Newman TK, Higley JD, Murray EA (2007) Genetic modulation of cognitive flexibility and socioemotional behavior in rhesus monkeys. Proc Natl Acad Sci U S A 104:14128-14133.

Izquierdo A, Belcher AM, Scott L, Cazares VA, Chen J, O'Dell SJ, Malvaez M, Wu T, Marshall JF (2010) Reversal-specific learning impairments after a binge regimen of methamphetamine in rats: possible involvement of striatal dopamine. Neuropsychopharmacology 35:505-514.

Jacobs BL, Fornal CA (1997) Serotonin and motor activity. Curr Opin Neurobiol 7:820-825.

Jakab RL, Goldman-Rakic PS (1998) 5-Hydroxytryptamine2A serotonin receptors in the primate cerebral cortex: possible site of action of hallucinogenic and antipsychotic drugs in pyramidal cell apical dendrites. Proc Natl Acad Sci U S A 95:735-740.

Jans LAW, Riedel WJ, Markus CR, Blokland A (2007a) Serotonergic vulnerability and depression: assumptions, experimental evidence and implications. Mol Psychiatry 12:522-543.

Jans LAW, Lieben CK, Blokland A (2007b) Influence of sex and estrous cycle on the effects of acute tryptophan depletion induced by a gelatin-based mixture in adult Wistar rats. Neuroscience 147:304-317.

Joel D, Weiner I, Feldon J (1997) Electrolytic lesions of the medial prefrontal cortex in rats disrupt performance on an analog of the Wisconsin Card Sorting Test, but do not disrupt latent inhibition: implications for animal models of schizophrenia. Behav Brain Res 85:187-201.

Jones S, Kauer JA (1999) Amphetamine depresses excitatory synaptic transmission via serotonin receptors in the ventral tegmental area. J Neurosci 19:9780-9787.

Jonnakuty C, Gragnoli C (2008) What do we know about serotonin? J Cell Physiol 217:301-306.

Kapur S, Remington G (1996) Serotonin-dopamine interaction and its relevance to schizophrenia. Am J Psychiatry 153:466-476.

Kehagia AA, Murray GK, Robbins TW (2010) Learning and cognitive flexibility: frontostriatal function and monoaminergic modulation. Curr Opin Neurobiol: 199-204.

Kilkens TO, Honig A, van Nieuwenhoven MA, Riedel WJ, Brummer RJ (2004) Acute tryptophan depletion affects brain-gut responses in irritable bowel syndrome patients and controls. Gut 53:1794-1800.

Knauer CS, Campbell JE, Galvan B, Bowman C, Osgood S, Buist S, Buchholz L, Henry B, Wong EH, Shahid M, Grimwood S (2008) Validation of a rat in vivo [(3)H] M100907 binding assay to determine a translatable measure of 5-HT_{2A} receptor occupancy. Eur J Pharmacol 591:136-141.

Knutson B, Taylor J, Kaufman M, Peterson R, Glover G (2005) Distributed neural representation of expected value. J Neurosci 25:4806-4812.

Kolb B (1984) Functions of the frontal cortex of the rat: a comparative review. Brain Res 320:65-98.

Kolb B, Nonneman AJ, Singh RK (1974) Double dissociation of spatial impairments and perseveration following selective prefrontal lesions in rats. J Comp Physiol Psychol 87:772-780.

Kringelbach ML (2005) The human orbitofrontal cortex: linking reward to hedonic experience. Nat Rev Neurosci 6:691-702.

Kringelbach ML, O'Doherty J, Rolls ET, Andrews C (2003) Activation of the human orbitofrontal cortex to a liquid food stimulus is correlated with its subjective pleasantness. Cereb Cortex 13:1064-1071.

Lansink CS, Bakker M, Buster W, Lankelma J, van der Blom R, Westdorp R, Joosten RNJMA, McNaughton BL, Pennartz CMA (2007) A split microdrive for simultaneous multi-electrode recordings from two brain areas in awake small animals. J Neurosci Methods 162:129-138.

Lapiz MD, Morilak DA (2006) Noradrenergic modulation of cognitive function in rat medial prefrontal cortex as measured by attentional set shifting capability. Neuroscience 137:1039-1049.

Li L, Shao J (1998) Restricted lesions to ventral prefrontal subareas block reversal learning but not visual discrimination learning in rats. Physiol Behav 65:371-379.

Lieben CK, van Oorsouw K, Deutz NE, Blokland A (2004a) Acute tryptophan depletion induced by a gelatin-based mixture impairs object memory but not affective behavior and spatial learning in the rat. Behav Brain Res 151:53-64.

Lieben CK, Blokland A, Westerink B, Deutz NE (2004b) Acute tryptophan and serotonin depletion using an optimized tryptophan-free protein-carbohydrate mixture in the adult rat. Neurochem Int 44:9-16.

Lieben CK, Schwarcz, R., Guidetti, P., Blokland, A. (2004c) Effects of an acute tryptophan depletion on the kynurenine pathway. University Maastricht, the Netherlands.

Lindefors N, Amberg G, Ungerstedt U (1989) Intracerebral microdialysis: I. Experimental studies of diffusion kinetics. J Pharmacol Methods 22:141-156.

Ludvig N, Mishra PK, Yan QS, Lasley SM, Burger RL, Jobe PC (1992) The combined EEG-intracerebral microdialysis technique: a new tool for neuropharmacological studies on freely behaving animals. J Neurosci Methods 43:129-137.

Ludvig N, Potter PE, Fox SE (1994) Simultaneous single-cell recording and microdialysis within the same brain site in freely behaving rats: a novel neurobiological method. J Neurosci Methods 55:31-40.

Ludvig N, Nguyen MC, Botero JM, Tang HM, Scalia F, Scharf BA, Kral JG (2000) Delivering drugs, via microdialysis, into the environment of extracellularly recorded hippocampal neurons in behaving primates. Brain Res Brain Res Protoc 5:75-84.

Manes F, Sahakian B, Clark L, Rogers R, Antoun N, Aitken M, Robbins T (2002) Decision-making processes following damage to the prefrontal cortex. Brain 125:624-639.

Marco EJ, Meek JL (1979) The effects of antidepressants on serotonin turnover in discrete regions of rat brain. Naunyn Schmiedebergs Arch Pharmacol 306:75-79.

Marek GJ, Carpenter LL, McDougle CJ, Price LH (2003) Synergistic action of 5-HT_{2A} antagonists and selective serotonin reuptake inhibitors in neuropsychiatric disorders. Neuropsychopharmacology 28:402-412.

Masaki D, Yokoyama C, Kinoshita S, Tsuchida H, Nakatomi Y, Yoshimoto K, Fukui K (2006) Relationship between limbic and cortical 5-HT neurotransmission and acquisition and reversal learning in a go/no-go task in rats. Psychopharmacology (Berl) 189:249-258.

McAlonan K, Brown VJ (2003) Orbital prefrontal cortex mediates reversal learning and not attentional set shifting in the rat. Behav Brain Res 146:97-103.

