Click to verify

 Intense feelings of well-being "Euphoric" redirects here. For other uses, see Euphoria (disambiguation) and Euphoric (disambiguation). Not to be confused with Euphorbia. Playing can induce an intense state of happiness and contentment, like this girl playing in the snow. Part of a series onEmotions Affect Classification In animals Emotional intelligence Mood Self-regulation Interpersonal Dysregulation Valence Emotions Acceptance Admiration Affection Amusement Anger Angst Anguish Annoyance Anticipation Anxiety Apathy Arousal Awe Belongingness Boredom Confidence Confusion Contempt Contentment Courage Curiosity Depression Desire Determination Disappointment Disgust Distrust Doubt Ecstasy Elevation Embarrassment Emotional detachment Empathy Enthusiasm Envy Euphoria Faith Fear Frustration Gratification Gratitude Greed Grief Guilt Happiness Hatred Hope Horror Hostility Hubris Humiliation Interest Jealousy Joy Kindness Limerence Loneliness Love Lust Nostalgia Outrage Panic Passion Pity Pleasure Pride Rage Regret Rejection Relief Remorse Resentment Sadness Saudade Schadenfreude Self-pity Shame Shock Shyness Social connection Sorrow Suffering Surprise Suspicion Trust Wonder Worry vte Euphoria (/juːˈfɔːriə/ yoo-FOR-ee-ə) is the experience (or affect) of pleasure or excitement and intense feelings of well-being and happiness.[1][2] Certain natural rewards and social activities, such as aerobic exercise, laughter, listening to or making music and dancing, can induce a state of euphoria.[3][4] Euphoria is also a symptom of certain neurological or neuropsychiatric disorders, such as mania.[5] Romantic love and components of the human sexual response cycle are also associated with the induction of euphoria.[6][7][8] Certain drugs, many of which are addictive, can cause euphoria, which at least partially motivates their recreational use.[9] Hedonic hotspots – i.e., the pleasure centers of the brain – are functionally linked. Activation of one hotspot results in the recruitment of the others. Inhibition of one hotspot results in the blunting of the effects of activating another hotspot.[10][11] Therefore, the simultaneous activation of every hedonic hotspot within the reward system is believed to be necessary for generating the sensation of an intense euphoria.[12] The word "euphoria" is derived from the Ancient Greek terms εὐφορία: εὖ eu meaning "well" and φέρω pherō meaning "to bear".[13][14] It is semantically opposite to dysphoria. A 1706 English dictionary defines euphoria as "the well bearing of the Operation of a Medicine, i.e., when the patient finds himself eas'd or reliev'd by it".[15] During the 1860s, the English physician Thomas Laycock described euphoria as the feeling of bodily well-being and hopefulness; he noted its misplaced presentation in the final stage of some terminal illnesses and attributed such euphoria to neurological dysfunction.[16] Sigmund Freud's 1884 monograph Über Coca described (his own) consumption of cocaine producing "the normal euphoria of a healthy person",[17] while about 1890 the German neuropsychiatrist Carl Wernicke lectured about the "abnormal euphoria" in patients with mania.[18] A 1903 article in The Boston Daily Globe refers to euphoria as "pleasant excitement" and "the sense of ease and well-being".[19] In 1920 Popular Science magazine described euphoria as "a high sounding name" meaning "feeling fit": normally making life worth living, motivating drug use, and ill formed in certain mental illnesses.[20] Robert S. Woodworth's 1921 textbook Psychology: A study of mental life, describes euphoria as an organic state which is the opposite of fatigue, and "means about the same as feeling good."[21] In 1940, The Journal of Psychology defined euphoria as a "state of general well being ... and pleasantly toned feeling."[22] A decade later, finding ordinary feelings of well being difficult to evaluate, American addiction researcher Harris Isbell redefined euphoria as behavioral changes and objective signs typical of morphine.[23] However, in 1957 British pharmacologist D. A. Cahal did not regard opioid euphoria as medically undesirable but an effect which "enhance[s] the value of a major analgesic."[24] The 1977 edition of A Concise Encyclopaedia of Psychiatry called euphoria "a mood of contentment and well-being," with pathologic associations when used in a psychiatric context. As a sign of cerebral disease, it was described as bland and out of context, representing an inability to experience negative emotion.[25] In the 21st century, euphoria is generally defined as a state of great happiness, well-being and excitement, which may be normal, or abnormal and inappropriate when associated with psychoactive drugs, manic states, or brain disease or injury.[26] Main article: Reward system § Pleasure centers Hedonic hotspots are functionally interrelated neural substrates/structures that (intrinsically or extrinsically) generate the feelings of pleasure. Activation of one hedonic hotspot involves the stimulation of the others. Inhibition of one hedonic hotspot blunts the activation the other ones.[10][11] Therefore, the simultaneous activation of every hedonic hotspot within the reward system is probably necessary for generating the sensation of euphoria.[12] Many different types of stimuli can induce euphoria, including psychoactive drugs, natural rewards, and social activities.[1][27][4][5] Affective disorders such as unipolar mania or bipolar disorder can involve euphoria as a symptom.[5] This section is an excerpt from Neurobiological effects of physical exercise § Exercise-induced euphoria.[edit] Continuous exercise can produce a transient state of euphoria – an emotional state involving the experience of pleasure and feelings of profound contentment, elation, and well-being – which is colloquially known as a "runner's high" in distance running or a "rower's high" in rowing.[28][29][30][31] Not everyone experiences this.[32] Further information: Frisson Euphoria can occur as a result of dancing to music, music-making, and listening to emotionally arousing music.[4][33][34] Neuroimaging studies have demonstrated that the reward system plays a central role in mediating music-induced pleasure.[34][35] Pleasurable emotionally arousing music strongly increases dopamine neurotransmission in the dopaminergic pathways that project to the striatum (i.e., the mesolimbic pathway and nigrostriatal pathway).[33][34][35] Approximately 5% of the population experiences a phenomenon termed "musical anhedonia", in which individuals do not experience pleasure from listening to emotionally arousing music despite having the ability to perceive the intended emotion that is conveyed in passages of music.[35] A clinical study from January 2019 that assessed the effect of a dopamine precursor (levodopa), dopamine antagonist (risperidone), and a placebo on reward responses to music – including the degree of pleasure experienced during musical chills, as measured by changes in electrodermal activity as well as subjective ratings – found that the manipulation of dopamine neurotransmission bidirectionally regulates pleasure cognition (specifically, the hedonic impact of music) in human subjects.[36][37] This research suggests that increased dopamine neurotransmission acts as a sine qua non condition for pleasurable hedonic reactions to music in humans.[36][37] The various stages of copulation may also be described as inducing euphoria in some people. Various analysts have described either the entire sexual act, the moments leading to orgasm, or the orgasm itself as the pinnacle of human pleasure or euphoria.[38] A large dose of methamphetamine causes a drug-induced euphoria.[39] A euphoriant is a type of psychoactive drug which tends to induce euphoria.[40] Most euphoriants are addictive drugs due to their reinforcing properties and ability to activate the brain's reward system.[5] Dopaminergic stimulants like amphetamine, methamphetamine, cocaine, MDMA, and methylphenidate are euphoriants.[1][5] Nicotine is a parasympathetic stimulant that acts as a mild euphoriant in some people.[5] Xanthines such as caffeine and theobromine may also be considered mild euphoriants by some.[medical citation needed] Chewing areca nut (seeds from the Areca catechu palm) with slaked lime (calcium hydroxide) – a common practice in South- and Southeast Asia – produces stimulant effects and euphoria.[41][42][43] The major psychoactive ingredients – arecoline (a muscarinic receptor partial agonist)[42][44] and arecaidine (a GABA reuptake inhibitor)[45][46] – are responsible for the euphoric effect.[47][48] Certain depressants can produce euphoria; some of those drugs in this class include alcohol in moderate doses,[49][50] γ-hydroxybutyric acid (GHB),[1][51] and ketamine.[1] Some barbiturates and benzodiazepines may cause euphoria. Euphoriant effects are determined by the drug's speed of onset,[52] increasing dose,[53] and with intravenous administration.[54] Barbiturates more likely to cause euphoria include amobarbital, secobarbital and pentobarbital.[55][56] Benzodiazepines more likely to cause euphoria are flunitrazepam, alprazolam and clonazepam.[52][57][58] Benzodiazepines also tend to enhance opioid-induced euphoria.[59] Pregabalin induces dose-dependent euphoria.[60][61] Occurring in a small percentage of individuals at recommended doses, euphoria is increasingly frequent at supratherapeutic doses (or with intravenous- or nasal administration).[62][61][60] At doses five times the maximum recommended, intense euphoria is reported.[60] Another GABA analogue, gabapentin, may induce euphoria.[63] Characterized as opioid-like but less intense,[clarification needed] it may occur at supratherapeutic doses, or in combination with other drugs, such as opioids or alcohol.[63] Ethosuximide and perampanel can also produce euphoria at therapeutic doses.[64][65][66] μ-Opioid receptor agonists are a set of euphoriants[5] that include drugs such as heroin, morphine, codeine, oxycodone, and fentanyl. By contrast, κ-opioid receptor agonists, like the endogenous neuropeptide dynorphin, are known to cause dysphoria,[5] a mood state opposite to euphoria that involves feelings of profound discontent. Cannabinoid receptor 1 agonists are a group of euphoriants that includes certain plant-based cannabinoids (e.g., THC from the cannabis plant), endogenous cannabinoids (e.g., anandamide), and synthetic cannabinoids.[5] Certain gases, like nitrous oxide (N2O, aka "laughing gas"), can induce euphoria when inhaled.[5][67] Traditional psychedelic drugs, such as LSD and psilocybin are capable of inducing euphoria despite lacking addictive qualities. The Global Drug Survey has revealed that out of 22,000 participant reports, MDMA, LSD, and psilocybin mushrooms were ranked most positively on the Net Pleasure Index of all recreational drugs included in the study.[68] Acute exogenous glucocorticoid administration is known to produce euphoria, but this effect is not observed with long-term exposure.