Cambridge University Press 978-0-521-79002-4 - Imaging Dopamine Paul Cumming Index <u>More information</u>

Index

AAADC activity assayed with [³H]DOPA in living rat brain, 50, 52 measured by FDOPA PET, 65 pharmacological modulation of, 52. 53, 62, 69-70 regulation by second messengers, 49 true magnitude of, 67 inhibition by NSD 1015, 30 kinetic properties and substrate specificity in vitro, 46, 47 substrates for PET studies of. 68 transcriptional regulation, 48 Acetylcholine striatal interneurons, 15 acidic metabolites efflux from brain blockade by haloperidol, 90 microdialysis study of kinetics, 93

rate for DOPAC, 91 sulfoconjugation in brain, 8, 92-94 adenylate cyclise, and regulation of TH activity, 16, 26 ADHD D₂-like dopamine receptors, 209-210 DAT-PET and SPET studies of. 156 **FDOPA-PET** results in, 70 aging D₁-like dopamine receptor binding, 170, 171 D₂-like dopamine receptor binding, 194 DAT binding changes, 139, 145, 146, 149 [¹¹C]DTBZ-PET studies of, 116, 119, 120 elimination rate constant of [¹⁸F]fluorodopamine, 67 FDOPA utilization in striatum, 61, 71 MAO activity, 103

Alcoholism, and D₂-like dopamine receptors, 196, 204 DAT-PET, 157 [¹¹C]DTBZ-PET, 121 FDOPA-PET, 76 Alzheimer's dementia, and D₁-like dopamine receptors, 172 D₂-like dopamine receptors, 198 DAT-PET, 155 amphetamines blockade at DAT, general mechanism, 9,128 blockade of VMAT2, 114 D₁-like dopamine receptor binding, invulnerability to, 173 [¹¹C]DTBZ PET, 121 effects of chronic use on DAT, 158 effects on D₂-like receptor binding, and, 183, 184, 189, 205 sensitization of, 207-208, 223

Cambridge University Press 978-0-521-79002-4 - Imaging Dopamine Paul Cumming Index More information

332 Index

amphetamines (cont.) sensitization of, 213 interstitial dopamine levels increased by, 124, 129 rewarding properties of, 16.207 AMPT blockade of TH by, 35 D₂-like receptor binding after, 206 evidence for quantal release of dopamine, 128 potential tracer for TH activity, 40 anaesthesia, effects on dopamine receptor binding, 182, 204, 214 anticonvulsants, and D₂-like dopamine receptor binding, 213 antipsychotic, atypical occupancy at D₂-like receptors in cortex, 201 possible action at dopamine D₄ receptors, 163 antipsychotic medication, typical activation of AAADC by, 49 activation of TH by, 22, 25, 30, 39 benzamides, binding kinetics in vivo, 175.182 effects on acidic metabolite transport, 91 effects on dopamine turnover evoked by, 87 modulation of FDOPA uptake by, 62

antizyme control of amino acid decarboxylases by, 49 Aphakia mice, 13 apomorphine inhibition of TH by, 27, 30 aromatic amino acid decarboxylase, see AAADC aryl-sulfotransferase biochemistry of, 81, 83 conjugation of acidic metabolites by, 92 asymmetry dopamine D₂-like receptors and, 196, 208-209 dopamine markers in hemi-parkinsonism and, 59, 60, 150, 152 attention deficit hyperactivity disorder, see ADHD autoreceptors control of TH activity by, 7, 22, 24-26, 30, 32-33, 39.44 modulation of AAADC activity, -53, 49, 52, 62,70 predominance in substantia nigra, 201 Ayahuasca, 103

basal ganglia direct and indirect pathways in, 13 neurochemical anatomy of, 11 neuropeptides in, 13 BH₄ biosynthesis of phenylalanine and tyrosine, 6 brain concentration, 23, 24

classical phenylketonuria, 21 dopamine release, effect on, 22, 24 Segawa's disease, 21 TH activity, affinity regulation of, 22, 24, 25 binding potential, definition of, 108 bipolar disorder D₂-like dopamine receptors in. 200 FDOPA-PET in, 76 blood brain barrier export of acidic metabolites through, 90-91 LNAA transport across, 6, 10, 55 P-glycoprotein in, 10 γ-butyrolactone brain dopamine concentration increased by, 128 TH activity decreased by, 33 butyrophenones first successful PET studies of dopamine receptors using, 18 invulnerability in most psychostimulant studies of, 185-186 pharmacological specificity and binding properties, of, 174-175 vulnerability to Ecstasy challenge of, 186