McNaughton BL, O'Keefe J, Barnes CA (1983) The stereotrode: a new technique for simultaneous isolation of several single units in the central nervous system from multiple unit records. J Neurosci Methods 8:391-397.

McQuade R, Sharp T (1997) Functional mapping of dorsal and median raphe 5-hydroxytryptamine pathways in forebrain of the rat using microdialysis. J Neurochem 69:791-796.

Miller EK (2000) The prefrontal cortex and cognitive control. Nat Rev Neurosci 1:59-65.

Miller EK, Cohen JD (2001) An integrative theory of prefrontal cortex function. Annu Rev Neurosci 24:167-202.

Moja EA, Cipolla P, Castoldi D, Tofanetti O (1989) Dose-response decrease in plasma tryptophan and in brain tryptophan and serotonin after tryptophan-free amino acid mixtures in rats. Life Sci 44:971-976.

Moja EA, Restani P, Corsini E, Stacchezzini MC, Assereto R, Galli CL (1991) Cycloheximide blocks the fall of plasma and tissue tryptophan levels after tryptophan-free amino acid mixtures. Life Sci 49:1121-1128.

Molliver ME (1987) Serotonergic neuronal systems: what their anatomic organization tells us about function. J Clin Psychopharmacol 7:3S-23S.

Moore P, Landolt HP, Seifritz E, Clark C, Bhatti T, Kelsoe J, Rapaport M, Gillin JC (2000) Clinical and physiological consequences of rapid tryptophan depletion. Neuropsychopharmacology 23:601-622.

Moret C, Briley M (1997) Ex vivo inhibitory effect of the 5-HT uptake blocker citalopram on 5-HT synthesis. J Neural Transm 104:147-160.

Morgan MA, Romanski LM, LeDoux JE (1993) Extinction of emotional learning: contribution of medial prefrontal cortex. Neurosci Lett 163:109-113.

Morgan MA, Schulkin J, LeDoux JE (2003) Ventral medial prefrontal cortex and emotional perseveration: the memory for prior extinction training. Behav Brain Res 146:121-130.

Neumeister A (2003) Tryptophan depletion, serotonin, and depression: where do we stand? Psychopharmacol Bull 37:99-115.

Neumeister A, Nugent AC, Waldeck T, Geraci M, Schwarz M, Bonne O, Bain EE, Luckenbaugh DA, Herscovitch P, Charney DS, Drevets WC (2004) Neural and behavioral responses to tryptophan depletion in unmedicated patients with remitted major depressive disorder and controls. Arch Gen Psychiatry 61:765-773.

Nilsson T, Longmore J, Shaw D, Pantev E, Bard JA, Branchek T, Edvinsson L (1999) Characterisation of 5-HT receptors in human coronary arteries by molecular and pharmacological techniques. Eur J Pharmacol 372:49-56.

Nishizawa S, Benkelfat C, Young SN, Leyton M, Mzengeza S, de Montigny C, Blier P, Diksic M (1997) Differences between males and females in rates of serotonin synthesis in human brain. Proc Natl Acad Sci U S A 94:5308-5313.

Niv Y, Joel D, Dayan P (2006) A normative perspective on motivation. Trends Cogn Sci 10:375-381.

Nonneman AJ, Voigt J, Kolb BE (1974) Comparisons of behavioral effects of hippocampal and prefrontal cortex lesions in the rat. J Comp Physiol Psychol 87:249-260.

O'Doherty J, Kringelbach ML, Rolls ET, Hornak J, Andrews C (2001) Abstract reward and punishment representations in the human orbitofrontal cortex. Nat Neurosci 4:95-102.

Obrenovitch TP, Sarna GS, Richards D, Symon L (1991) Microdialysis combined with electroencephalogram and DC potential recordings. In: 5th international Conference on In Vivo Methods, pp 349-351. Noordwijkerhout, the Netherlands.

Olivier JD, Jans LA, Korte-Bouws GA, Korte SM, Deen PM, Cools AR, Ellenbroek BA, Blokland A (2008) Acute tryptophan depletion dose dependently impairs object memory in serotonin transporter knockout rats. Psychopharmacology (Berl) 200:243-254.

Ongür D, Price JL (2000) The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans. Cereb Cortex 10:206-219.

Park SB, Coull JT, McShane RH, Young AH, Sahakian BJ, Robbins TW, Cowen PJ (1994) Tryptophan depletion in normal volunteers produces selective impairments in learning and memory. Neuropharmacology 33:575-588.

Passetti F, Chudasama Y, Robbins TW (2002) The frontal cortex of the rat and visual attentional performance: dissociable functions of distinct medial prefrontal subregions. Cereb Cortex 12:1254-1268.

Passingham RE (1998) Attention to action. In: The prefrontal cortex: Executive and cognitive functions, Eds. Roberts AC, Robbins TW, Weiskrantz L, Oxford University Press; 131-143.

Paxinos G, Watson C (1998) The brain in stereotaxic coordinates: Academic, San Diego.

Paxinos G, Watson C (2005) The rat brain in stereotaxic coordinates, 5th ed.: Elsevier, the Netherlands.

Pennartz CM, Berke JD, Graybiel AM, Ito R, Lansink CS, van der Meer M, Redish AD, Smith KS, Voorn P (2009) Corticostriatal Interactions during Learning, Memory Processing, and Decision Making. J Neurosci 29:12831-12838.

Petersen SE, van Mier H, Fiez JA, Raichle ME (1998) The effects of practice on the functional anatomy of task performance. Proc Natl Acad Sci U S A 95:853-860.

Porter RJ, Gallagher P, O'Brien JT (2007) Effects of rapid tryptophan depletion on salivary cortisol in older people recovered from depression, and the healthy elderly. J Psychopharmacol 21:71-75.

Praschak-Rieder N, Hussey D, Wilson AA, Carella A, Lee M, Dunn E, Willeit M, Bagby RM, Houle S, Meyer JH (2004) Tryptophan depletion and serotonin loss in selective serotonin reuptake inhibitor-treated depression: an [(18)F] MPPF positron emission tomography study. Biol Psychiatry 56:587-591.

Pratt WE, Kelley AE (2004) Nucleus accumbens acetylcholine regulates appetitive learning and motivation for food via activation of muscarinic receptors. Behav Neurosci 118:730-739.

Price MT, Murray GN, Fibiger HC (1977) Schedule dependent changes in operant responding after lesions of the dorsal tegmental noradrenergic projection. Pharmacol Biochem Behav 6:11-15.

Ragozzino ME, Detrick S, Kesner RP (1999a) Involvement of the prelimbic-infralimbic areas of the rodent prefrontal cortex in behavioral flexibility for place and response learning. J Neurosci 19:4585-4594.

Ragozzino ME, Wilcox C, Raso M, Kesner RP (1999b) Involvement of rodent prefrontal cortex subregions in strategy switching. Behav Neurosci 113:32-41.

Ragozzino ME, Kim J, Hassert D, Minniti N, Kiang C (2003) The contribution of the rat prelimbic-infralimbic areas to different forms of task switching. Behav Neurosci 117:1054-1065.