[5] The following is a full list of euphoriant or rewarding/reinforcing drugs:[69][70][71] GABAA receptor PAMsTooltip positive allosteric modulators (e.g., alcohol, benzodiazepines, Z-drugs, barbiturates,) and agonists (e.g., muscimol, gaboxadol)[72][73][74] Nicotinic acetylcholine receptor agonists (e.g., nicotine)[75] Classical dopamine reuptake inhibitors (e.g., cocaine, methylphenidate) and dopamine releasing agents (e.g., amphetamine, methamphetamine) (psychostimulants)[76][77][78] μ-Opioid receptor agonists (opioids) (e.g., morphine, heroin, fentanyl, hydrocodone, oxycodone)[79] Cannabinoid CB1 receptor agonists (cannabinoids) (e.g., Δ9-THCTooltip delta9-tetrahydrocannabinol, nabilone)[80][81] NMDA receptor antagonists (dissociatives) (e.g., ketamine, phencyclidine, nitrous oxide, dextromethorphan)[82][83] Gabapentinoids (α2δ ligands) (e.g., gabapentin, pregabalin, phenibut)[84][85] γ-Hydroxybutyrate (GHB) and analogues (GHB and GABAB receptor agonists) (e.g., GHBTooltip γ-hydroxybutyrate, GBLTooltip γ-butyrolactone, 1,4-BDTooltip 1,4-butanediol)[86] AMPA receptor antagonists (e.g., perampanel)[66] Serotonin releasing agents (entactogens) (e.g., MDMA, MBDB, MDAI, MEAI)[87][88] Serotonergic psychedelics (non-selective serotonin receptor agonists) (e.g., LSDTooltip lysergic acid diethylamide, psilocybin, mescaline, DMTTooltip dimethyltryptamine) (mixed/variable and non-addictive)[89][90][91] Glucocorticoid receptor agonists (glucocorticoids or corticosteroids) (e.g., hydrocortisone, dexamethasone)[92][93] Fasting has been associated with improved mood, well-being, and sometimes euphoria. Various mechanisms have been proposed and possible applications in treating depression considered.[94] Euphoria is also strongly associated with both hypomania and mania, mental states characterized by a pathological heightening of mood, which may be either euphoric or irritable, in addition to other symptoms, such as pressured speech, flight of ideas, and grandiosity.[95][96] Although hypomania and mania are syndromes with multiple etiologies (that is, ones that may arise from any number of conditions), they are most commonly seen in bipolar disorder, a psychiatric illness characterized by alternating periods of mania and depression.[95][96] Euphoria may occur during auras of seizures[97][98] typically originating in the temporal lobe, but affecting the anterior insular cortex. This euphoria is symptomatic of a rare syndrome called ecstatic seizures,[99][100] often also involving mystical experiences.[101] Euphoria (or more commonly dysphoria) may also occur in periods between epileptic seizures. This condition, interictal dysphoric disorder, is considered an atypical affective disorder.[102][103] Persons who experience feelings of depression or anxiety between or before seizures occasionally experience euphoria afterwards.[104] Some persons experience euphoria in the prodrome – hours to days before the onset – of a migraine headache.[105][106][107] Similarly, a euphoric state occurs in some persons following the migraine episode.[105][107] Euphoria sometimes occurs in persons with multiple sclerosis as the illness progresses. This euphoria is part of a syndrome originally called euphoria sclerotica, which typically includes disinhibition and other symptoms of cognitive and behavioral dysfunction.[108][109] Gender euphoria is satisfaction or enjoyment felt by a person due to consistency between their gender identity and gendered features associated with a gender different to the sex they were assigned at birth. It is considered to be the positive counterpart of gender dysphoria.[110] Related euphorias have also been recorded in studies of alignments between sexual identity and social recognition such as support in schools for lesbian and gay people, and experiences of intersex variation and their diagnoses such as receiving a diagnosis of congenital adrenal hyperplasia which explained physical differences for example.[111] Peak experience Psychological Dysphoria Euthymia Hyperthymia Sense of wonder Pharmacological Anxiolytic Designer drug Recreational drug use ^ a b c d e Bearn J, O'Brien M (2015). "Chapter Ten - "Addicted to Euphoria": The History, Clinical Presentation, and Management of Party Drug Misuse". In Taba P, Lees A, Sikk K (eds.). The Neuropsychiatric Complications of Stimulant Abuse. International Review of Neurobiology. Vol. 120. Academic Press. pp. 205–33. doi:10.1016/bs.irn.2015.02.005. ISBN 9780128029787. PMID 26070759. Eating, drinking, sexual activity and parenting invoke pleasure, an emotion that promotes repetition of these behaviors, are essential for survival. Euphoria, a feeling or state of intense excitement and happiness, is an amplification of pleasure, aspired to one's essential biological needs that are satisfied. People use party drugs as a shortcut to euphoria. Ecstasy (3,4-methylenedioxymethamphetamine), γ-hydroxybutyric acid, and ketamine fall under the umbrella of the term "party drugs," each with differing neuropharmacological and physiological actions. ^ Alcaro A, Panksepp J (2011). "The SEEKING mind: primal neuro-affective substrates for appetitive incentive states and their pathological dynamics in addictions and depression". Neuroscience and Biobehavioral Reviews. 35 (9): 1805–1820. doi:10.1016/j.neubiorev.2011.03.002. PMID 21396397. S2CID 6613696. Recent human data have demonstrated that the SEEKING brain circuitry, as predicted, is involved in the emergence of a characteristic appetitive affective state, which may be described as "enthusiastic positive excitement" or "euphoria" (Drevets et al., 2001; Volkow and Swanson, 2003) and that do not resemble any kind of sensory pleasure (Heath, 1996; Panksepp et al., 1985) ... However, in our view, cognitive processes, are only one "slice of the pie", and gamma oscillations may be more globally viewed as the overall emotional–motivational neurodynamics through which the SEEKING disposition is expressed, accompanied by a feeling of excitement/euphoria (not 'pleasure') that is evolutionarily designed to achieve a diversity of useful outcomes ^ "Key DSM-IV Mental Status Exam Phrases" (Content adapted from "Brain Calipers, 2nd Edition, David J. Robinson, MD".). Gateway Psychiatric Services. Mood and Affect. Archived from the original on 13 November 2013. Retrieved 17 February 2014. ^ a b c Cohen EE, Ejsmond-Frey R, Knight N, Dunbar RI (2010). "Rowers' high: behavioural synchrony is correlated with elevated pain thresholds". Biol. Lett. 6 (1): 106–8. doi:10.1098/rsbl.2009.0670. PMC 2817271. PMID 19755532. This heightened effect from synchronized activity may explain the sense of euphoria experienced during other social activities (such as laughter, music-making and dancing) that are involved in social bonding in humans and possibly other vertebrates. ^ a b c d e f g h i j k Malenka RC, Nestler EJ, Hyman SE (2009). Sydor A, Brown RY (eds.). Molecular Neuropharmacology: A Foundation for Clinical Neuroscience (2nd ed.). New York: McGraw-Hill Medical. pp. 191, 350–351, 367–368, 371–375. ISBN 9780071481274. Changes in appetite and energy may reflect abnormalities in various hypothalamic nuclei. Depressed mood and anhedonia (lack of interest in pleasurable activities) in depressed individuals, and euphoria and increased involvement in goal-directed activities in patients, who experience mania, may reflect opposing abnormalities in the nucleus accumbens, medial prefrontal cortex, amygdala, or other structures. ... Although short-term administration of glucocorticoids often produces euphoria and increased energy, the impact of long-lasting increases in endogenous glucocorticoids produced during depression can involve complex adaptations such as those that occur in Cushing syndrome (Chapter 10). ... Exposure to addictive chemicals not only produces extreme euphoric states that may initially motivate drug use, but also causes equally extreme adaptations in reinforcement mechanisms and motivated behavior that eventually lead to compulsive use. Accordingly, the evolutionary design of human and animal brains that has helped to promote our survival also has made us vulnerable to addiction. ^ Georgiadis JR, Kringelbach ML (July 2012). "The human sexual response cycle: brain imaging evidence linking sex to other pleasures" (PDF). Prog. Neurobiol. 98 (1): 49–81. doi:10.1016/j.pneurobio.2012.05.004. PMID 22609047. S2CID 3793929. Archived (PDF) from the original on 13 August 2016. Retrieved 13 November 2016 – via Hedonia. Strong feelings of pleasure and euphoria, as well as marked alterations in cognitive processing, self-referential thought, and physiological arousal are defining features of sexual consummation, especially during orgasm (Mah and Binik, 2001). ^ Blum K, Werner T, Carnes S, Carnes P, Bowirrat A, Giordano J, Oscar-Berman M, Gold M (March 2012). "Sex, drugs, and rock 'n' roll: hypothesizing common mesolimbic activation as a function of reward gene polymorphisms". Journal of Psychoactive Drugs. 44 (1): 38–55. doi:10.1080/02791072.2012.662112. PMC 4040958. PMID 22641964. Early-stage romantic love can induce euphoria, is a cross-cultural phenomenon, and is possibly a developed form of a mammalian drive to pursue preferred mates. ... Under normal conditions, it is not surprising that sexual activity is physiologically regulated by the reward circuitry of the brain, specifically by dopaminergic pathways (see Figure 1). Moreover, the early stages of a new, romantic relationship can be a powerful and absorbing experience. Individuals in new romantic relationships report feeling euphoric and energetic. They also become emotionally dependent on, desire closeness with, and have highly focused attention on their partner (Reynaud et al. 2010; Young 2009). Human neuroimaging studies have shown that feelings experienced during the early stages of a romantic relationship are associated with neural activations in several reward-system and affect-processing regions of the brain (Young 2009; Aron et al. 2005; Bartels & Zeki 2000; Mashek, Aron & Fisher 2000). ^ Jankowiak, William; Paladino, Thomas (2013). "Chapter 1. Desiring Sex, Longing for Love: A Tripartite Conundrum". In Jankowiak, William R. (ed.). Intimacies: Love and Sex Across Cultures. Columbia University Press. p. 13. ISBN 9780231508766 – via Google Books. These emotional states may also be manifested behaviorally as "labile psychophysical responses to the loved person, including exhilaration, euphoria, buoyancy, spiritual feelings, increased energy, sleeplessness, loss of appetite, shyness, awkwardness ... in the presence of the loved person" (Fisher 1998:32). The presence of similar neurological mechanisms and brain patterns may account for the ability to readily identify when someone is romantically involved or erotically excited (Fisher 1998:32; Fisher 1995). ^ Roache JD (2010). "Role of the Human Laboratory in the Development of Medications for Alcohol and Drug Dependence". In Johnson BA (ed.). Addiction Medicine: Science and Practice. Springer Science & Business Media. p. 133. ISBN 9781441903389 – via Google Books. It has been observed that drugs of abuse as diverse as alcohol, barbiturates, opiates, and psychomotor stimulants all share a profile of psychoactive effects characterized as euphoria. It is generally accepted that euphoria is at least a partial explanation why these drugs are abused. ^ a b Berridge KC, Kringelbach ML (May 2015). "Pleasure systems in the brain". Neuron (Review). 86 (3): 646–664. doi:10.1016/j.neuron.2015.02.018. PMC 4425246. PMID 25950633. ^ a b Castro, DC; Berridge, KC (24 October 2017). "Opioid and orexin hedonic hotspots in rat orbitofrontal cortex and insula". Proceedings of the National Academy of Sciences of the United States of America (Research article). 114 (43): E9125 – E9134. Bibcode:2017PNAS..114E9125C. doi:10.1073/pnas.1705753114. PMC 5664503. PMID 29073109. ^ a b Kringelbach ML, Berridge KC (2012). "The Joyful Mind" (PDF). Scientific American. 