Ca2+ concentration in interstitial fluid, 125 MPTP and 6-OHDA toxicity, role in, 12 Cambridge University Press 978-0-521-79002-4 - Imaging Dopamine Paul Cumming Index More information

Index 333

vesicular fusion, role in, 113 Calcium, see Ca2+ cannabis COMT, and risk of psychosis, 83, 216 effects on D2-like dopamine receptors, 216 Carlsson, Arvid discovery of autoreceptor regulation of dopamine synthesis, 24 receives Nobel Prize in Medicine, 3 schematic model of catecholamine fibre, 5.7 catechol-O-methyltransferase, see COMT cerebellum, validity as reference tissue, 177 c-fos expression adrenal medulla and, 48 MAO-B knockout mice and, 103 stimulation of dopamine receptors and, 16, 164 choreoathetosis, and [¹¹C]DTBZ-PET, 121 Cloninger, see personality and cognition, relation with cocaine abuse of D₂-like dopamine receptors and, 204, 210-211 DAT-PET and, 157 blockade of DAT, 9 as a PET tracer, 141 rewarding properties, 16, 158

interstitial dopamine levels and, 124, 126, 130 relation with impulsivity in rats and, 218 coffee, effect on D2-receptor availability, 213 cognition, see personality and cognition, relation with competition model in vivo against D₁-like receptors, failure to demonstrate, 173 D₂-like receptors, and invulnerablity of butyrophenone ligands, 185 labelled with antagonist ligands, 182, 184 particular vulnerability of agonist ligands, 185 DAT imaging, 148 **MAO-PET**, 110 COMT activity with respect to brain DOPA, 39 alleles, 83 D1-like dopamine receptor binding and, 172 distrubution in brain, 82 enzyme biochemistry, 80 inhibition and inhibitors FDOPA-PET, 63 microdialysis studies, 93 target as antipsychotic treatment, 98 metabolism of plasma FDOPA by, 55 prolongation of DOPA therapeutic action by, 82

concentration gradients for DOPAC between brain compartments, 123 dopamine across the plasma membrane, 127, 129 dopamine between vesicle and cytosolic space, 124 LNAAs across BBB, 10 cyclic nucleotides phosphorylation of TH and, 25–26 regulation of AAADC and, 49

D₁-like dopamine receptor absolute abundance of. 190-192, 227-228 agonists claims for existence of distinct affinity states, 167 internalization evoked by, 165 PET ligands for, 168 signal transduction pathways of, 9, 16, 160, 163, 165 D₂-like dopamine receptor absolute abundance of, 170, 227-228 agonists dubious claims for existence of distinct affinity states, 167, 178, 213, 227, 233 internalization evoked by, 166 ligands for, 178-180 particular vulnerability in competition models, 185, 189, 192, 193

Cambridge University Press 978-0-521-79002-4 - Imaging Dopamine Paul Cumming Index More information

334 Index

D₂-like dopamine receptor (cont.) allelic variants D2-like dopamine receptors and, 19 DAT-PET studies, 151 FDOPA-PET studies of, 75 butyrophenone ligands in vivo, 166, 175 D₃ receptors, 163, 177 high and low affinity benzamide ligands cortical binding sites measured by PET, 191, 200, 201 general aspects, 176-177, 194 vulnerability to psychostimulants, 184, 187 long and short, forms of. 161 occupancy by agonists, 202 antipsychotics, 201 oligomeric associations of, 180 signal transduction pathways of, 9, 16, 161.163 upregulation in striatum after dopamine depletion, 181 receptor blockade, 203 DAT density in brain, 145-146 extent of hemilesion and turning rate, 133, 138 knockout, and dopamine dynamics behavioural effects, 140 dopamine dynamics measured by