Ragozzino ME (2007) The contribution of the medial prefrontal cortex, orbitofrontal cortex, and dorsomedial striatum to behavioral flexibility. Ann N Y Acad Sci 1121:355-375.

Raichle ME, Fiez JA, Videen TO, MacLeod AM, Pardo JV, Fox PT, Petersen SE (1994) Practice-related changes in human brain functional anatomy during nonmotor learning. Cereb Cortex 4:8-26.

Ramage AG, Villalón CM (2008) 5-hydroxytryptamine and cardiovascular regulation. Trends Pharmacol Sci 29:472-481.

Recce ML, O'Keefe J (1989) The tetrode: an improved technique for multi-unit extracellular recording. Soc Neuroscience Abstr, p 15:1250. Phoenix, Arizona.

Reilly JG, McTavish SF, Young AH (1997) Rapid depletion of plasma tryptophan: a review of studies and experimental methodology. J Psychopharmacol 11:381-392.

Remijnse PL, Nielen MM, Uylings HBM, Veltman DJ (2005) Neural correlates of a reversal learning task with an affectively neutral baseline: an event-related fMRI study. Neuroimage 26:609-618.

Rice ME, Gerhardt GA, Hierl PM, Nagy G, Adams RN (1985) Diffusion coefficients of neurotransmitters and their metabolites in brain extracellular fluid space. Neuroscience 15:891-902.

Rich EL, Shapiro M (2009) Rat prefrontal cortical neurons selectively code strategy switches. J Neurosci 29:7208-7219.

Ridderinkhof KR, Ullsperger M, Crone EA, Nieuwenhuis S (2004) The role of the medial frontal cortex in cognitive control. Science 306:443-447.

Riedel WJ (2004) Cognitive changes after acute tryptophan depletion: what can they tell us? Psychol Med 34:3-8.

Riedel WJ, Klaassen T, Deutz NE, van Someren A, van Praag HM (1999) Tryptophan depletion in normal volunteers produces selective impairment in memory consolidation. Psychopharmacology (Berl) 141:362-369.

Riedel WJ, Klaassen T, Schmitt JA (2002) Tryptophan, mood, and cognitive function. Brain Behav Immun 16:581-589.

Robbins TW (2000) Chemical neuromodulation of frontal-executive functions in humans and other animals. Exp Brain Res 133:130-138.

Robbins TW (2005) Chemistry of the mind: neurochemical modulation of prefrontal cortical function. J Comp Neurol 493:140-146.

Roberts DC, Loh EA, Baker GB, Vickers G (1994) Lesions of central serotonin systems affect responding on a progressive ratio schedule reinforced either by intravenous cocaine or by food. Pharmacol Biochem Behav 49:177-182.

Roberts AC, Wallis JD (2000) Inhibitory control and affective processing in the prefrontal cortex: neuropsychological studies in the common marmoset. Cereb Cortex 10:252-262.

Robinson ES, Dalley JW, Theobald DE, Glennon JC, Pezze MA, Murphy ER, Robbins TW (2008) Opposing roles for 5-HT_{2A} and 5-HT_{2C} receptors in the nucleus accumbens on inhibitory response control in the 5-choice serial reaction time task. Neuropsychopharmacology 33:2398-2406.

Robinson OJ, Sahakian BJ (2009) A double dissociation in the roles of serotonin and mood in healthy subjects. Biol Psychiatry 65:89-92.

Robinson OJ, Cools R, Crockett MJ, Sahakian BJ (2010) Mood state moderates the role of serotonin in cognitive biases. J Psychopharmacol 24:573-583.

Robinson PW, Storm RH (1978) Effects of error and errorless discrimination acquisition on reversal learning. J Exp Anal Behav 29:517-525.

Rogers RD, Blackshaw AJ, Middleton HC, Matthews K, Hawtin K, Crowley C, Hopwood A, Wallace C, Deakin JF, Sahakian BJ, Robbins TW (1999a) Tryptophan depletion impairs stimulus-reward learning while methylphenidate disrupts attentional control in healthy young adults: implications for the monoaminergic basis of impulsive behaviour. Psychopharmacology (Berl) 146:482-491.

Rogers RD, Everitt BJ, Baldacchino A, Blackshaw AJ, Swainson R, Wynne K, Baker NB, Hunter J, Carthy T, Booker E, London M, Deakin JF, Sahakian BJ, Robbins TW (1999b) Dissociable deficits in the decision-making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers: evidence for monoaminergic mechanisms. Neuropsychopharmacology 20:322-339.

Rogers RD, Tunbridge EM, Bhagwagar Z, Drevets WC, Sahakian BJ, Carter CS (2003) Tryptophan depletion alters the decision-making of healthy volunteers through altered processing of reward cues. Neuropsychopharmacology 28:153-162.

Roiser JP, Blackwell AD, Cools R, Clark L, Rubinsztein DC, Robbins TW, Sahakian BJ (2006) Serotonin transporter polymorphism mediates vulnerability to loss of incentive motivation following acute tryptophan depletion. Neuropsychopharmacology 31:2264-2272.

Rolls ET (1996) The orbitofrontal cortex. Philos Trans R Soc Lond B Biol Sci 351:1433-1443.

Rolls ET, Hornak J, Wade D, McGrath J (1994) Emotion-related learning in patients with social and emotional changes associated with frontal lobe damage. J Neurol Neurosurg Psychiatry 57:1518-1524.

Rolls ET, Critchley HD, Mason R, Wakeman EA (1996) Orbitofrontal cortex neurons: role in olfactory and visual association learning. J Neurophysiol 75:1970-1981.

Rose JE, Woolsey CN (1948) The orbitofrontal cortex and its connections with the mediodorsal nucleus in rabbit, sheep and cat. Res Publ Assoc Res Nerv Ment Dis 27 (1 vol.):210-232.

Rosenkilde CE, Bauer RH, Fuster JM (1981) Single cell activity in ventral prefrontal cortex of behaving monkeys. Brain Res 209:375-394.

Rubia K, Lee F, Cleare AJ, Tunstall N, Fu CH, Brammer M, McGuire P (2005) Tryptophan depletion reduces right inferior prefrontal activation during response inhibition in fast, event-related fMRI. Psychopharmacology (Berl) 179:791-803.

Rubinsztein JS, Rogers RD, Riedel WJ, Mehta MA, Robbins TW, Sahakian BJ (2001) Acute dietary tryptophan depletion impairs maintenance of "affective set" and delayed visual recognition in healthy volunteers. Psychopharmacology (Berl) 154:319-326.

Ruhé HG, Mason NS, Schene AH (2007) Mood is indirectly related to serotonin, norepinephrine and dopamine levels in humans: a meta-analysis of monoamine depletion studies. Mol Psychiatry 12:331-359.

Russo S, Kema IP, Fokkema MR, Boon JC, Willemse PH, de Vries EG, den Boer JA, Korf J (2003) Tryptophan as a link between psychopathology and somatic states. Psychosom Med 65:665-671.