307 (2): 44–45. Bibcode:2012SciAm.307b..40K. doi:10.1038/scientificamerican0812-40. PMID 22844850. Archived (PDF) from the original on 29 March 2017. Retrieved 17 January 2017. So it makes sense that the real pleasure centers in the brain – those directly responsible for generating pleasurable sensations – turn out to lie within some of the structures previously identified as part of the reward circuit. One of these so-called hedonic hotspots lies in a subregion of the nucleus accumbens called the medial shell. A second is found within the ventral pallidum, a deep-seated structure near the base of the forebrain that receives most of its signals from the nucleus accumbens. ... On the other hand, intense euphoria is harder to come by than everyday pleasures. The reason may be that strong enhancement of pleasure – like the chemically induced pleasure bump we produced in lab animals – seems to require activation of the entire network at once. Defection of any single component dampens the high. Whether the pleasure circuit – and in particular, the ventral pallidum – works the same way in humans is unclear. ^ Liddell HG, Scott R (1940). A Greek-English Lexicon. Revised and augmented throughout by Sir Henry Stuart Jones, with the assistance of Roderick McKenzie. Oxford: Clarendon Press. Perseus – via Tufts University. ^ "Online Etymology Dictionary". Archived from the original on 21 December 2008. Retrieved 11 May 2008. ^ Kersey J, Phillips E (1706). The new world of words: or, Universal English dictionary. London: Printed for J. Phillips. pp. EU. ^ Laycock T (4 January 1862). The Medical Times & Gazette. London: John Churchill. pp. 1. Not unfrequently, indeed, the appearance of the patient is more diagnostic than his feelings. This is the case in some very grave diseases, in which that portion of the nervous system which subserves to the feeling of bodily well-being,—termed, in psychological phrase, euphoria—is morbidly modified as to function. • Laycock T (17 May 1864). The Medical Times & Gazette. London: John Churchill. pp. 500. The morbid hopefulness of phthisis, physiologically termed euphoria, is seen more particularly in this class of patients. I have often called attention to it at the bedside, and shown that it ushers in the last stage. It is really a disease of the nervous system of a low type, a sort of insanity, and is of the worst significance. ^ Freud S (1884). Über Coca., cited in, NIDA Research Monograph #13 Siegel RK (1977). "Chapter VI Cocaine: Recreational Use and Intoxication" (PDF). In Petersen RC, Stillman RC (eds.). NIDA Research Monograph #13. U.S. Government Printing Office. p. 130. The psychic effect (of cocaine) consists of exhilaration and lasting euphoria, which does not differ in any way from the normal euphoria of a healthy person.... One senses an increase of self-control and feels more vigorous and more capable of work; on the other hand, if one works, one misses the heightening of the mental powers which alcohol, tea, or coffee induce. One is simply normal, and soon finds it difficult to believe that one is under the influence of any drug at all.[permanent dead link] ^ Miller R, Dennison J (2015). "Lecture 31". An Outline of Psychiatry in Clinical Lectures: The Lectures of Carl Wernicke. Springer. p. 216. ISBN 9783319180519 – via Google books. [R]ational judgment of actual ability is lost, and a feeling of increased capacity arises, ... it induces feelings of happiness, to the point of abnormal euphoria; but here too, assuming that some degree of psychic ability prevails, self-awareness of the change in personality may be enabled—an autopsychic paraesthesia in the above sense. Consequently, the Affective state of abnormal euphoria which determines the clinical picture often shows up as transitions to autopsychic disarray. ^ "Paris Doctors Say That Scorching is Like Effects of Drugs". Paris Herald. 1903. reprinted in The Boston Daily Globe, 13 May 1903. p. 6 ^ "Have You Euphoria?". Popular Science. 97 (6): 79. December 1920 – via Google books. It takes a doctor to give a high-sounding name to a well known phenomenon. "Euphoria" means "feeling fit." It is as much a physiological fact as scarlet fever. Nature makes it worth while to be alive simply through euphoria. The joy of making a good tennis stroke, the delight that a Woodsman gets in the open air, the artist's rhapsody—all are due to euphoria. Why do we drink alcohol—when we can get it or smoke tobacco? To affect euphoria. When a lunatic thinks that he is Napoleon and demands the homage due an emperor; he has euphoria in its worst form. Too little is known about euphoria. Since it can be affected by drugs and chemicals, who knows but it may have its seat in some gland? ^ Woodworth, RS (1921). "Chapter VII: Emotion: Various organic states, and the conscious states that go with them". Psychology, a study of mental life. New York: Henry Holt and Company. pp. 119–120. Retrieved 16 April 2017 – via Internet archive. Something was said before about "organic states", under the general head of tendencies to reaction. Fatigue was an example. Now we could include fatigue under the term, "stirred-up state of the organism"; at least, if not precisely "stirred-up", it is uneasy. It is a deviation from the normal or neutral state. Also, it is often a conscious state, as when we speak of the "tired feeling"; not a purely cognitive state, either not simply a recognition of the fact that we are fatigued but a state of disinclination to work any longer. Though fatigue is thus so much like an emotion that it fits under our definition, it is not called an emotion, but a sensation or complex of sensations.... Many other organic states are akin to emotion in the same way. The opposite of fatigue, the "warmed-up" condition, brought on by a certain amount of activity after rest, is a case in point. It is a deviation from the average or neutral condition, in the direction of greater readiness for activity. The warmed-up person feels ready for business, full of "ginger" or "pep" in short, full of life. The name "euphoria", which means about the same as "feeling good", is given to this condition. Drowsiness is another of these emotion-like states; but hunger and thirst are as typical examples as any. ^ Bousfield WA (1940). "The Relation of the Euphoric Attitude to the Quality of Sleep". The Journal of Psychology. 9 (2): 393–401. doi:10.1080/00223980.1940.9917707. Euphoria is a term aptly denoting the state of general well being, and while it involves a relatively enduring and pleasantly toned feeling, its psychological significance derives primarily from its being a semi-emotional attitude of considerable determining power. ^ Keats AS, Beecher HK (1952). "Analgesic activity and toxic effects of acetylmethadol isomers in man". The Journal of Pharmacology and Experimental Therapeutics. 105 (2): 210–215. doi:10.1016/S0022-3565(25)05029-3. ISSN 0022-3565. PMID 14928223. Archived from the original on 22 September 2016. Retrieved 17 September 2016. [Footnote 3] Since matters of some interest hang upon the definition of 'euphoria', direct enquiry of Dr. Isbell brought the following comment (letter of November 1, 1951). 'I think it would be wise to exercise a certain degree of care in our use of the term "euphoria". We use it here in the sense of a train of effects similar to those seen after the administration of morphine. These effects include changes in behavior and objective signs, such as constriction of the pupil, depression of the respiratory rate and volume, drop in rectal temperature, etc. We do not use it in the sense of "feeling of well-being", as this is something that I have been utterly unable to evaluate.' The present authors prefer to limit the definition of euphoria to 'a sense of well-being'. • Isbell H, Vogel VH (1949). "The addiction liability of methadon (amidone, dolophine, 10820) and its use in the treatment of the morphine abstinence syndrome". The American Journal of Psychiatry. 105 (12): 909–914. doi:10.1176/ajp.105.12.909. ISSN 0002-953X. PMID 18127077. • Jaffe JH, Jaffe FK (1989). "4. Historical Perspectives on the Use of Subjective Effects Measures in Assessing the Abuse Potential of Drugs". In Fischman MW, Mello NK (eds.). Testing for Abuse Liability of Drugs in Humans. National Institute on Drug Abuse Research Monograph Series. Vol. 92. Rockville, MD: National Institute on Drug Abuse. ^ Cahal DA (1957). "Analgesic activity of dipipanone hydrochloride in student volunteers". British Journal of Pharmacology and Chemotherapy. 12 (1): 97–99. doi:10.1111/j.1476-5381.1957.tb01368.x. ISSN 0366-0826. PMC 1509651. PMID 13413158. Not all of these effects can be regarded as undesirable. Drowsiness, euphoria, sleep, and 'detachment,' for instance, are effects which enhance the value of a major analgesic. ^ Leigh D, Pare CM, Marks J (1977). A Concise Encyclopaedia of Psychiatry. Springer Science & Business Media. p. 152. ISBN 9789401159135 – via Google books. A mood of contentment and wellbeing. Euphoria in psychiatric terms always has a pathological connotation and is often an important early sign of organic cerebral disease. It differs from elation in subtle but important ways. It has no infectious quality and no element of gaiety, for its bland contentment is based on lack of awareness and inability to experience sadness or anxiety rather than on anything positive. It may be seen in any condition involving extensive cerebral damage, particularly if the frontal lobes are involved. It occurs sooner or later in senile and arteriosclerotic dementias (q.v.), in disseminated sclerosis and in Huntington's chorea (q.v.) and is often seen also after severe head injury and old-fashioned forms of leucotomy (q.v.). Euphoria is sometimes seen in Addison's disease (q.v.). ^ "definition of euphoria in English". Oxford Dictionaries. Archived from the original on 28 July 2016. Retrieved 16 December 2016. a feeling or state of intense excitement and happiness • "definition of euphoria". Dictionary.com. Archived from the original on 29 December 2016. Retrieved 16 December 2016. a state of intense happiness and self-confidence (psychology) a feeling of happiness, confidence, or well-being sometimes exaggerated in pathological states as mania • Sadock B, Sadock V (2009). Kaplan and Sadock's Comprehensive Textbook of Psychiatry (9th ed.). pp. 411–412, 923. Refers to a persistent and unrealistic sense of well-being, without the increased mental or motor rate of mania. Exaggerated feeling of well-being that is inappropriate to real events. Can occur with drugs such as opiates, amphetamines, and alcohol. • Mosby's Medical Dictionary (8th ed.). 2009. Archived from the original on 2 July 2017. Retrieved 29 December 2016. 1. a feeling or state of well-being or elation. 2. an exaggerated or abnormal sense of physical and emotional well-being not based on reality or truth, disproportionate to its cause, and inappropriate to the situation, as commonly seen in the manic stage of bipolar disorder, some forms of schizophrenia, organic mental disorders, and toxic and drug-induced states ^ Schultz W (2015). "Neuronal reward and decision signals: from theories to data". Physiological Reviews. 95 (3): 853–951. doi:10.1152/physrev.00023.2014. PMC 4491543. PMID 26109341. The feeling of high that is experienced by sports people during running or swimming, the lust evoked by encountering a ready mating partner, a sexual orgasm, the euphoria reported by drug users, and the parental affection to babies constitute different forms (qualities) rather than degrees of pleasure (quantities). ^ Cunha GS, Ribeiro JL, Oliveira AR (June 2008). "[Levels of beta-endorphin in response to exercise and overtraining]". Arq Bras Endocrinol Metabol (in Portuguese). 