electrochemistryd, 126, 139 dopamine dynamics measured by microdialysis, 129 ligands for [¹¹C]cocaine, 141 molecular biologyd, 137, 151 Tropane ligands for SPET studies, 141-147 Parkinson's disease, 152-154 PET studies of aging, 149 Dementia, see Alzheimer's dementia, and depolarization block chronic antipsychotic treatment, 15 FDOPA PET study of, 70 depression, see major depressive disorder dihydrotetrabenazine, see reserpine-like alkaloids dihydroxyphenylacetic acid, see acidic metabolites distribution volume [¹¹C]DTBZ, 118 [¹¹C]harmine in pig brain, 108 definition of, 41 hungry chicken model of, 42 DOPA brain metabolism compartmental model of, 51 multiple fates in living brain, or branching ratio, 7, 52 synthesis rate in rat striatum, 30, 31

effect in receptor competition models, 149 reanimation of reserpinized rabbits, 2 treatment for Parkinson's disease 3 DOPAC, see acidic metabolites DOPA decarboxylase, see AAADC dopamine biosynthesis of, 6 concentration in interstitial fluid. 125 prediction error coding, and, 17 turnover, calculated from accumulation in rat striatum after pargyline, 87 conjugation by arylsulfotransferase, 81 decline in rat striatum after AMPT, 35, 86-88 fractional rate constant for breakdown by MAO, 87 washout of [18F] fluorodopamine in FDOPA-PET. 67 dopamine D₃ or D₄ receptors, see D2-like dopamine receptor dopamine D₅ receptors, see D₂-like dopamine receptor dopamine neurons autoreceptors apomorphine and, 27, 32 control of dopamine metabolism, 24

Cambridge University Press 978-0-521-79002-4 - Imaging Dopamine Paul Cumming Index More information

discovery by Carlsson, 24

possible contribution to motor fluctuation of Parkinson's disease, 33 postnatal development of. 25 size and abundance, 11, 12 firing properties, and depolarization block, 15 reward, 17 MPTP model of parkinsonism, 72 dopamine receptors, see D₁-like dopamine receptor, D₂-like dopamine receptor dopamine transporter, see DAT DOPA-responsive dystonia, see Segawa's disease dystonia, D₂-like dopamine receptors in, 198 ecstasy, see MDMA, effect on D₂-like dopamine receptor binding EEDQ and evidence for receptor reserve, 168 electrochemistry in vivo, 125-126 estrogen, and dopamine receptor binding, 179 ethanol, effect on D2-like dopamine receptor availability, 213 euphoria, see reward, relation with dopamine release extracellular fluid. see interstititial fluid FDG, early application of

PET, 18

FDOPA clinical PET studies aging, 71 MPTP model of parkinsonism, 72 rate of progression of Parkinson's disease, 73 schizophrenia, 75, 76, 77 threshold for detection of nigostriatal degeneration, 73 common partition volume with LNAAs in brain. 61, 63 quantitative PET methods compartmental model of metabolism, 55, 58, 63.65 linear graphic analysis with arterial input, 58.60 linear graphic analysis with reference tissue input (Hartvig), 58-61 steady-state kinetics in brain, 64, 66 studies of personality and cognition, 78 time-activity curves in monkey brain, 56 [¹⁸F]fluorodeoxyglucose, see FDG, early application of PET 6-[¹⁸F[fluoro-L-DOPA, see FDOPA 6-[¹⁸F]fluoro-metatyrosine, see FMT feeding, and dopamine release, 143, 221 fluordopamine, washout from brain, 64, 67

FMT acquired parkinsonism in monkeys, 72 alternate AAADC substrate for PET studies, 69 forskolin, and activation of adenylate cyclise, 165 GABA effects of γ-vinyl-GABA on [¹¹C]raclopride binding, 213 medium spiny neurons of striatum, 13 gender differences D2-like dopamine receptors and amphetamine challenge, 191, 195, 222 DAT binding, 151 FDOPA kinetics, 76 Gjedde-Patlak plot, see linear graphic analysis **G**-proteins association with VMAT2, 114 control of TH activity, 32

233 haloperdiol, *see* antipsychotic medication, typical Hartvig plot, *see* FDOPA, quantitative PET methods heroin, *see* opiates high performance liquid chromatography, *see* HPLC homovanillic acid, *see* acidic metabolites

lack of PET tracers for

signal transduction,

Index 335

Cambridge University Press 978-0-521-79002-4 - Imaging Dopamine Paul Cumming Index More information