Rutten K, Lieben C, Smits L, Blokland A (2007) The PDE4 inhibitor rolipram reverses object memory impairment induced by acute tryptophan depletion in the rat. Psychopharmacology (Berl) 192:275-282.

Sakai K, Crochet S (2000) Serotonergic dorsal raphe neurons cease firing by disfacilitation during paradoxical sleep. Neuroreport 11:3237-3241.

Sakai K, Crochet S (2001) Role of dorsal raphe neurons in paradoxical sleep generation in the cat: no evidence for a serotonergic mechanism. Eur J Neurosci 13:103-112.

Salazar RF, White W, Lacroix L, Feldon J, White IM (2004) NMDA lesions in the medial prefrontal cortex impair the ability to inhibit responses during reversal of a simple spatial discrimination. Behav Brain Res 152:413-424.

Sambeth A, Blokland A, Harmer CJ, Kilkens TO, Nathan PJ, Porter RJ, Schmitt JA, Scholtissen B, Sobczak S, Young AH, Riedel WJ (2007) Sex differences in the effect of acute tryptophan depletion on declarative episodic memory: a pooled analysis of nine studies. Neurosci Biobehav Rev 31:516-529.

Sandberg M, Butcher SP, Hagberg H (1986) Extracellular overflow of neuroactive amino acids during severe insulin-induced hypoglycemia: in vivo dialysis of the rat hippocampus. J Neurochem 47:178-184.

Santana N, Bortolozzi A, Serrats J, Mengod G, Artigas F (2004) Expression of serotonin1A and serotonin2A receptors in pyramidal and GABAergic neurons of the rat prefrontal cortex. Cereb Cortex 14:1100-1109.

Sato Y, Yasui-Furukori N, Nakagami T, Saito M, Kaneko S (2009) Augmentation of antidepressants with perospirone for treatment-resistant major depressive disorder. Prog Neuropsychopharmacol Biol Psychiatry 33:416-418.

Schaechter JD, Wurtman RJ (1990) Serotonin release varies with brain tryptophan levels. Brain Res 532:203-210.

Schmitt JA, Jorissen BL, Sobczak S, van Boxtel MP, Hogervorst E, Deutz NE, Riedel WJ (2000) Tryptophan depletion impairs memory consolidation but improves focussed attention in healthy young volunteers. J Psychopharmacol 14:21-29.

Schoenbaum G, Chiba AA, Gallagher M (1998) Orbitofrontal cortex and basolateral amygdala encode expected outcomes during learning. Nat Neurosci 1:155-159.

Schoenbaum G, Chiba AA, Gallagher M (1999) Neural encoding in orbitofrontal cortex and basolateral amygdala during olfactory discrimination learning. J Neurosci 19:1876-1884.

Schoenbaum G, Nugent SL, Saddoris MP, Setlow B (2002) Orbitofrontal lesions in rats impair reversal but not acquisition of go, no-go odor discriminations. Neuroreport 13:885-890.

Schoenbaum G, Setlow B, Ramus SJ (2003a) A systems approach to orbitofrontal cortex function: recordings in rat orbitofrontal cortex reveal interactions with different learning systems. Behav Brain Res 146:19-29.

Schoenbaum G, Setlow B, Saddoris MP, Gallagher M (2003b) Encoding predicted outcome and acquired value in orbitofrontal cortex during cue sampling depends upon input from basolateral amygdala. Neuron 39:855-867.

Schoenbaum G, Roesch M (2005) Orbitofrontal cortex, associative learning, and expectancies. Neuron 47:633-636.

Schoenbaum G, Setlow B, Saddoris MP, Gallagher M (2006) Encoding changes in orbitofrontal cortex in reversal-impaired aged rats. J Neurophysiol 95:1509-1517.

Schoenbaum G, Roesch MR, Stalnaker TA, Takahashi YK (2009) A new perspective on the role of the orbitofrontal cortex in adaptive behaviour. Nat Rev Neurosci 10:885-892.

Schultz W (1998) Predictive reward signal of dopamine neurons. J Neurophysiol 80:1-27.

Schultz W (2000) Multiple reward signals in the brain. Nat Rev Neurosci 1:199-207.

Schultz W (2006) Behavioral theories and the neurophysiology of reward. Annu Rev Psychol 57:87-115.

Shohamy D, Myers CE, Hopkins RO, Sage J, Gluck MA (2009) Distinct hippocampal and basal ganglia contributions to probabilistic learning and reversal. J Cogn Neurosci 21:1821-1833.

Shufflebotham J, Hood S, Hendry J, Hince DA, Morris K, Nutt D, Probert C, Potokar J (2006) Acute tryptophan depletion alters gastrointestinal and anxiety symptoms in irritable bowel syndrome. Am J Gastroenterol 101:2582-2587.

Sorensen SM, Kehne JH, Fadayel GM, Humphreys TM, Ketteler HJ, Sullivan CK, Taylor VL, Schmidt CJ (1993) Characterization of the 5-HT_2 receptor antagonist MDL 100907 as a putative atypical antipsychotic: behavioral, electrophysiological and neurochemical studies. J Pharmacol Exp Ther 266:684-691.

Soubrié P (1986) Reconciling the role of central serotonin in human and animal behavior. Behav Brain Sci 9:319-364.

Stalnaker TA, Roesch MR, Franz TM, Burke KA, Schoenbaum G (2006) Abnormal associative encoding in orbitofrontal neurons in cocaine-experienced rats during decision-making. Eur J Neurosci 24:2643-2653.

Stalnaker TA, Takahashi Y, Roesch MR, Schoenbaum G (2009) Neural substrates of cognitive inflexibility after chronic cocaine exposure. Neuropharmacology 56 Suppl 1:63-72.

Stancampiano R, Melis F, Sarais L, Cocco S, Cugusi C, Fadda F (1997a) Acute administration of a tryptophan-free amino acid mixture decreases 5-HT release in rat hippocampus in vivo. Am J Physiol 272:R991-994.

Stancampiano R, Cocco S, Melis F, Cugusi C, Sarais L, Fadda F (1997b) The decrease of serotonin release induced by a tryptophan-free amino acid diet does not affect spatial and passive avoidance learning. Brain Res 762:269-274.

Steffens AB (1969) A method for frequent sampling of blood and continuous infusion of fluids in the rat without disturbing the animal. Physiol Behav 4:833-836.

Stenfors C, Ross SB (2004) Changes in extracellular 5-HIAA concentrations as measured by in vivo microdialysis technique in relation to changes in 5-HT release. Psychopharmacology (Berl) 172:119-128.

Storey JD, Robertson DA, Beattie JE, Reid IC, Mitchell SN, Balfour DJ (2006) Behavioural and neurochemical responses evoked by repeated exposure to an elevated open platform. Behav Brain Res 166:220-229.

Tait DS, Brown VJ, Farovik A, Theobald DE, Dalley JW, Robbins TW (2007) Lesions of the dorsal noradrenergic bundle impair attentional set-shifting in the rat. Eur J Neurosci 25:3719-3724.