52 (4): 589–598. doi:10.1590/S0004-27302008000400004. hdl:10183/40053. PMID 18604371. ^ Boecker H, Sprenger T, Spilker ME, Henriksen G, Koppenhoefer M, Wagner KJ, Valet M, Berthele A, Tolle TR (2008). "The runner's high: opioidergic mechanisms in the human brain". Cereb. Cortex. 18 (11): 2523–2531. doi:10.1093/cercor/bhn013. PMID 18296435. The runner's high describes an euphoric state resulting from long-distance running. ^ Raichlen DA, Foster AD, Gerdeman GL, Seillier A, Giuffrida A (2012). "Wired to run: exercise-induced endocannabinoid signaling in humans and cursorial mammals with implications for the 'runner's high'". J. Exp. Biol. 215 (Pt 8): 1331–1336. Bibcode:2012JExpB.215.1331R. doi:10.1242/jeb.063677. PMID 22442371. S2CID 5129200. ^ Cohen EE, Ejsmond-Frey R, Knight N, Dunbar RI (2010). "Rowers' high: behavioural synchrony is correlated with elevated pain thresholds". Biol. Lett. 6 (1): 106–108. doi:10.1098/rsbl.2009.0670. PMC 2817271. PMID 19755532. ^ Friedman, Danielle (30 July 2024). "How to Optimize Your Workout to Boost Your Mood". The New York Times. ISSN 0362-4331. Retrieved 29 January 2025. ^ a b Salimpoor VN, Benovoy M, Larcher K, Dagher A, Zatorre RJ (2011). "Anatomically distinct dopamine release during anticipation and experience of peak emotion to music". Nat. Neurosci. 14 (2): 257–262. doi:10.1038/nn.2726. PMID 21217764. S2CID 205433454. Music, an abstract stimulus, can arouse feelings of euphoria and craving, similar to tangible rewards that involve the striatal dopaminergic system. ... the caudate was more involved during the anticipation and the nucleus accumbens was more involved during the experience of peak emotional responses to music. ... Notably, the anticipation of an abstract reward can result in dopamine release in an anatomical pathway distinct from that associated with the peak pleasure itself. ^ a b c Mavridis IN (March 2015). "Music and the nucleus accumbens". Surg Radiol Anat. 37 (2): 121–125. doi:10.1007/s00276-014-1360-0. PMID 25102783. S2CID 25768771. The functional connectivity between brain regions mediating reward, autonomic and cognitive processing provides insight into understanding why listening to music is one of the most rewarding and pleasurable human experiences. Musical stimuli can significantly increase extracellular DA levels in the NA. NA DA and serotonin were found significantly higher in animals exposed to music. Finally, passive listening to unfamiliar although liked music showed activations in the NA. ... Music can arouse feelings of euphoria and craving, similar to tangible rewards that involve the striatal DAergic system [16]. Reward value for music can be coded by activity levels in the NA, whose functional connectivity with auditory and frontal areas increases as a function of increasing musical reward [19]. ... Listening to pleasant music induces a strong response and significant activation of the VTA-mediated interaction of the NA with the hypothalamus, insula and orbitofrontal cortex [1].ConclusionsListening to music strongly modulates activity in a network of mesolimbic structures involved in reward processing including the NA. Music, acting as a positive pleasant emotion, increases NA DAergic activity. Specifically the NA is more involved during the experience of peak emotional responses to music. Reward value of music can be predicted by increased functional connectivity of auditory cortices, amygdala and ventromedial prefrontal regions with the NA. Further research is needed to improve our understanding of the NA role in the influence of music in our lives. ^ a b c Zatorre RJ (March 2015). "Musical pleasure and reward: mechanisms and dysfunction". Ann. N. Y. Acad. Sci. 1337 (1): 202–211. Bibcode:2015NYASA1337..202Z. doi:10.1111/nyas.12677. PMID 25773636. S2CID 22212386. Archived from the original on 19 October 2019. Retrieved 19 October 2019. Most people derive pleasure from music. Neuroimaging studies show that the reward system of the human brain is central to this experience. Specifically, the dorsal and ventral striatum release dopamine when listening to pleasurable music, and activity in these structures also codes the reward value of musical excerpts. Moreover, the striatum interacts with cortical mechanisms involved in perception and valuation of musical stimuli. ... Development of a questionnaire for music reward experiences has allowed the identification of separable factors associated with musical pleasure, described as music-seeking, emotion-evocation, mood regulation, sensorimotor, and social factors. Applying this questionnaire to a large sample uncovered approximately 5% of the population with low sensitivity to musical reward in the absence of generalized anhedonia or depression. Further study of this group revealed that there are individuals who respond normally both behaviorally and psychophysiologically to rewards other than music (e.g., monetary value) but do not experience pleasure from music despite normal music perception ability and preserved ability to identify intended emotions in musical passages. ^ a b Ferreri L, Mas-Herrero E, Zatorre RJ, Ripollés P, Gomez-Andres A, Alicart H, Olivé G, Marco-Pallarés J, Antonijoan RM, Valle M, Riba J, Rodriguez-Fornells A (January 2019). "Dopamine modulates the reward experiences elicited by music". Proceedings of the National Academy of Sciences of the United States of America. 116 (9): 3793–3798. Bibcode:2019PNAS..116.3793F. doi:10.1073/pnas.1811878116. PMC 6397525. PMID 30670642. Listening to pleasurable music is often accompanied by measurable bodily reactions such as goose bumps or shivers down the spine, commonly called "chills" or "frissons." ... Overall, our results straightforwardly revealed that pharmacological interventions bidirectionally modulated the reward responses elicited by music. In particular, we found that risperidone impaired participants' ability to experience musical pleasure, whereas levodopa enhanced it. ... Here, in contrast, studying responses to abstract rewards in human subjects, we show that manipulation of dopaminergic transmission affects both the pleasure (i.e., amount of time reporting chills and emotional arousal measured by EDA) and the motivational components of musical reward (money willing to spend). These findings suggest that dopaminergic signaling is a sine qua non condition not only for motivational responses, as has been shown with primary and secondary rewards, but also for hedonic reactions to music. This result supports recent findings showing that dopamine also mediates the perceived pleasantness attained by other types of abstract rewards (37) and challenges previous findings in animal models on primary rewards, such as food (42, 43). ^ a b Goupil L, Aucouturier JJ (February 2019). "Musical pleasure and musical emotions". Proceedings of the National Academy of Sciences of the United States of America. 116 (9): 3364–3366. Bibcode:2019PNAS..116.3364G. doi:10.1073/pnas.1900369116. PMC 6397567. PMID 30770455. In a pharmacological study published in PNAS, Ferreri et al. (1) present evidence that enhancing or inhibiting dopamine signaling using levodopa or risperidone modulates the pleasure experienced while listening to music. ... In a final salvo to establish not only the correlational but also the causal implication of dopamine in musical pleasure, the authors have turned to directly manipulating dopaminergic signaling in the striatum, first by applying excitatory and inhibitory transcranial magnetic stimulation over their participants' left dorsolateral prefrontal cortex, a region known to modulate striatal function (5), and finally, in the current study, by administrating pharmaceutical agents able to alter dopamine synaptic availability (1), both of which influenced perceived pleasure, physiological measures of arousal, and the monetary value assigned to music in the predicted direction. ... While the question of the musical expression of emotion has a long history of investigation, including in PNAS (6), and the 1990s psychophysiological strand of research had already established that musical pleasure could activate the autonomic nervous system (7), the authors' demonstration of the implication of the reward system in musical emotions was taken as inaugural proof that these were veridical emotions whose study has full legitimacy to inform the neurobiology of our everyday cognitive, social, and affective functions (8). Incidentally, this line of work, culminating in the article by Ferreri et al. (1), has plausibly done more to attract research funding for the field of music sciences than any other in this community.The evidence of Ferreri et al. (1) provides the latest support for a compelling neurobiological model in which musical pleasure arises from the interaction of ancient reward/valuation systems (striatal–limbic–paralimbic) with more phylogenetically advanced perception/predictions systems (temporofrontal). ^ Goldstein A, Hansteen RW (1977). "Evidence against involvement of endorphins in sexual arousal and orgasm in man". Archives of General Psychiatry. 34 (10): 1179–1180. doi:10.1001/archpsyc.1977.01770220061006. PMID 199128. ^ "Methamphetamine | InfoFacts | The National Institute on Drug Abuse (NIDA)". Archived from the original on 28 September 2011. Retrieved 28 September 2011. ^ "Merrian-Webster definition". Archived from the original on 7 January 2015. Retrieved 18 February 2015. ^ Cox S, Ullah M, Zoellner H (2016). "Oral and Systemic Health Effects of Compulsive Areca Nut Use". In Preedy VR (ed.). Neuropathology of Drug Addictions and Substance Misuse Volume 3: General Processes and Mechanisms, Prescription Medications, Caffeine and Areca, Polydrug Misuse, Emerging Addictions and Non-Drug Addictions. Academic Press. p. 791. ISBN 9780128006771. The areca nut is the fourth most used drug after nicotine, alcohol, and caffeine. The effects are described as pleasurable and generally stimulating, inducing a sense of well-being, euphoria, heightened alertness, a warm sensation throughout the body, and an increased capacity to work. ^ a b Garg A, Chaturvedi P, Gupta PC (June 2014). "A review of the systemic adverse effects of areca nut or betel nut". Indian Journal of Medical and Paediatric Oncology. 35 (1): 3–9. doi:10.4103/0971-5851.133702. PMC 4080659. PMID 25006276. It is one of the most widely consumed addictive substances in the world after nicotine, ethanol and caffeine, and is consumed by approximately 10% of the world's population.... The users of areca nut believe that it is helpful for the digestive system and has mild euphoric effects. ... The major parasympathetic and muscarinic effects of areca nut are due to arecoline. ^ Sharan RN, Mehrotra R, Choudhury Y, Asotra K (August 2012). "Association of Betel Nut with Carcinogenesis: Revisit with a Clinical Perspective". PLOS ONE. 7 (8): e42759. Bibcode:2012PLoSO...742759S. doi:10.1371/journal.pone.0042759. ISSN 1932-6203. PMC 3418282. PMID 22912735. ^ Riviere JE, Papich MG (2013). Veterinary Pharmacology and Therapeutics. John Wiley & Sons. p. 165. ISBN 9781118685907. Pilocarpine, arecoline and muscarine are rather selective parasympathetic agents; i.e., their cholinomimetic activity is exerted primarily at muscarinic sites with minimal nicotinic effects. ^ Liu YJ, Peng W, Hu MB, Xu M, Wu CJ (November 2016). "The pharmacology, toxicology and potential applications of arecoline: a review". Pharmaceutical Biology. 