336 Index

HPLC ketamine, see NMDA dopamine metabolites in antagonists brain and interstitial fluid, 93, 122 large neutral amino acids, plasma metabolites see LNAA carrier Lesch-Nyhan syndrome of PET tracers, 55, DAT-PET, 155 104.106 Huntington's disease FDOPA-PET, 75 D₁-like dopamine linear graphic analysis applied to [¹¹C]tyrosine receptors, 172 D₂-like dopamine influx to monkey receptors, 198 brain, 42 applied to FDOPA DAT PET, 155 [¹¹C]DTBZ-PET, 120 metabolite-corrected FDOPA-PET, 155 arterial input, HVA, see acidic metabolites 58,60 6-hydroxydopamine, reference tissue input see 6-OHDA method of Hartvig, 58-61 interstititial fluid linkage to dopamine behavioral correlates of receptors, 9, 160, 228 dopamine release, LNAA carrier 131-132 blood brain barrier, 6 dopamine concentration by countertransport of brain zero net flux OMD.8 DOPA transport, 50 microdialysis cortex, 140 molecular biology of, 10 striatum, 9, 124, 139 locus ceruleus dopamine release Parkinson's disease, altered D₂-like dopamine degeneration in, 78 receptor binding, TH expression in, 29 184 Logan plot BH₄ effect on dopamine ^{[11}C]DTBZ binding, 118-119 release, 22 [¹¹C]harmine uptake, 107 MAO inhibition, effect on benzamide binding, 176 dopamine bias, tendency for, 184 metabolites, 93 LSD, competition against precursor loading, and dopamine D₂-like effect on, 20, 25 receptors, 215 unaltered D₂-like dopamine receptor Machado-Joseph disease, see binding, 207, 214 spinocerebellar microdialysis, general ataxias, and DAT-

major depressive disorder D₁-like dopamine receptors, 171 D₂-like dopamine receptors, 211 DAT-PET, 156, 157 **MAO-PET**, 110 MAO activity with respect to dopamine in vivo, 87 biochemistry, enzymology, and substrate specificity, 100 catabolism of dopamine, 8.87 clinical PET studies of depression, 110 epilepsy, 109 smoking, 109 knockouts and Norrie Disease, 103 MPTP toxicity and endogenous Parkinson's disease, 103 neurochemical anatomy, 102 PET tracers [¹¹C]clorgyline, 106 ^{[11}C]deprenyl, difficulties in kinetic modelling, 105 [¹¹C]harmine, favourable kinetics, 107 others. 109 MAO inhibitors AAADC activity, regulation of, 48, 53 acidic metabolites, turnover of, 93 D₂-like dopamine receptors, effect on. 185 DAT binding, effects on, 57

aspects of, 123

SPET

Cambridge University Press 978-0-521-79002-4 - Imaging Dopamine Paul Cumming Index More information

> TH activity, regulation of, 32 MDMA, effect on D₂-like dopamine receptor binding, 189 methamphetamine, see amphetamines methoxytyamine, see 3MT α-methyl-para-tryrosine, see AMPT methylphenidate DAT-PET, tracer for, 148, 152, 158, 159 dopamine metabolites in striatal slices, 22 effects on benzamide binding, 184, 210 FDOPA utilization, effect of chronic treatment, 70 NADPH diaphorase unmasks small binding changes in [¹¹C]raclopride PET, 221 microdialysis, see interstititial fluid monoamine neurons revealed fluorescence histology, 2 TH immunohistochemistry, 11 monoamine oxidase, see MAO monoamine vesicles, see vesicles movement and motor learning availability of D₂-like dopamine receptors, 195, 217, 222 interstitial dopamine release, 131-132 MPTP D₁-like dopamine receptors, 167 D₂-like dopamine receptors, 181

DAT-PET and SPET studies of, 146, 150, 152 [¹¹C]DTBZ-PET studies of, 118, 119 FDOPA-PET studies of, 56-62, 72 model of Parkinson's disease, and toxicity for dopamine neurons, 12 3MT forked path of dopamine metabolism, 6 kinetics in vivo, 93, 96 steady state concentrations in brain, 95 patch-matrix compartments, 14 striatal interneurons, 11 neurochemical anatomy dopamine inervation, 13 dopamine neurons, 11 dopamine receptors, 161-162 MAO, 102 neuropeptide

coexpression, 13-15 neuromelanin, and von Economo's encephalopathy, 3 neuronal ceroid lipofuscinosis D1-like dopamine receptors binding, 172 FDOPA uptake, 75 neuropeptides, coexpression in striatal neurons, 13 - 15nicotine and smoking D₁-like dopamine receptors, 171