Tang C, Pawlak AP, Prokopenko V, West MO (2007) Changes in activity of the striatum during formation of a motor habit. Eur J Neurosci 25:1212-1227.

Tehovnik EJ, Sommer MA (1997) Effective spread and timecourse of neural inactivation caused by lidocaine injection in monkey cerebral cortex. J Neurosci Methods 74:17-26.

Thorpe SJ, Rolls ET, Maddison S (1983) The orbitofrontal cortex: neuronal activity in the behaving monkey. Exp Brain Res 49:93-115.

Tobler PN, Fiorillo CD, Schultz W (2005) Adaptive coding of reward value by dopamine neurons. Science 307:1642-1645.

Tossman U, Wieloch T, Ungerstedt U (1985) gamma-Aminobutyric acid and taurine release in the striatum of the rat during hypoglycemic coma, studied by microdialysis. Neurosci Lett 62:231-235.

Tran-Nguyen LT, Bellew JG, Grote KA, Neisewander JL (2001) Serotonin depletion attenuates cocaine seeking but enhances sucrose seeking and the effects of cocaine priming on reinstatement of cocaine seeking in rats. Psychopharmacology (Berl) 157:340-348.

Tremblay L, Schultz W (1999) Relative reward preference in primate orbitofrontal cortex. Nature 398:704-708.

Tremblay L, Schultz W (2000) Reward-related neuronal activity during go-nogo task performance in primate orbitofrontal cortex. J Neurophysiol 83:1864-1876.

Trulson ME (1985) Dietary tryptophan does not alter the function of brain serotonin neurons. Life Sci 37:1067-1072.

Trulson ME, Jacobs BL (1975) Raphe neurons: depression of activity by L-5-hydroxytryptophan. Brain Res 97:350-355.

Udo de Haes JI, Bosker FJ, Van Waarde A, Pruim J, Willemsen AT, Vaalburg W, Den Boer JA (2002) 5-HT_{1A} receptor imaging in the human brain: effect of tryptophan depletion and infusion on [(18)F]MPPF binding. Synapse 46:108-115.

Uylings HBM, Groenewegen HJ, Kolb B (2003) Do rats have a prefrontal cortex? Behav Brain Res 146:3-17.

Vallender EJ, Lynch L, Novak MA, Miller GM (2009) Polymorphisms in the 3' UTR of the serotonin transporter are associated with cognitive flexibility in rhesus macaques. Am J Med Genet B Neuropsychiatr Genet 150B:467-475.

van de Werd HJ, Uylings HBM (2008) The rat orbital and agranular insular prefrontal cortical areas: a cytoarchitectonic and chemoarchitectonic study. Brain Struct Funct 212:387-401.

van der Does AJ (2001) The effects of tryptophan depletion on mood and psychiatric symptoms. J Affect Disord 64:107-119.

van der Meulen JAJ, Bilbija L, Joosten RNJMA, de Bruin JPC, Feenstra MGP (2003) The NMDA-receptor antagonist MK-801 selectively disrupts reversal learning in rats. Neuroreport 14:2225-2228.

van der Meulen JAJ, Joosten RNJMA, de Bruin JPC, Feenstra MGP (2007) Dopamine and noradrenaline efflux in the medial prefrontal cortex during serial reversals and extinction of instrumental goal-directed behavior. Cereb Cortex 17:1444-1453.

van der Plasse G, Meerkerk DT, Lieben CK, Blokland A, Feenstra MGP (2007a) Lack of evidence for reduced prefrontal cortical serotonin and dopamine efflux after acute tryptophan depletion. Psychopharmacology (Berl) 195:377-385.

van der Plasse G, La Fors SS, Meerkerk DT, Joosten RNJMA, Uylings HBM, Feenstra MGP (2007b) Medial prefrontal serotonin in the rat is involved in goal-directed behaviour when affect guides decision making. Psychopharmacology (Berl) 195:435-449.

van der Stelt HM, Broersen LM, Olivier B, Westenberg HGM (2004) Effects of dietary tryptophan variations on extracellular serotonin in the dorsal hippocampus of rats. Psychopharmacology (Berl) 172:137-144.

van der Stelt HM, Breuer ME, Olivier B, Westenberg HGM (2005) Permanent deficits in serotonergic functioning of olfactory bulbectomized rats: an in vivo microdialysis study. Biol Psychiatry 57:1061-1067.

van der Veen FM, Mies GW, van der Molen MW, Evers EAT (2008) Acute tryptophan depletion in healthy males attenuates phasic cardiac slowing but does not affect electro-cortical response to negative feedback. Psychopharmacology (Berl) 199:255-263.

van Duuren E, Escamez FA, Joosten RN, Visser R, Mulder AB, Pennartz CMA (2007a) Neural coding of reward magnitude in the orbitofrontal cortex of the rat during a five-odor olfactory discrimination task. Learn Mem 14:446-456.

van Duuren E, van der Plasse G, van der Blom R, Joosten RNJMA, Mulder AB, Pennartz CMA, Feenstra MGP (2007b) Pharmacological manipulation of neuronal ensemble activity by reverse microdialysis in freely moving rats: a comparative study of the effects of tetrodotoxin, lidocaine, and muscimol. J Pharmacol Exp Ther 323:61-69.

van Duuren E, Lankelma J, Pennartz CMA (2008) Population coding of reward magnitude in the orbitofrontal cortex of the rat. J Neurosci 28:8590-8603.

van Duuren E, van der Plasse G, Lankelma J, Joosten RNJMA, Feenstra MGP, Pennartz CMA (2009) Single-cell and population coding of expected reward probability in the orbitofrontal cortex of the rat. J Neurosci 29:8965-8976.

van Nieuwenhoven MA, Valks SD, Sobczak S, Riedel WJ, Brummer RJ (2004) Acute tryptophan depletion slows gastric emptying in females. Br J Nutr 91:351-355.

Vertes RP (1991) A PHA-L analysis of ascending projections of the dorsal raphe nucleus in the rat. J Comp Neurol 313:643-668.

Vezzani A, Ungerstedt U, French ED, Schwarcz R (1985) In vivo brain dialysis of amino acids and simultaneous EEG measurements following intrahippocampal quinolinic acid injection: evidence for a dissociation between neurochemical changes and seizures. J Neurochem 45:335-344.

Ward BO, Wilkinson LS, Robbins TW, Everitt BJ (1999) Forebrain serotonin depletion facilitates the acquisition and performance of a conditional visual discrimination task in rats. Behav Brain Res 100:51-65.

Watanabe M (1996) Reward expectancy in primate prefrontal neurons. Nature 382:629-632.

Watson DJ, Stanton ME (2009) Intrahippocampal administration of an NMDA-receptor antagonist impairs spatial discrimination reversal learning in weanling rats. Neurobiol Learn Mem 92:89-98.

West AR, Moore H, Grace AA (2002) Direct examination of local regulation of membrane activity in striatal and prefrontal cortical neurons in vivo using simultaneous intracellular recording and microdialysis. J Pharmacol Exp Ther 301:867-877.