54 (11): 2753–2760. doi:10.3109/13880209.2016.1160251. ISSN 1744-5116. PMID 27046150. ^ Peng W, Liu YJ, Wu N, Sun T, He XY, Gao YX, Wu CJ (April 2015). "Areca catechu L. (Arecaceae): a review of its traditional uses, botany, phytochemistry, pharmacology and toxicology". Journal of Ethnopharmacology. 164: 340–56. doi:10.1016/j.jep.2015.02.010. ISSN 1872-7573. PMID 25681543. Previous investigations indicated that the arecaidine and guvacine isolated from the A. catechu are effective antagonists of GABA, with IC50 values 122712 μM and 871 μM, respectively (Johnston et al., 1975; Lodge et al., 1977). ^ Arif A, Westermeyer J (2012). Manual of Drug and Alcohol Abuse: Guidelines for Teaching in Medical and Health Institutions. New York: Springer Science & Business Media. pp. 159–160. ISBN 9781461595168. ^ Aronson, J. K. (2009). Meyler's Side Effects of Herbal Medicines. Elsevier. p. 53. ISBN 9780444532695. The lime in the betel quid [areca nut, lime and Piper betle leaves] causes hydrolysis of arecoline to arecailide, a central nervous stimulant, which accounts, together with the essential oil of the betel pepper, for the eucphoric effects of chewing betel quid. ^ Gilman JM, Ramchandani VA, Davis MB, Bjork JM, Hommer DW (2008). "Why we like to drink: a functional magnetic resonance imaging study of the rewarding and anxiolytic effects of alcohol". J. Neurosci. 28 (18): 4583–4591. doi:10.1523/JNEUROSCI.0086-08.2008. PMC 2730732. PMID 18448634. ^ Morgan CJ, Badawy AA (2001). "Alcohol-induced euphoria: exclusion of serotonin". Alcohol and Alcoholism. 36 (1): 22–25. doi:10.1093/alcalc/36.1.22. PMID 11139411. ^ Busardò FP, Jones AW (2015). "GHB Pharmacology and Toxicology: Acute Intoxication, Concentrations in Blood and Urine in Forensic Cases and Treatment of the Withdrawal Syndrome". Current Neuropharmacology. 13 (1): 47–70. doi:10.2174/1570159X13666141210215423. ISSN 1570-159X. PMC 4462042. PMID 26074743. ^ a b Mack AH, Brady KT, Miller SI, Frances RJ (2016). Clinical Textbook of Addictive Disorders, Fourth Edition. Guilford Publications. p. 249. ISBN 9781462521708. ^ McCuistion LE, Kee JL, Hayes ER (2014). Pharmacology: A Patient-Centered Nursing Process Approach. Elsevier Health Sciences. p. 54. ISBN 9780323293488. ^ Doweiko HE (2014). Concepts of Chemical Dependency. Cengage Learning. p. 79. ISBN 9781285457178. ^ Galizio M, Maisto SA (2013). Determinants of Substance Abuse: Biological, Psychological, and Environmental Factors. Springer Science & Business Media. p. 205. ISBN 9781475799903. ^ Psychotropic Agents: Part III: Alcohol and Psychotomimetics, Psychotropic Effects of Central Acting Drugs. Springer Science & Business Media. 2012. p. 420. ISBN 9783642677700. ^ McCrady, Barbara S.; Epstein, Elizabeth E. (2013). Addictions: A Comprehensive Guidebook. OUP USA. p. 163. ISBN 9780199753666. ^ Ruiz P, Strain EC (2011). Lowinson and Ruiz's Substance Abuse: A Comprehensive Textbook. Lippincott Williams & Wilkins. p. 258. ISBN 9781605472775. ^ Staats PS, Silverman SM (2016). Controlled Substance Management in Chronic Pain: A Balanced Approach. Springer. p. 77. ISBN 9783319309644. ^ a b c Martinotti G, Papazisis G, Santacroce R, Kouvelas D, Cinosi E, Lupi M, di Giannantonio M (2016). "Pregabalin Abuse and Addiction". In Preedy VR (ed.). Neuropathology of Drug Addictions and Substance Misuse Volume 3: General Processes and Mechanisms, Prescription Medications, Caffeine and Areca, Polydrug Misuse, Emerging Addictions and Non-Drug Addictions. London: Academic Press. pp. 948–949. ISBN 9780128006771. Exceeding the therapeutic doses, pregabalin is described as an 'ideal psychotropic drug' for recreational purposes, including alcohol/GHB/benzodiazepine-like effects, euphoria, entactogenic feelings, and dissociation. ... Up to 1200mg ... euphoria ... Over 1500mg ... intense euphoria ^ a b Schjerning O, Rosenzweig M, Pottegård A, Damkier P, Nielsen J (January 2016). "Abuse Potential of Pregabalin: A Systematic Review" (PDF). CNS Drugs. 30 (1): 9–25. doi:10.1007/s40263-015-0303-6. ISSN 1179-1934. PMID 26767525. S2CID 3800377. Archived (PDF) from the original on 13 August 2017. Retrieved 29 April 2017. Pregabalin is, in some cases, used for recreational purposes and it has incurred attention among drug abusers for causing euphoric and dissociative effects when taken in doses exceeding normal therapeutic dosages or used by alternative routes of administration, such as nasal insufflation or venous injection. ^ "Lyrica". Drugs.com. Archived from the original on 13 August 2017. Retrieved 20 August 2016. ^ a b Smith RV, Havens JR, Walsh SL (2016). "Gabapentin misuse, abuse, and diversion: A systematic review". Addiction. 111 (7): 1160–1174. doi:10.1111/add.13324. PMC 5573873. PMID 27265421. Several case studies mentioned experiencing euphoria after gabapentin misuse that was reminiscent of, but not as strong as, opioids. This feeling was achieved in combination with other drugs (e.g., buprenorphine/naloxone, methadone, baclofen, quetiapine, alcohol) as well as by using gabapentin alone, in dosages ranging from 1500–12000 mg, though only three articles give actual amounts misused. ^ Rossi, S, ed. (July 2017). "Ethosuximide". Australian Medicines Handbook. Adelaide, Australia: Australian Medicines Handbook Pty Ltd. Retrieved 12 August 2017. ^ Rossi, S, ed. (July 2017). "Perampanel". Australian Medicines Handbook. Adelaide, Australia: Australian Medicines Handbook Pty Ltd. Retrieved 12 August 2017. ^ a b Hawkins KL, Gidal BE (December 2017). "When adverse effects are seen as desirable: Abuse potential of the newer generation antiepileptic drugs". Epilepsy Behav. 77: 62–72. doi:10.1016/j.yebeh.2017.10.007. PMID 29111505. ^ Huang C, Johnson N (2016). "Nitrous Oxide, From the Operating Room to the Emergency Department". Current Emergency and Hospital Medicine Reports. 4: 16. doi:10.1007/s40138-016-0092-3. ISSN 2167-4884. PMC 4819505. PMID 27073749. The term 'laughing gas' is a common layman's term for nitrous oxide, given its ability to create a sense of euphoria in the user. In addition, as noted earlier, it has an opioid-like effect, which accounts for its analgesic properties. ^ "Drug Pleasure Ratings | Global Drug Survey". ^ Volkow ND, Michaelides M, Baler R (October 2019). "The Neuroscience of Drug Reward and Addiction". Physiol Rev. 99 (4): 2115–2140. doi:10.1152/physrev.00014.2018. PMC 6890985. PMID 31507244. ^ Jones JD, Arout CA, Luba R, Murugesan D, Madera G, Gorsuch L, Schusterman R, Martinez S (July 2024). "The influence of drug class on reward in substance use disorders". Pharmacol Biochem Behav. 240: 173771. doi:10.1016/j.pbb.2024.173771. PMC 11162950. PMID 38670466. ^ Tzschentke TM (September 2007). 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The side effects of Gaboxadol have, however, been described as mild and similar in quality to those of other GABA-mimetics (Hoehn-Saric, 1983). This combination of analgesic and anxiolytic effects of THIP obviously has therapeutic prospects. ^ Schoedel KA, Rosen LB, Alexander R, Wang J, Snavely D, Murphy MG, Chodakewitz J, Mengel H, Romach MK, Sellers EM (16 January 2009). "Poster Session I (PI 1-89): PI-44: A single-dose randomized, double-blind, crossover abuse liability study to evaluate the subjective and objective effects of gaboxadol and zolpidem in recreational drug users". Clinical Pharmacology & Therapeutics. 85 (S1 [Supplement: Abstracts of the 2009 Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics. National Harbor, Maryland, USA. March 18–21, 2009]): S9–S36 (S22–S22). doi:10.1038/sj.clpt.2008.283. ISSN 0009-9236. ^ Kalman D (February 2002). 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Archived (PDF) from the original on 19 July 2018. Retrieved 14 November 2018. ^ a b "Bipolar and Related Disorders". Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (5th ed.). American Psychiatric Association. 2013. ISBN 9780890425572. ^ a b Ruggero CJ, Kotov R, Watson D, Kilmer JN, Perlman G, Liu K (June 2014). "Beyond a single index of mania symptoms: structure and validity of subdimensions". J. Affect. Disord. 161: 8–15. doi:10.1016/j.jad.2014.02.044. PMID 24751301. ^ Dahl J, Lundgren TL (2007). "Conditioning mechanisms, behavior technology, and contextual behavior therapy". In Holmes GL, Schachter SC, Kasteleijn-Nolst Trenite DG (eds.). Behavioral Aspects of Epilepsy: Principles and Practice. Demos Medical Publishing. p. 248. ISBN 9781934559888. [S]eizures themselves may be stimulating or may induce euphoria. Dostoyevsky describes his seizure experience as follows 'the air was filled with a big noise and I tried to move. I felt the heaven was going down upon the earth and that it had engulfed me. I have really touched God. He came into me myself. Yes, God exists. I cried, and I don't remember anything else. You all, healthy people ... can't imagine the happiness we epileptics feel during the second before our fit ... I don't know if this felicity lasts for seconds, hours, or months but believe me, for all the joys that life may bring, I would not exchange this one'. [emphasis added] ^ Kanner AM (2011). "Peri-ictal psychiatric phenomena". In Trimble MR, Schmitz B (eds.). The Neuropsychiatry of Epilepsy. Cambridge University Press. p. 57. ISBN 9781139497893. The classic expression of an ictal psychiatric symptom is an "aura," presenting as feelings of fear, sadness, or euphoria. ^ Gschwind M, Picard F (January 2016). "Ecstatic Epileptic Seizures: A Glimpse into the Multiple Roles of the Insula". Frontiers in Behavioral Neuroscience. 10: 21. doi:10.3389/fnbeh.2016.00021. PMC 4756129. PMID 26924970. In a table listing cases of ecstatic seizures reported in the literature, descriptions include: "Euphoric and talkative", "calm euphoria", "Pleasant feeling, euphoria", "Pleasant feeling, and feels euphoria", "short euphoric states"; others are within the definition of euphoria: "Sudden feeling of extreme well-being", "Ineffable joy. Intense pleasure without match in reality (perhaps music)", "Extreme happiness", "intense (non-sexual) pleasure", "Intense happy feeling", "Sudden indescribably pleasant and joyous feeling", "Sensation of intense well-being", "Intense pleasant feeling", "Intense feelings of bliss and well-being". ^ Picard F, Friston K (September 2014). "Predictions, perception, and a sense of self". Neurology. 83 (12): 1112–8. doi:10.1212/WNL.0000000000000798. ISSN 0028-3878. PMC 4166359. PMID 25128179. ^ Devinsky O, Lai G (May 2008). "Spirituality and religion in epilepsy". Epilepsy & Behavior. 