D₂-like dopamine receptors

pharmacological challenge studies, 212-213, 221 possible relationship with tardive dyskinesia, 203 **DAT-PET. 157** FDOPA-PET, 76 MAO-PET, 109 rewarding properties, 16, 130 NMDA antagonists AAADC activity, modulation by, 53, 214 D₂-like dopamine receptor availability, effects on. 214 NMSP, see butyrophenones Norrie disease, 103 novelty seeking personality, see personality and cognition, relation with NSD 1015 TH activity, assay of, 29 tryptophan hydroxylase activity, assay of. 31 nucleus accumbens, and dopamine D₃ receptors, 162

6-OHDA D₂-like dopamine receptors, upregulation by, 181 detection of dopaminergic grafts, 143 interstitial dopamine concentration, 125 priming of response to agonists, 164

Index 337

Cambridge University Press 978-0-521-79002-4 - Imaging Dopamine Paul Cumming Index More information

338 Index

6-OHDA (cont.) Trojan horse toxicity for dopamine neurons, 12 turning behaviour, 132, 138 olivopontocerebllar atrophy, [¹¹C]DTBZ-PET findings, 120 O-methyl-FDOPA, see OMFD OMFD constrained compartmental model for FDOPA, 63 formation in plasma from FDOPA, 55 subtraction of calculated brain concentrations, 66 opiates D₂-like dopamine receptor availability, 214 interstitial dopamine, 131 opioid receptors, distribution in patch matrix compartments, 14 pain, and [¹¹C]raclopride binding changes, 219 pargyline, see MAO inhibitors Parkinson's disease D₁-like dopamine receptors, 170, 171 D₂-like dopamine receptors PET baseline levels, 191, 197 transcranial magnetic stimulation and deep brain stimulation, 216-217 treatment effects, 202, 211-212

DAT-PET evidence for down-regulation of, 138, 152 studies of, 146, 152-154 FDOPA-PET studies of, 61, 62, 65, 72, 78 genetics and relationship with dopamine receptor alleles, 75 rate of progression of disease, 73, 74 washout of [¹⁸F]fluorodopamine, 67 [¹¹C]DTBZ-PET studies of, 116, 120 HVA levels in CSF. 95 link with von Economo's encephalopathy, 2 motor fluctuations, possible effects of autoreceptors in, 33 partial volume effects AAADC activity measured by FDOPA-PET, 68 limited spatial resolution and, 230 personality and cognition, relation with D₂-like dopamine receptors, 195, 217 DAT binding sites, 151 FDOPA-PET, 77, 78 description of, 17 watch smashing, end of, 9 phenylalanine, competitive inhibition of TH, 20 phenylalanine hydroxylase classical phenylketonuria, 21 inhibition by pPCA, 20

synthesis of tyrosine in brain, 6 phenylketonuria biochemistry of, 21 FDOPA-PET, 62 pheochromocytoma AAADC in, 48 TH expression in, 27 placebo, and dopamine competition paradigm, 223 plasma metbolites of PET tracers [¹¹C]harmine, 107 FDOPA and [¹¹C]DOPA, 54-56 positron emission tomography, see PET prediction error, and dopamine signalling, 17 probenecid, blockade of acidic metabolite transport, at BBB, 90, 92 protein precursor pool for brain tyrosine salvage, 40 synthesis in brain measured with $[^{11}C]$ tyrosine PET, 43 protein kinases D₁-like receptor binding, 171 DAT, phosphorylation by, 137 TH, phosphorylation by, 26, 27

raclopride, *see* antipsychotic medications, typical reserpine-like alkaloids D₁-like dopamine receptor binding, invulnerability to, 170, 173 Cambridge University Press 978-0-521-79002-4 - Imaging Dopamine Paul Cumming Index More information