Westerink BH (1995) Brain microdialysis and its application for the study of animal behaviour. Behav Brain Res 70:103-124.

Whishaw IQ (1985) Formation of a place learning-set by the rat: a new paradigm for neurobehavioral studies. Physiol Behav 35:139-143.

Williams WA, Shoaf SE, Hommer D, Rawlings R, Linnoila M (1999) Effects of acute tryptophan depletion on plasma and cerebrospinal fluid tryptophan and 5-hydroxyindoleacetic acid in normal volunteers. J Neurochem 72:1641-1647.

Williams WA, Carson RE, Momeman R, Lang L, Heinz A, Bjork J, Geyer C, Rawlings R, Phillips M, Johnson B, Excleman WC, Hommer D, Herscovitch P (2002) Effects of acute plasma tryptophan depletion on serotonin receptor occupancy using PET in healthy human subjects. Soc Neuroscience Abstr, p 826.824. Orlando, Florida.

Wilson MA, McNaughton BL (1993) Dynamics of the hippocampal ensemble code for space. Science 261:1055-1058.

Winstanley CA, Dalley JW, Theobald DE, Robbins TW (2003) Global 5-HT depletion attenuates the ability of amphetamine to decrease impulsive choice on a delay-discounting task in rats. Psychopharmacology (Berl) 170:320-331.

Winstanley CA, Dalley JW, Theobald DE, Robbins TW (2004a) Fractionating impulsivity: contrasting effects of central 5-HT depletion on different measures of impulsive behavior. Neuropsychopharmacology 29:1331-1343.

Winstanley CA, Theobald DE, Dalley JW, Glennon JC, Robbins TW (2004b) 5-HT_{2A} and 5-HT_{2C} receptor antagonists have opposing effects on a measure of impulsivity: interactions with global 5-HT depletion. Psychopharmacology (Berl) 176:376-385.

Winstanley CA, Theobald DE, Dalley JW, Robbins TW (2005) Interactions between serotonin and dopamine in the control of impulsive choice in rats: therapeutic implications for impulse control disorders. Neuropsychopharmacology 30:669-682.

Winstanley CA, Theobald DE, Dalley JW, Cardinal RN, Robbins TW (2006) Double dissociation between serotonergic and dopaminergic modulation of medial prefrontal and orbitofrontal cortex during a test of impulsive choice. Cereb Cortex 16:106-114.

Wittmann BC, Schott BH, Guderian S, Frey JU, Heinze HJ, Duzel E (2005) Reward-related FMRI activation of dopaminergic midbrain is associated with enhanced hippocampus-dependent long-term memory formation. Neuron 45:459-467.

Yamane F, Okazawa H, Blier P, Diksic M (2001) Reduction in serotonin synthesis following acute and chronic treatments with paroxetine, a selective serotonin reuptake inhibitor, in rat brain: an autoradiographic study with alpha-[14C] methyl-L-tryptophan. Biochem Pharmacol 62:1481-1489.

Yatham LN, Liddle PF, Shiah IS, Lam RW, Adam MJ, Zis AP, Ruth TJ (2001) Effects of rapid tryptophan depletion on brain 5-HT_2 receptors: a PET study. Br J Psychiatry 178:448-453.

Yokoyama C, Tsukada H, Watanabe Y, Onoe H (2005) A dynamic shift of neural network activity before and after learning-set formation. Cereb Cortex 15:796-801.

Young SN, Smith SE, Pihl RO, Ervin FR (1985) Tryptophan depletion causes a rapid lowering of mood in normal males. Psychopharmacology (Berl) 87:173-177.

Young SN, Ervin FR, Pihl RO, Finn P (1989) Biochemical aspects of tryptophan depletion in primates. Psychopharmacology (Berl) 98:508-511.

Young SN, Teff KL (1989) Tryptophan availability, 5-HT synthesis and 5-HT function. Prog Neuropsychopharmacol Biol Psychiatry 13:373-379.

Young SN, Leyton M (2002) The role of serotonin in human mood and social interaction. Insight from altered tryptophan levels. Pharmacol Biochem Behav 71:857-865.

Yun IA, Nicola SM, Fields HL (2004) Contrasting effects of dopamine and glutamate receptor antagonist injection in the nucleus accumbens suggest a neural mechanism underlying cue-evoked goal-directed behavior. Eur J Neurosci 20:249-263.

Zhuravin IA, Bures J (1991) Extent of the tetrodotoxin induced blockade examined by pupillary paralysis elicited by intracerebral injection of the drug. Exp Brain Res 83:687-690.

Zimmer L, Rbah L, Giacomelli F, Le Bars D, Renaud B (2003) A reduced extracellular serotonin level increases the 5-HT_{1A} PET ligand 18F-MPPF binding in the rat hippocampus. J Nucl Med 44:1495-1501.

Nederlandse samenvatting

Serotonine en cognitieve flexibiliteit; gedrags-, neurochemische-, en electrofysiologische studies in ratten.

De aansturing van doelgericht gedrag en de mogelijkheid om flexibel om te gaan met een veranderende omgeving wordt cognitieve flexibiliteit genoemd en is een belangrijke functie van de prefrontale cortex (PFC). Onderzoek heeft uitgewezen dat verschillende hersengebieden binnen de PFC nauw betrokken zijn bij specifieke cognitieve taken en dat een verminderde PFC functie leidt tot een verminderde cognitieve flexibiliteit. Daarnaast heeft de PFC een belangrijke rol in de integratie van motivationele informatie in de keuze en de uitvoering van beslissingen. De vraag hoe deze functies gereguleerd worden door de neurotransmitter serotonine (5-HT) staat centraal in dit proefschrift.

Vanuit verschillende invalshoeken is deze vraagstelling onderzocht. Met behulp van acute tryptofaan depletie onderzochten wij het effect van verminderde beschikbaarheid van serotonine op een cognitieve taak voor flexibiliteit (hoofdstuk 2). In de hoofdstukken 3 en 4 zijn wij vervolgens dieper ingegaan op eerdere bevindingen van onderzoek met tryptofaan depletie op cognitie en affect, evenals de mate waarin veranderingen in 5-HT afgifte bepalend zijn voor de gevonden effecten. Vervolgens hebben wij met behulp van locale neurotoxische 5-HT depletie de rol van serotonerge innervatie in de prefrontale cortex getest. In deze studie (hoofdstuk 5) hebben wij naast tests voor cognitieve flexibiliteit ook de affectieve waarde van de beloner gevarieerd met als doel de rol van 5-HT op affectieve processen te onderzoeken. Het proefschrift wordt besloten met metingen aan individuele neuronen in de prefrontale cortex gedurende de uitvoering van een gedragstaak voor flexibiliteit. Bovendien hebben wij in deze experimenten (hoofdstukken 6 en 7) direct het effect gemeten van locale toediening van farmaca op (taak gerelateerde) neurale activiteit.

Acute tryptofaan depletie en de rol van 5-HT in cognitieve flexibliteit en affect.