12 (4): 636–643. doi:10.1016/j.yebeh.2007.11.011. ISSN 1525-5050. PMID 18171635. S2CID 8768458. ^ Levenson JL, ed. (2011). "Neurology and Neurosurgery". The American Psychiatric Publishing Textbook of Psychosomatic Medicine: Psychiatric Care of the Medically Ill. American Psychiatric Publishing. p. 777. ISBN 9781585623792. ^ Mulu M (2010). "The Interictal Dysphoric Disorder of Epilepsy". In Miyoshi K, Morimura Y, Maeda K (eds.). Neuropsychiatric Disorders. Springer Science & Business Media. pp. 106–107. ISBN 9784431538714. ^ Engel J (2013). Seizures and Epilepsy. Oxford University Press. pp. 332, 383. ISBN 9780195328547. Archived from the original on 23 April 2017. Retrieved 23 April 2017. Patients who are aware of increased depression or tension prior to generalized tonic-clonic or limbic seizures occasionally report a feeling of euphoria or release during the postictal period.... [P]atients with interictal or preictal depression can report relief or euphoria postictally, which is consistent with the well-known beneficial effect of electroconvulsive shock therapy (ECT). Postictal hypomania can occur, particularly after repeated limbic seizures. ^ a b Dodick DW, Silberstein SD (2016). Migraine (3rd ed.). Oxford University Press. pp. 2, 15. ISBN 9780199793693. More than 70% of migraineurs experience premonitory phenomena hours to days before headache onset. Psychological symptoms include anxiety, depression, euphoria, irritability, restlessness, mental slowness, hyperactivity, fatigue, and drowsiness. Following the headache, the patient may have impaired concentration or feel tired, washed out, irritable, and listless. Some people, however, feel unusually refreshed or euphoric after an attack. [emphasis added] ^ Green MW, Colman R (2015). "6. Complicated Migraine". In Diamond S (ed.). Headache and Migraine Biology and Management. Academic Press. p. 51. ISBN 9780128011621. [P]remonitory symptoms can occur hours to a day or more prior to a migraine attack (with or without aura). Prodromal symptoms include various combinations of fatigue, stiff neck, sensitivity to light or sounds, difficulty in concentrating, depression or euphoria, cold hands and feet, blurred vision, yawning, nausea and pallor. [emphasis added] ^ a b Walling AD (2013). "63. Headache". In Taylor RB (ed.). Family Medicine: Principles and Practice (6th ed.). Springer Science & Business Media. p. 532. ISBN 9780387217444. Patients in the 'classic' subgroup (approximately 20% of all migraineurs) experience a characteristic aura before the onset of migraine head pain.... A much larger proportion of patients describe prodromal symptoms, which may be visceral, such as diarrhea or nausea, but are more commonly alterations in mood or behavior. Food cravings, mild euphoria (conversely, yawning), and heightened sensory perception, particularly of smell, are surprisingly common.... The attack often terminates with sleep.... Many patients report a 'hangover' on waking after a migraine, but others report complete freedom from symptoms and a sense of euphoria. [emphasis added] ^ Haussleiter IS, Brüne M, Juckel G (January 2009). "Psychopathology in multiple sclerosis: diagnosis, prevalence and treatment". Ther. Adv. Neurol. Disord. 2 (1): 13–29. doi:10.1177/1756285608100325. PMC 3002616. PMID 21180640. ^ Romano S, Nocentini U (2012). "Euphoria, Pathological Laughing and Crying". In Nocentini U, Caltagirone C, Tedeschi G (eds.). Neuropsychiatric Dysfunction in Multiple Sclerosis. Springer Science & Business Media. ISBN 9788847026766. ^ Ashley, Florence; Ells, Carolyn (2 December 2018). "In Favor of Covering Ethically Important Cosmetic Surgeries: Facial Feminization Surgery for Transgender People" (PDF). The American Journal of Bioethics. 18 (12): 23–25. doi:10.1080/15265161.2018.1531162. ISSN 1526-5161. PMID 31159694. S2CID 81006262. ^ Jones, Tiffany (2023). Euphorias in gender, sex and sexuality variations : positive experiences. Cham, Switzerland. ISBN 978-3-031-23756-0. OCLC 1371240775.{{cite book}}: CS1 maint: location missing publisher (link) The dictionary definition of euphoria at Wiktionary Retrieved from " 2Psychoactive drug Not to be confused with tusi, a recreational drug in pink-dyed powder form that contains a mixture of different drugs. Pharmaceutical compound 2C-B2C-B structure3D representation of a 2C-B moleculeClinical dataOther names4-Bromo-2,5-dimethoxyphenethylamine; 2,5-Dimethoxy-4-bromophenethylamine; Nexus; Venus; Bromo; Bees; Erox; Synergy; Performax; Toonies[1]Routes ofadministrationBy mouth, insufflation, rectalDrug classSerotonergic psychedelic; Hallucinogen; Serotonin 5-HT2A receptor agonistATC codeNoneLegal statusLegal status AU: S9 (Prohibited substance) BR: Class F2 (Prohibited psychotropics) CA: Schedule III DE: Anlage I (Authorized scientific use only) UK: Class A US: Schedule I UN: Psychotropic Schedule II Pharmacokinetic dataMetabolismLiver (MAO and CYP450)[5][1]MetabolitesBDMPE, BDMPAA, BDMBA, and others[2]Onset of actionOral: 20–90 min[2]Elimination half-life1.2–2.5 hours[3][4]Duration of actionOral: 2–8 hours[5][2][1]ExcretionUrine[2][1]Identifiers IUPAC name 2-(4-Bromo-2,5-dimethoxyphenyl)ethanamine CAS Number66142-81-2PubChem CID98527DrugBankDB01537ChemSpider88978UNIIV77772N32HKEGGC22775ChEBICHEBI:189669ChEMBLChEMBL292821CompTox Dashboard (EPA)DTXSID10216332 ECHA InfoCard100.164.088 Chemical and physical dataFormulaC10H14BrNO2Molar mass260.131 g·mol−13D model (JSmol)Interactive image SMILES COc1cc(CCN)c(OC)cc1Br

InChI InChI=1S/C10H14BrNO2/c1-13-9-6-8(11)10(14-2)5-7(9)3-4-12/h5-6H,3-4,12H2,1-2H3Key:YMHOBZXQZVXHBM-UHFFFAOYSA-N 2C-B, also known as 4-bromo-2,5-dimethoxyphenethylamine or by the slang name Nexus, is a synthetic psychedelic drug of the 2C family, mainly used as a recreational drug.[2][1][6] It was first synthesized by Alexander Shulgin in 1974 for use in psychotherapy. To date, there is limited scientific information regarding the drug's pharmacokinetics and pharmacological effects in humans. The existing studies primarily classify 2C-B as a stimulant and hallucinogen, and less commonly an entactogen.[7] 2C-B is also known by a number of slang names and appears on the illicit market in multiple forms:[8][9] as a powder, in capsules or pills. For recreational use, the substance is generally consumed orally or nasally. 1000mg of 2C-B 2C-B became briefly popular in the United States as substitute for the street drug ecstasy (MDMA) when the latter became illegal in 1985.[10] Many 2C-B users are young adults who attend raves.[8] Although 2C-B is still used in the rave subculture (commonly mistaken for and/or sold as ecstasy), more knowledgeable use has become more widespread in the 2000s.[11] There are claims that 2C-B was used as entheogen by the Sangoma, Nyanga, and Amagqirha people in place of their traditional plants; they refer to the chemical as Ubulawu Nomathotholo, which roughly translates to "Medicine of the Singing Ancestors".[12][13][14] In Shulgin's book PiHKAL, the oral dosage range is listed as 12 to 24 mg.[15] The common oral recreational dose per Erowid is around 15 to 25 mg.[16] Shulgin and others describe 2C-B as having a steep dose-response curve, such that a small increase in dose can result in an unexpectedly large increase in effects.[15][17] 2C-B dosage[citation needed] Oral Insufflated ED50 10 mg 4–6 mg Moderate 15–25 mg 5–9 mg Strong 26–35 mg 10–20 mg Extremely Intense >35 mg >20 mg Duration 4–8 hours 2–4 hours When sold as "Ecstasy", tablets containing 2C-B often contain about 5 mg of the drug, an amount which produces stimulatory effects that mimic the effects of MDMA; in contrast, tablets marketed as 2C-B have larger quantities of the drug (10–20 mg) which cause hallucinogenic effects.[18] When orally consumed, 2C-B has a much longer delay before the onset of effects than when it is insufflated. Oral ingestion generally takes roughly 45–75 minutes for the effects to be felt, plateau lasts 2–4 hours, and coming down lasts 1–2 hours. Rectal administration onset varies from 5 to 20 minutes. Insufflated onset takes 1–10 minutes for effects to be felt. The duration can last from 4 to 12 hours depending on route of administration, dose, and other factors.[19] With insufflation, the effects are more abrupt and intense but have a significantly shorter duration, while oral usage results in a milder, longer experience. When insufflated, the onset happens very rapidly, usually reaching the peak at about 20–40 minutes and plateauing for 2–3 hours. 2C-B is also considered one of the most painful drugs to insufflate, with users reporting intense nasal burning.[20] The sudden intensity of the experience combined with the pain can often start the experience with a negative imprint and nausea is also increased with insufflation, compounding the issue. 2C-B pill with heart logo Little academic research has been conducted on the effects of 2C-B in humans. The information available is largely anecdotal and limited. Effects are often described as being more easily managed than other psychedelics;[20][17] it is often compared to a mixture of a serotonergic psychedelic and MDMA.[21] At 5–10 mg, experiments with young chickens have shown it to produce effects similar to a low dosage of amphetamines.[22] The anecdotal effects of 2C-B that have been reported by users on online discussion forums include:[19][23][24] At low doses, the experience may shift in intensity from engaging to mild/undetectable. Experienced users report the ability to take control of the effects and switch from engaged to sober at will. The hallucinations have a tendency to decrease and then increase in intensity, giving the users a sense of "waves" or even glowing. These are popularly described as "clichéd '70s visuals" or objects taking on "water color"-like textures. While the effects of the drug often render users unable to concentrate deeply on anything in particular, some can become engrossed in an activity such as watching a movie or playing a video game, thus distracting themselves from the visual and auditory effects of the drug. Excessive giggling or smiling is common, as is a tendency for deeper "belly laughs". Some users say that the effects are more intense when listening to music and report that they can see sounds and noises. Some users experience a decrease in visual acuity, although others report sharper vision. Through increased awareness of one's body, attention may be brought to perceived "imperfections" or internal body processes.The following effects are highly dose-dependent. Open eye visuals (OEVs), such as cartoon-like distortions and red or green halos around objects. Closed eye visuals (CEVs) are more common than OEVs. Affects and alters ability to communicate, engage in deep thought, or maintain attention span. Some users report experiencing frightening or fearful effects during the experience. Users describe feeling frigid or cold on reaching a plateau, while others feel wrapped in comfortable blankets/ultimate pleasure. Coordination may be affected; some users lose balance or have perceptual distinction problems. Onset time of 2C-B is highly dose dependent, but usually from 45 to 75 minutes. Taken on a full stomach, the onset time is increased to two hours or more. Before it was scheduled, 2C-B was sold in small doses as an aphrodisiac (see: § History). Some users report aphrodisiac effects at lower doses.[15][23] Clinical studies in humans suggest that 2C-B is a psychedelic with some possible entactogen-like effects.[7][3][25] Specific effects have included slight hallucinogenic states, perceptual changes, ego dissolution, time dilation, euphoria, feelings of well-being, reduced anger, increased reactivity to negative emotional stimuli, decreased ability to recognize expressions of happiness, augmented emotionality in speech, and mild sympathomimetic effects such as pressor effects, among others.[7][3][25] Some users report mild "jitters" (body tremors), shuddering breath, and/or mild muscle spasms after insufflating 2C-B. Whether or not these effects are enjoyable depends on the user; Mild to intense diarrhea, gas, nausea, and general gastrointestinal discomfort; Severe headaches after coming down from large doses have been reported. However, many users report a lack of "comedown" or "crash", instead noting a gradual return to sobriety; At doses over 30–40 mg the user may experience frightening hallucinations, as well as tachycardia, hypertension, and hyperthermia;[26] 2C-B HCl is very painful to insufflate. Anecdotal evidence suggests that 2C-B HBr, the hydrobromide salt with greater water solubility, is less irritating to the mucous membranes lining the nose but slightly less potent when compared dose-for-dose with the HCl salt;[27] Rectal administration of a water-based solution of 2C-B is known to be less painful than insufflation and much more potent than oral administration. Severe adverse reactions are rare, but use of 2C-B was linked to significant brain injury in one case report; the alleged "2C-B" was never actually discovered by testing so the only evidence suggesting 2C-B was the cause was the victim's own words, without taking into consideration that adulteration and impurities are very common in illicit drugs.