> D₂-like dopamine receptor binding, vulnerability to, 186-190 discovery of antiparkinsonian action of DOPA, 2 TH, activation by, 33 VMAT2 activation by, 114 PET ligands for, 115, 116 restless legs syndrome D₂-like receptor availability, 198 FDOPA-PET, 75 reward, relation with dopamine release, 16, 158, 159, 207, 213, 220-222 S-adenosylmethionine, see SAM, co-substrate for COMT SAM, co-substrate for COMT. 80.81 schizophrenia D₁-like dopamine receptor binding in, 168.172 D₂-like dopamine receptor binding in amphetamine challenge paradigm, 205 controversy about, 192, 198-299 FDOPA-PET studies of. 62. 65,76 [¹¹C]DTBZ-PET, **121** DAT-PET, 155 depolarization block after chronic antipsychotic medication, 15, 70

steady-state FDOPA trapping reduced in, 77 washout of [¹⁸F]fluorodopamine increased in, 76 Segawa's disease BH₄ synthesis and, 21 empty vesicles visualized with [¹¹C]DTBZ-PET, 120 self-administration, see reward, relation with dopamine release serotonin binding sites cocaine action at. 140 biosynthesis, 31 D₂-like dopamine receptor availability, modulation by, 215 antipsychotic medication, atypical, occupancy by, 201 dopamine ligands, cross-talk wiht, 141, 142, 169, 174, 203 neurons DOPA metabolism within. 50 TH activity, modulation by agonists of, 34 sexual behaviour, and dopamine release, 138 smoking, see nicotine and smoking spinocerebellar ataxias, and DAT-SPET, 155 spiperone, see butyrophenones

stress dopamine release evoked by, 135, 220 striatum interneurons, 15 patch-matrix compartments, 13-14, 139 slices methylphenidateevoked dopamine overflow, 22 properties of, 123 substance P, see neuropeptides substantia nigra dopamine neurons in, 11.12 loss of pigmented neurons in 3 subthalamic stimulation, lack of effect on [¹¹C]raclopride binding, 216 synaptosomes general properties of, 123 TH activity in striatum, 20, 26

tetrahydrobiopterin, see BH₄ TH activity assayed with intracerebroventricular [³H]tyrosine infusion, 36 assayed with intravenous [³H]tyrosine injection, 36 assayed by NSD 1015 method, 29, 31 assayed by push-pull cannula, 35

Cambridge University Press 978-0-521-79002-4 - Imaging Dopamine Paul Cumming Index More information

340 Index

TH (cont.) autoreceptor regulation of, 7, 22, 24-26, 30, 32-33, 39, 44 PET study with ^{[11}C]tyrosine, 41 pharmacological modulation of, 34 biochemical properties of, 19, 23, 27 classical rate limiting step for catecholamine synthesis, 7, 22, 24 immunohistochemical localization in brain, 11 phenylalanine as a substrate in brain, 20 phosphorylation and transcriptional regulation, 25, 27 transgenic mice overexpressing, 28 Tourette's syndrome, and [¹¹C]DTBZ- PET, 121 DAT imaging, 156 trace amines synthesis in rat striatum, 47 turnover in rodent brain, 88 vesicular amine storage, 111. 129

transcranial magnetic stimulation, effects on [¹¹C]raclopride binding, 216-217 tryptophan hydroxylase, activity in striatum, 31 Tyrosine compartmental model of metabolism, 37, 38 effects of loading on DOPA synthesis, 25 formation in liver, 5 precursor for brain protein synthesis, 7 unidirectional blood-brain clearance, 39, 41, 43 tyrosine hydroxylase, see TH ventral tegmental area, see VTA neurons vesicles capacitance change during fusion of, 112 dopamine quanta, concept of, 126, 128 vesicular monoamine transporter, see VMAT1, VMAT2 VMAT1 chromaffin granules, used for studies of exocytosis, 112

dopamine concentration gradient, 113 MPTP toxicity, resistance to, imparted by, 111 VMAT2 ATP, required for dopamine gradient, 9 dopamine, storage via, 8 molecular biology and knockouts, 111, 114 binding properties of radioligands for, 115-117 kinetic modelling, 117-118 Parkinson's disease and dementias. decreased in. 120 PET studies with [¹¹C]DTBZ, 120 von Economo's encephalopathy, 3 VTA neurons autoreceptor regulation, notably weak in, 24, 33 burst firing of, 15 dopamine D₃ receptors in, 162 precursor loading, dependence on, 25 TH immunohistochemistry of. 11