De beperkende factor in de synthese van 5-HT is de beschikbaarheid van het essentieel aminozuur tryptofaan. Een verlaging van inname van tryptofaan via de voeding leidt tot een verminderde synthese van 5-HT, een verlaagde hersenconcentratie, en, naar algemeen wordt aangenomen, een verlaagde serotonerge neurotransmissie. Vanwege de korte werking en omkeerbaarheid van deze serotonine depletie en de toepasbaarheid in

mensgebonden onderzoek is acute tryptofaan depletie (ATD) een populaire methode om de rol van serotonine te onderzoeken.

In hoofdstuk 2 is een experiment beschreven waarin de rol van 5-HT in cognitieve flexibiliteit is onderzocht met behulp van ATD. Om te meten of 5-HT betrokken is bij de uitvoering van een 'reversal-taak' werden ratten getest nadat ze een tryptofaan depletie hadden ondergaan. In de betreffende taak worden twee stimuli aangeboden die elk geassocieerd zijn met een bepaalde respons en uitkomst, één beloond en één onbeloond. Zodra de associaties zijn geleerd wordt de respons – uitkomst relatie omgekeerd en moet de respons worden aangepast om de beloning te krijgen. De resultaten van deze experimenten gaven een eerste indicatie dat 5-HT niet betrokken is bij de uitvoering van een 'reversal' taak die spatieel van opzet is. Het bleef echter onduidelijk in welke mate de tryptofaan depletie de afgifte van 5-HT had verminderd. Om een beter inzicht te krijgen in de relatie tussen de mate van 5-HT reductie in de PFC en de resultaten van de gedragsstudie hebben wij vervolgens de afgifte van 5-HT na ATD gemeten met behulp van microdialyse.

Hoofdstuk 3 beschrijft deze studie waarin gemeten werd hoe groot het effect is van ATD op de afgifte van 5-HT in de prefrontale cortex. In mensgebonden studies wordt het effect van ATD op de afgifte van 5-HT slechts indirect gemeten. Om die reden wordt een verlaging van plasma tryptofaan, ook in dierexperimentele studies, vaak als maat gezien voor het succes van de behandeling. Dat deze maat geen afspiegeling is van de afgifte van 5-HT blijkt uit de microdialyse metingen. De resultaten geven aan dat ATD weliswaar een verlaging induceerde van plasma tryptofaan, zoals dat ook in andere studies is gezien, maar dat deze verlaging niet leidde tot de verwachtte verlaging van afgifte van 5-HT in de prefrontale cortex. Deze bevinding geeft aan dat de relatie tussen ATD en serotonine functie niet zo eenduidig is al algemeen voorondersteld en dat ATD-geïnduceerde effecten mogelijk niet enkel serotonerg van aard zijn.

In Hoofdstuk 4 wordt een overzicht van bewijs voor ATD geïnduceerde effecten op 5-HT transmissie gegeven. Een belangrijk punt dat in dit overzicht naar voren komt is het gebrek aan direct bewijs dat ATD de afgifte van 5-HT verlaagt en dat een causale relatie tussen 5-HT en effecten van ATD moeilijk aan te tonen is. De effectiviteit van ATD in induceren van cognitieve effecten lijkt in sterke mate afhankelijk van de gevoeligheid van het test subject voor veranderingen van serotonine spiegels. Tot deze zogenaamde kwetsbare groepen behoren (familieleden van) patiënten met een verleden van depressie, vrouwen, en personen met een bepaalde mutatie van de serotonine transporter gen. Daarnaast wordt in dit hoofdstuk de mogelijkheid besproken dat de effecten van ATD op gedrag en cognitie mogelijk veroorzaakt worden door een interactie tussen een directe modulatie van autonome activiteit (bv. hartslag, bloeddruk en viscerale perceptie) en cognitieve processen.

Hoewel deze bevindingen zeer belangrijk zijn voor het onderzoek naar functies van het serotonerge systeem met behulp van ATD, duiden ze erop dat de belangrijkste conclusie van hoofdstuk 2, namelijk dat 5-HT niet betrokken is bij flexibiliteit van spatiele informatie, mogelijk niet gefundeerd is. Er zal naar onze mening enige terughoudendheid moeten worden betracht met het toeschrijven van de effekten van ATD aan een verlaging van 5-HT transmissie. Alleen onder specifieke condities is aangetoond dat ATD de afgifte van 5-HT verlaagd. Dit kan na verlaagde synthese of een verhoogd verbruik van 5-HT.

Mediaal PFC 5-HT en affect

Hoofdstuk 5 beschrijft een experiment waarin wij opnieuw onze hypothese testen dat prefrontaal 5-HT belangrijk is voor flexibiliteit. Deze rol wordt weer onderzocht met behulp van reversal leren, maar daarnaast hebben wij in deze experimenten ook bestudeerd wat de impact is van een verandering in affectieve waarde van de beloning. Hiertoe werd tijdens de uitvoering van de taak het type beloning dat verdiend kon worden veranderd vangewoon voer in een suiker pellet.

Depletie van 5-HT in de mediale PFC leidde niet tot een verslechtering van de taakuitvoering van spatiele reversal en dat stemt dus overeen met onze eerdere bevindingen uit hoofdstuk 2. Echter, wanneer het type beloning werd veranderd zagen wij een sterk effect op de taak uitvoering. De resultaten lieten zien dat wanneer 5-HT verminderd aanwezig is in de mPFC de ratten niet langer in staat waren om de veranderde waarde van de beloning in de taakuitvoering te integreren. Daarmee hebben wij kunnen laten zien dat mediale PFC 5-HT belangrijk is voor gedrag wanneer affectieve informatie het gedrag kan beïnvloeden. De betrokkenheid van de mPFC 5-HT is hierin wel anders dan die voor de oPFC 5-HT en reversal-leren. In het laatste geval uit een verslechterde taakuitvoering zich door een groter aantal verkeerde responsen door een veranderde relatie tussen de respons en uitkomst. In onze experimenten bleken de ratten goed in staat om een reversal te volbrengen maar lieten ze zich niet leiden door de huidige waarde van de beloning. Deze uitkomsten ondersteunen bevindingen in humaan onderzoek dat 5-HT een belangrijke rol vervuld in de verwerking van beloningsgerelateerde- en emotionele informatie. Serotonerge innervatie van de mPFC vervult hierin een belangrijke complementaire rol in het medieren van cognitieve flexibiliteit in het algemeen en reversal leren in het bijzonder.

Codering van beloningsgerelateerde informatie en 5-HT in de orbitale PFC

Een belangrijke punt dat tot op heden nauwelijks onderzocht is, is de vraag hoe 5-HT in de orbitale PFC bij de uitvoering van een reversal taak betrokken is op neuronaal niveau. Om deze vraag te beantwoorden ontwikkelden wij een ‘combidrive’ waarmee

tegelijkertijd neuronale activiteit gemeten kan worden en locaal in dezelfde neuronale populatie een farmakologisch aktieve stof toegediend kan worden. De afsluitende hoofdstukken hebben betrekking tot de effecten van locale toediening van farmaca op neurale activiteit (hoofdstuk 6) en de codering van taakgerelateerde informatie (hoofdstuk 7).