[28] There is a case report of acquired synesthesia following a single very high dose of 2C-B.[29] There is also a case report of persistent psychosis following a single dose of 2C-B.[30] The lethal dosage is unknown. It was reported in PiHKAL, by Alexander Shulgin, that a psychologist had accidentally taken a 100 mg dose orally without apparent harm.[15] See also: Psychedelic drug § Interactions, and Trip killer § Serotonergic psychedelic antidotes 2C-B is metabolized by the monoamine oxidase (MAO) enzymes MAO-A and MAO-B.[31][32] Monoamine oxidase inhibitors (MAOIs) such as phenelzine, tranylcypromine, moclobemide, and selegiline may potentiate the effects of 2C-B.[31][32][33] This may result in overdose and serious toxicity.[33][31] 2C-B may also have interactions with other medications and drugs.[5] 2C-B activities Target Affinity (Ki, nM) 5-HT1A 130–311 5-HT1B 104 5-HT1D 26 5-HT1E 120 5-HT1F ND 5-HT2A 0.66–32 (Ki)1.20–689 (EC50Tooltip half-maximal effective concentration)4–101% (EmaxTooltip maximal efficacy) 5-HT2B 13.5–97 (Ki)12.6–130 (EC50)52–97% (Emax) 5-HT2C 32–90 (Ki)0.03–493 (EC50)50–116% (Emax) 5-HT3 >10,000 5-HT4 ND 5-HT5A >10,000 5-HT6 320 5-HT7 210 α1A >10,000 α1B >10,000 α1D ND α2A 309–320 α2B >10,000 α2C 103 β1 >10,000 β2 >10,000 β3 ND D1 12,000 D2 2,200–25,200 D3 7,116–10,000 D4 >10,000 D5 >10,000 H1–H4 >10,000 M1–M2 >10,000 M3 822 M4–M5 >10,000 I1 2,155 σ1 >10,000 σ2 >10,000 TAAR1Tooltip Trace amine-associated receptor 1 90–3,000 (Ki) (rodent)3,300–7,190 (EC50) (human) SERTTooltip Serotonin transporter 9,700–13,300 (Ki)18,000–312,900 (IC50Tooltip half-maximal inhibitory concentration) NETTooltip Norepinephrine transporter 27,400–31,000 (Ki)44,000–67,100 (IC50) DATTooltip Dopamine transporter 6,500–>30,000 (Ki)231,000 (IC50) MAO-ATooltip Monoamine oxidase A 125,000 (IC50) MAO-BTooltip Monoamine oxidase B 58,000 (IC50) Notes: The smaller the value, the more avidly the drug binds to the site. All proteins are human unless otherwise specified. Refs: [34][35][36][37][1][38][39][40][41][42][43][44][45][46] Unlike most psychedelics, 2C-B has been shown to be a low efficacy human serotonin 5-HT2A and 5-HT2C receptor partial agonist.[47] This suggests that activation of the 5-HT2A-coupled phospholipase D pathway[47] or functional antagonism of 5-HT2A may also play a role. The rank order of 5-HT2A receptor antagonist potency for this family of drugs in Xenopus is 2C-I > 2C-B > 2C-D > 2C-H.[48] Although 2C-B itself was not evaluated, other closely related members of the 2C series, including 2C-C, 2C-D, 2C-E, 2C-I, and 2C-T-2, all showed no activity as monoamine releasing agents of serotonin, norepinephrine, or dopamine (EC50Tooltip half-maximal effective concentration = >100,000 nM or "inactive").[49][50] Likewise, these other 2C derivatives showed little activity as serotonin 5-HT1A receptor agonists (EC50 = >3,000 nM).[50] The September 1998 issue of Journal of Analytical Toxicology reported that very little data exists about the pharmacological properties, metabolism, and toxicity of 2C-B.[citation needed] With 30 mg 2C-B by oral administration, its peak concentrations (mean ± SD) were 5.4 ± 1.7 ng/mL and its time to peak concentrations were 2.3 ± 1.0 hours.[4] 2C-B has been shown to be metabolized by liver hepatocytes, resulting in deamination and demethylation that produces several products. Oxidative deamination results in the 2-(4-bromo-2,5-dimethoxyphenyl)ethanol (BDMPE) and 4-bromo-2,5-dimethoxyphenylacetic acid (BDMPAA) metabolites. Additionally, 4-bromo-2,5-dimethoxybenzoic acid (BDMBA) can be produced by oxidative deamination. Further metabolism of BDMPE and BDMPAA may occur by demethylation. Alternatively, the later metabolites can be generated by demethylation of 2C-B followed by oxidative deamination.[26] Deamination of 2C-B is mediated by the monoamine oxidase (MAO) enzymes MAO-A and MAO-B.[31][32][4] There is species differentiation in the metabolism of 2C-B. Mice hepatocytes produce 4-bromo-2,5-dimethoxyphenol (BDMP), a previously unknown metabolite. Meanwhile, human, monkey, and rabbit hepatocytes produce 2-(4-bromo-2-hydroxy-5-methoxyphenyl)-ethanol (B-2-HMPE), but dog, rat, and mouse hepatocytes do not.[26] 2C-B's metabolites BDMPAA and 4-bromo-2-hydroxy-5-methoxyphenylacetic acid (B-2-HMPAA) in humans occur at peak concentrations 280-fold and 17-fold higher than those of 2C-B with oral administration of 2C-B, respectively.[4] The elimination half-life of 2C-B in humans is 1.2 to 2.5 hours.[3][4] Analogues and derivatives of 2C-B: 25-N: 25B-N1POMe 25B-NAcPip 25-NB: 25B-N(BOMe)2 25B-NB 25B-NB23DM 25B-NB25DM 25B-NB3OMe 25B-NB4OMe 25B-NBF 25B-NBMD 25B-NBOH 25B-NBOMe (NBOMe-2CB) 2C-B-DRAGONFLY-NBOH 2CBCB-NBOMe DMBMPP 2CBFly-NBOMe (NBOMe-2CB-Fly) 25-NM: 25B-NMe7BF 25B-NMe7BT 25B-NMe7Bim 25B-NMe7Box 25B-NMe7DHBF 25B-NMe7Ind 25B-NMe7Indz 25B-NMePyr Substituted benzofurans: 2C-B-FLY 2C-B-BUTTERFLY 2C-B-DRAGONFLY DOB-FLY DOB-2-DRAGONFLY-5-BUTTERFLY N-(2C)-fentanyl: N-(2C-B) fentanyl[51] N-(2C-B-FLY) fentanyl[52] Other: BOB BOH-2C-B, β-Hydroxy-2C-B, βOH-2CB[53][54] BMB 2C-B-5-hemifly 2C-B-aminorex (2C-B-AR) 2C-B-AN 2C-B-BZP 2C-B-FLY-NB2EtO5Cl 2C-B-PP 2CB-Ind βk-2C-B (beta-keto 2C-B) N-Ethyl-2C-B TCB-2 (2C-BCB) A variety of N-substituted derivatives of 2C-B have been tested, including N-methyl-2CB, N,N-dimethyl-2CB, N-ethyl-2CB and N-benzyl-2CB. Most simple alkyl derivatives were considerably less potent than 2C-B, with N-ethyl-2CB for instance having a 40 times lower affinity for the 5-HT2A receptor. The N-benzyl derivative however was found to have higher binding affinity than 2C-B itself, with N-(4-bromobenzyl)-2CB binding even more tightly.[55] This initial research did not include functional assays of activity, but later led to the development of potent substituted N-benzyl derivatives such as 25B-NBOMe,[56] and 25B-NBOH. βk-2C-B shows dramatically reduced potency and efficacy as a serotonin 5-HT2A receptor agonist compared to 2C-B.[42] ASR-2001 (2CB-5PrO) is another notable analogue of 2C-B which is under development for treatment of psychiatric disorders.[57][58][59] Exposing compounds to the reagents gives a colour change which is indicative of the compound under test. Marquis Mecke Mandelin Liebermann Froehde Robadope Yellow to green Yellow to olive brownish green Yellow to black Yellow to green Slow pink Ehrlich Hofmann Simon's Scott Folin No reaction No reaction No reaction No reaction (Light) purple 2C-B was synthesized from 2,5-dimethoxybenzaldehyde by American chemist Alexander Shulgin in 1974. It first saw use among the psychiatric community as an aid during therapy, but was abandoned due to gastrointestinal effects and the lack of empathogenic effects.[1] 2C-B was first sold commercially as a purported aphrodisiac[60] under the trade name "Erox", which was manufactured by the German pharmaceutical company Drittewelle.[61] For several years, it was available as tablets in Dutch smart shops under the name "Nexus" and "B-Dub".[citation needed] Street purity of 2C-B, when tested, has been found to be relatively high.[62] Researchers in Spain found that 2C-B samples in the country doubled between 2006 and 2009, switched from primarily powder form to tablets, and exhibited "low falsification rates".[21] An analysis of street samples in the Netherlands found impurities "in small percentages"; only one of the impurities, the N-acetyl derivative of 2C-B, could be identified, and comprised 1.3% of the sample. The authors suggested that this compound was a by-product of 2C-B synthesis.[18] In 2011, street prices in the United States ranged between $10 and $30 per tablet when purchased in small quantities.[8] Larger retail purchases cost between $200 and $500 per gram. Wholesale purchases of 2C-B would lower the price ($100 to $300 per gram in 2001, $30 to $100 on the darknet in 2020).[60] The UN Commission on Narcotic Drugs added 2C-B to Schedule II of the Convention on Psychotropic Substances in March 2001.[63] 2C-B is a scheduled drug in most jurisdictions.[64] The following is a partial list of territories where the substance has been scheduled. 2C-B is controlled under the List 1, as well as similar substances like 2C-I or 2C-T-2.[65] 2C-B is controlled in Australia and on the list of substances subject to import and export controls (Appendix B). It was placed on Schedule One of the Drugs Misuse and Trafficking Act when it first came to notice in 1994, when in a showcase legal battle chemist R. Simpson was charged with manufacturing the substance in Sydney. Alexander Shulgin came to Australia to testify on behalf of the defense, to no avail. 2C-B is not specifically listed in the Australia Poisons Standard (October 2015), however similar drugs such as 2C-T-2 and 2C-I are making 2C-B fall under the Australian analogue act.[66] In Belgium, 2C-B is a controlled substance making production, distribution, and possession illegal. In Brazil, 2C-B is a controlled substance making production, distribution, and possession illegal. In Canada, 2C-B is classified under Controlled Drugs and Substances Act as Schedule III as "4-bromo-2,5-dimethoxybenzeneethanamine and any salt, isomer or salt of isomer thereof".[67] 2C-B has been rescheduled (Schedule III), in a new amendment, taking effect on October 31, 2016. This is to include the other 2C-x analogues.[68] In August 2007, 2C-B, along with many other psychologically active substances,[69] was added to Ley 20.000, known as the Ley de Drogas [es]. Possession of more than 200 mg of 2C-B is punishable with a two years jail sentence.[70] Smaller amount is punishable by a fine. The 200 mg threshold is merely a guideline which the court can reconsider depending on circumstances. In Denmark, 2C-B is listed as a category B drug.[71] In Estonia, 2C-B is classified as Schedule I. In Germany, 2C-B is controlled in the Betäubungsmittelgesetz (BtMG) Anlage I as "Bromdimethoxyphenethylamin" (BDMPEA). 2C-B is schedule I (tabella I).[72] In Japan, 2C-B was scheduled in 1998. It was previously marketed as "Performax". In Luxembourg, 2C-B is a prohibited substance since 2001.[73] In the Netherlands, 2C-B was scheduled on July 9, 1997. In the Netherlands, 2C-B became a list I substance of the Opium Law despite no health incidents occurring. Following the ban, other phenethylamines were sold in place of 2C-B until the Netherlands became the first country in the world to ban 2C-I, 2C-T-2 and 2C-T-7 alongside 2C-B. In Norway, 2C-B was classified as Schedule II on March 22, 2004, listed as 4-bromo-2,5-dimethoxyphenethylamine.[74] 2C-B is schedule I (I-P group) in Poland. Banned as a narcotic drug with a criminal penalty for possession of at least 10 mg.[75] In Spain, 2C-B was added to Category 2 prohibited substances in 2002. 2C-B is currently classified as Schedule I in Sweden. 2C-B was first classified as "health hazard" under the act Lagen om förbud mot vissa hälsofarliga varor (Act on the Prohibition of Certain Goods Dangerous to Health) as of April 1, 1999, under SFS 1999:58[76] that made it illegal to sell or possess. Then it became schedule I as of June 1, 2002, published in LVFS 2002:4[77] but mislabeled "2-CB" in the document. However, this was corrected in a new document, LVFS 2009:22[78] effective December 9, 2009. In Switzerland, 2C-B is listed in Anhang D of the DetMV and is illegal to possess.[79] All drugs in the 2C family are Class A under the Misuse of Drugs Act which means they are illegal to produce, supply or possess. Possession carries a maximum sentence of seven years imprisonment while supply is punishable by life imprisonment and an unlimited fine.[80] In the United States, 2C-B is classified as a Schedule I controlled substance. This became permanent law on June 2, 1995,[81] following a proposal by the Drug Enforcement Administration in December 1994.[82]