Voor deze experimenten hebben wij gebruik gemaakt van een speciale 'drive' die de mogelijkheid biedt om zeer locaal neuronen te meten en tegelijk een farmacon toe te dienen. Voor de validatie experimenten (hoofdstuk 6) hebben wij het effect onderzocht van veel gebruikte inhiberende farmaca en in hoofdstuk 7, een specifieke 5-HT_{2A} antagonist voor het effect van serotonerge manipulatie op de codering van beloningsgerelateerde informatie.

De validatie experimenten beschreven in hoofdstuk 6 toonden aan dat de voor deze experimenten ontworpen drive geschikt is om locaal farmaca toe te dienen in een gebied waarin tegelijk de neurale activiteit gemeten kan worden. Om dit aan te tonen hebben we 3 veelgebruikte remmers van neuronale activiteit toegediend en laten zien dat deze activiteit in een dosisafhankelijke manier verlagen. Verschillen tussen lidocaine, muscimol en tetrodotoxine (TTX) gaven bovendien aan dat korte, maar onvolledige, inactivatie het best met lidocaine bewerkstelligd wordt, maar voor langere, en meer complete, inactivatie, muscimol of TTX gebruikt kan worden. Waarbij TTX langer werkt maar mogelijk tot celdood kan leiden.

Hoofdstuk 7 beschrijft een experiment waarin het effect van 5-HT_{2A} receptor blokkade op de codering van beloningsgerelateerde informatie in de oPFC is onderzocht. Neuronale activiteit in de oPFC werd gemeten tijdens de uitvoering van een reversal-taak, waarbij er in het meetgebied een antagonist of controle oplossing werd geinfundeerd. De resultaten laten zien dat blokkade van de 5-HT_{2A} receptor verstorend werkt op de codering van beloningsgerelateerde informatie. In de controle conditie liet het merendeel van de uitkomstgevoelige neuronen een verandering van vuuractiviteit zien in relatie tot de beloonde trials, een minderheid van neuronen reageerde op onbeloonde trials. Dit onderscheid was niet aanwezig in de sessies waarin de antagonist werd geinfundeerd. Mogelijk dat deze verstoorde codering ten grondslag ligt aan de veranderde gevoeligheid voor positieve- en negatieve stimuli zoals dat eerder in mensgebonden onderzoek is gevonden. De antagonist had geen effect op het onderscheid dat neuronen maken tussen de verschillende beloningen; in beide condities maakten neuronen onderscheid tussen geprefereerde- en niet geprefereerd beloningen.

Daarnaast werd onderzocht of antagonisme van de 5-HT_{2A} receptor mogelijk van invloed is op stimulusgevoelige neuronen die hun respons aanpassen na een taak reversal. Een dergelijke interactie zou mogelijk kunnen verklaren hoe 5-HT depletie de uitvoering van een reversal taak kan verstoren. Echter, in deze experimenten kwam

naar voren dat neuronen in de oPFC slechts zeer sporadisch hun respons 'omdraaien' na een taak reversal. Veel vaker verdwijnen bestaande correlaten en worden er nieuwe gevormd volgens de nieuwe 'stimulus – beloning' relatie.

Deze resultaten zijn de eerste waarin direct het effect bestudeerd werd van een lokale toediening van een farmacon op de codering van beloningsgerelateerde informatie tijdens een gedragstaak. De resultaten suggereren dat een verslechterde taakuitvoering na 5-HT depletie mogelijk een gevolg is van een verstoorde codering van beloningsgerelateerde informatie.

Publications

5-HT_{2A} receptor antagonism impairs encoding of reward-related information in the rat orbital prefrontal cortex. (in preparation).

Feenstra MGP, **van der Plasse G** (2010). Tryptophan depletion and serotonin release - a critical reappraisal. In: Handbook of the Behavioral Neurobiology of Serotonin, Eds.: Müller CP and Jacobs BL, Academic press, San Diego, Ch. 2.7.

van Duuren E, **van der Plasse G**, Lankelma J, Joosten RN, Feenstra MG, Pennartz CM.Single-cell and population coding of expected reward probability in the orbitofrontal cortex of the rat. J Neurosci. 2009 Jul 15;29(28):8965-76.

van der Plasse G, Feenstra MGP. Serial reversal learning and acute tryptophan depletion. Behav Brain Res. 2008 Jan 10;186(1):23-31.

Cailotto C, van Heijningen C, van der Vliet J, **van der Plasse G**, Habold C, Kalsbeek A, Pévet P, Buijs RM.Daily rhythms in metabolic liver enzymes and plasma glucose require a balance in the autonomic output to the liver. Endocrinology. 2008 Apr;149(4):1914-25.

van der Plasse G, La Fors SS, Meerkerk DT, Joosten RNJMA, Uylings HBM, Feenstra MGP. Medial prefrontal serotonin in the rat is involved in goal-directed behaviour when affect guides decision making. Psychopharmacology (Berl). 2007 Dec;195(3):435-494.

van der Plasse G, Meerkerk DT, Lieben CK, Blokland A, Feenstra MGP. Lack of evidence for reduced prefrontal cortical serotonin and dopamine efflux after acute tryptophan depletion. Psychopharmacology (Berl). 2007 Dec;195(3):377-85.

van Duuren E*, **van der Plasse G***, van der Blom R, Joosten RNJMA, Mulder AB, Pennartz CMA, Feenstra MGP. Pharmacological manipulation of neuronal ensemble activity by reverse microdialysis in freely moving rats: a comparative study of the effects of tetrodotoxin, lidocaine, and muscimol. J Pharmacol Exp Ther. 2007 Oct;323(1):61-9.
*equal contribution

McGregor IS, Clemens KJ, **van der Plasse G**, Li KM, Hunt GE, Chen F, Lawrence AJ. Increased anxiety 3 months after brief exposure to MDMA ("Ecstasy") in rats: association with altered 5-HT transporter and receptor density. Neuropsychopharmacology. 2003 Aug;28(8):1472-84.


Matthijs
Esther
Stefano
Damiaan
Henk
Jelle
Harry
Louk
Jan
Ruud
Rinus
Roshan
Tonny
Chris
Hanny
Henry
Arjan
Jilles
Velentia
Thanks
Aimin
Caitlijn
Paula
Marcel
Caroline
Paul
Nanneke
Jenneke
Marijn
Ronald
Rein
Dirk
Carlyn
Lwout
Jingjun
Patrna
RMI colleagues
Rawien
Sabina
Eunjeong
Annemiek
Roman
Michel
Jamilja
grazie
Bedankt
Carlien
Jeffrey
Lisbeth
Tini
Serge
Jennifer
Joop
Maarten
Mam
Nel
Wilma
Alexander
Cindy
Mark
Herman
Arja
Dick
Marcia
Peter
Nienke
Nico
Olga
Joris
Martin
Dorie
Merci
Dimitra
Roy
Sabrina
Freddy
Adriaan
Matthew
Barbara
Iain
Cyriel
Gijs