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Retrieved from " 3 Pharmaceutical compound 2C-iBuClinical dataOther names2,5-Dimethoxy-4-isobutylphenethylamine; 4-Isobutyl-2,5-dimethoxyphenethylamine; 2C-iBu; 2C-IB; ELE-02; ELE02; ELEU02Routes ofadministrationOral;[1] Ophthalmic[2][3]Drug classSerotonin 5-HT2A receptor agonist; Serotonergic psychedelic; Hallucinogen; Anti-inflammatory drugPharmacokinetic dataProtein binding74%[4]Duration of action20 hours[1]Identifiers IUPAC name 2-[2,5-dimethoxy-4-(2-methylpropyl)phenyl]ethanamine PubChem CID57486931Chemical and physical dataFormulaC14H23NO2Molar mass237.343 g·mol−13D model (JSmol)Interactive image SMILES CC(C)CC1=C(C=C(C(=C1)OC)CCN)OC InChI InChI=1S/C14H23NO2/c1-10(2)7-12-9-13(16-3)11(5-6-15)8-14(12)17-4/h8-10H,5-7,15H2,1-4H3Key:FLBABUVVTQBINW-UHFFFAOYSA-N 2,5-Dimethoxy-4-isobutylphenethylamine (2C-iBu or 2C-IB), also known by its developmental code name ELE-02, is a serotonin 5-HT2A receptor agonist, serotonergic psychedelic, and anti-inflammatory drug which is under development for the treatment of inflammation.[2][3][4][5][6][7] It is a member of the phenethylamine and 2C families of compounds.[4][5][7] The drug is being developed as a topical eye drop for treatment of inflammatory eye conditions.[2][3] There is also interest in 2C-iBu and related drugs for treatment of systemic inflammation and neuroinflammation.[8][9][10][11][12][5] 2C-iBu was not assessed or discovered by Alexander Shulgin and was not described in PiHKAL (Phenethylamines I Have Known and Loved) (1991).[7][13] However, he did include 2C-iBu (as "2C-IB") as a DOM analogue in a table in The Shulgin Index, Volume One: Psychedelic Phenethylamines and Related Compounds (2011).[1] In addition, he stated in a footnote that a 5 mg oral dose of 2C-iBu produces threshold activity and has a long duration of about 20 hours.[1] The cited source for these observations, however, was only a 2006 personal communication with "M. Mueller."[1] 2C-iBu was subsequently more thoroughly characterized by Charles D. Nichols and colleagues at Louisiana State University School of Medicine as a novel anti-inflammatory drug in the late 2010s.[4][7] Eleusis has licensed 2C-iBu intellectual property from LSU and the drug has reached the preclinical research stage of development, but no recent development has been reported as of October 2023.[2][3] 2C-iBu molecular targets[4] Target Affinity (pKi) 2C-iBu (R)-DOI 5-HT1A 7.1 5.9 5-HT1B 7.3 5.6 5-HT1D 7.2 ND 5-HT2A 8.9 10.4 5-HT2B 7.8 8.6 5-HT2C 9.6 9.2 5-HT6 5.9 ND 5-HT7 6.5 ND 2C-iBu is a highly potent and robustly efficacious serotonin 5-HT2A receptor agonist.[4] Its EC50Tooltip half-maximal effective concentration values are 1.3 nM for calcium mobilization and 57.5 nM for β-arrestin-2 recruitment, whereas its EmaxTooltip maximal efficacy values are 103% for calcium mobilization and 77% for β-arrestin-2 recruitment relative to serotonin.[4] The drug showed higher potency and efficacy as a serotonin 5-HT2A receptor agonist than several other 2C drugs, including 2C-NP, 2C-B, 2C-I, 2C-H, and 2C-iP, whereas its activities were more comparable to or less than those of the DOx drugs DOIB, (R)-DOB, (R)-DOI, and DOiP.[4] 2C-iBu has also been assessed and found to bind to other serotonin receptors, including the serotonin 5-HT2C, 5-HT2B, 5-HT1B, 5-HT1D, 5-HT1A, 5-HT7, and 5-HT6 receptors, in that order of affinity and with varying avidities.[4] 2C-iBu dose-dependently produces the head-twitch response (HTR), a behavioral proxy of psychedelic effects, in rodents.[4] In terms of ED50Tooltip median effective dose, 2C-iBu is about 3-fold less potent than (R)-DOI in producing the HTR.[4] According to Eleusis, it is expected to have "greatly reduced" psychoactivity or hallucinogenic effects compared to related drugs like other members of the 2C family.[6][14] The drug is effective in an allergic asthma model in rodents and showed similar potency as (R)-DOI.[4] Due to its reduced potency in producing the HTR but retained anti-inflammatory potency, 2C-iBu is expected to show greater separation between the desired anti-inflammatory and the undesired psychedelic effects in humans compared to (R)-DOI.[4] In contrast to certain other anti-inflammatory drugs like corticosteroids, serotonin 5-HT2A receptor agonists like 2C-iBu are not immunosuppressants.[14] 2C-iBu, also known as 2,5-dimethoxy-4-isobutylphenethylamine, is a phenethylamine and 2C derivative.[4][5][7] Related drugs to 2C-iBu include 2C-Bu (the butyl analogue), 2C-tBu (the tert-butyl analogue), 2C-sBu (the sec-butyl analogue), and 2C-CPM (the cyclopropylmethyl analogue).[4] In addition, 2C-iBu is related to DOx drugs such as DOIB (DOiBu).[4][15] According to Charles D. Nichols, 2,5-dimethoxyamphetamine (2,5-DMA) has potent anti-inflammatory activity with weak or no hallucinogenic effects.[7][15] Moreover, DOTFM has potent psychedelic effects with no anti-inflammatory activity.[7][16][17] Hence, it appears that the anti-inflammatory effects and psychedelic effects of serotonin 5-HT2A receptor agonists can be fully dissociated.[7] The chemical synthesis of 2C-iBu has been described.[4][1] 2C-iBu was developed as a novel anti-inflammatory drug by Charles D. Nichols and colleagues at Eleusis in the late 2010s.[7][4] They are developing it for treatment of inflammatory conditions.[2][3] Eleusis was acquired by and merged into Beckley Psytech in October 2022.[2][18][19] The drug has reached the preclinical research stage of development, but no recent development has been reported as of October 2023.[2][3] Eleusis has licensed intellectual property surrounding 2C-iBu and has patent protection for 2C-iBu.[6][4] 2C-iBu is not a controlled substance in the United States as of 2020.[6] 5-HT2A receptor § Anti-inflammatory effects

^ a b c d e f Shulgin A, Manning T, Daley PF (2011). "#60. DOM". The Shulgin Index, Volume One: Psychedelic Phenethylamines and Related Compounds. Vol. 1. Berkeley, CA: Transform Press. pp. 118–129. ISBN 978-0-9630096-3-0. OCLC 709667010. 2C-IB: [...] (15) Synthesis (from 2,5-dimethoxyisobutylbenzene) (Mueller, 2006); although this compound was reported here, a structure-search in Chemical Abstracts does not produce a CAS registry number (16) Threshold activity in humans at 5 mg orally; long duration (about 20 hours; Mueller, 2006). [...] Mueller, M. (2006) Personal communication with A.T. Shulgin. ^ a b c d e f g "ELE 02". AdisInsight. 28 October 2023. Retrieved 16 February 2025. ^ a b c d e f "Delving into the Latest Updates on ELE-02 with Synapse". Synapse. 23 January 2025. Retrieved 16 February 2025. ^ a b c d e f g h i j k l m n o p q r s WO published 2020210823, Nichols CD, Billac G, Nichols DE, "Compounds and methods for treating inflammatory disorders", published 15 October 2020 ^ a b c d Raz S (February 2020). Eleusis Drug Development Overview. LSX World Congress 2020. ^ a b c d Newvine C (8 July 2020). "Eleusis Draws on Research Into Psychedelics To Develop New Medicines for Inflammation". Lucid News - Psychedelics, Consciousness Technology, and the Future of Wellness. Retrieved 16 February 2025. ^ a b c d e f g h i Hamilton Morris (14 November 2021). "PODCAST 33: An interview with Dr. Charles D. Nichols". The Hamilton Morris Podcast (Podcast). Patreon. Event occurs at 48:22–53:56. Retrieved 20 January 2025. ^ Nichols DE, Johnson MW, Nichols CD (February 2017). "Psychedelics as Medicines: An Emerging New Paradigm". Clin Pharmacol Ther. 101 (2): 209–219. doi:10.1002/cpt.557. PMID 28019026. ^ Flanagan TW, Nichols CD (2022). 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"Researcher Charles Nichols Studies the Impact of Psychedelic Substances on Inflammation". Lucid News - Psychedelics, Consciousness Technology, and the Future of Wellness. Retrieved 16 February 2025. ^ a b Flanagan TW, Billac GB, Landry AN, Sebastian MN, Cormier SA, Nichols CD (April 2021). "Structure-Activity Relationship Analysis of Psychedelics in a Rat Model of Asthma Reveals the Anti-Inflammatory Pharmacophore". ACS Pharmacol Transl Sci. 4 (2): 488–502. doi:10.1021/acsptsci.0c00063. PMC 8033619. PMID 33860179. The nature of the 4-position substituent of phenethylamine psychedelics has been previously linked to 5-HT2 receptor selectivity as well as agonist properties at 5-HT2 receptors.40 Analysis of the 4-position demonstrated that the identity of the moiety at this position was rather flexible. Fully efficacious substitutions at the 4-position included the halogens iodine and bromine (R)-DOI (Figure 3), 2C-B (Figure 7A), methoxy (TMA-2) (Figure 7G), short-chain hydrocarbons (R)-DOM (Figure 7H), (R)-DOET) (Figure 7I), and a branched hydrocarbon (DOiBu) (Figure 7J). [...] In a comparison of PenH-AUC values determined for each drug as a proxy measure of anti-inflammatory efficacy (Figure 8A) to either EC50 or EMax for calcium mobilization downstream of 5- HT2A receptor activation (Table 1), [...] ^ Flanagan TW, Billac G, Nichols CD (2022). "Differential Regulation of Inflammatory Responses Following 5-HT 2 Receptor Activation in Pulmonary Tissues". The FASEB Journal. 36 (S1). doi:10.1096/fasebj.2022.36.S1.R2617. ISSN 0892-6638. ^ Flanagan TW, Foster TP, Galbato TE, Lum PY, Louie B, Song G, et al. (February 2024). "Serotonin-2 Receptor Agonists Produce Anti-inflammatory Effects through Functionally Selective Mechanisms That Involve the Suppression of Disease-Induced Arginase 1 Expression". ACS Pharmacology & Translational Science. 7 (2): 478–492. doi:10.1021/acsptsci.3c00297. PMC 10863441. PMID 38357283. The effects of (R)-DOTFM were examined in the head-twitch response (HTR) assay. (R)-DOTFM produced a strong HTR with a potent ED 50 of 0.60 μmol/kg. These values are equivalent to (R)-DOI, as previously determined. ^ Gunther M (26 October 2022). "What's the Future of Eleusis Therapeutics After Acquisition by Beckley Psytech?". Lucid News - Psychedelics, Consciousness Technology, and the Future of Wellness. Retrieved 17 February 2025. ^ "Beckley Psytech Strengthens Pipeline and Development Team With Acquisition of Eleusis Therapeutics Limited". Psychedelic Alpha. 24 October 2022. Retrieved 17 February 2025. 2C-IB - isomer design PODCAST 33: An interview with Dr. Charles D. Nichols (November 14, 2021) - The Hamilton Morris Podcast (discusses 2C-iBu/ELE-02 from 48:22 to 53:56)

Retrieved from " 4 Pharmaceutical compound 2C-BuClinical dataOther names2,5-Dimethoxy-4-butylphenethylamine; 4-Butyl-2,5-dimethoxyphenethylamine; 2C-BUIdentifiers IUPAC name 2-(4-butyl-2,5-dimethoxyphenyl)ethan-1-amine CAS Number2888537-44-6PubChem CID172187929Chemical and physical dataFormulaC14H23NO2Molar mass237.343 g·mol−13D model (JSmol)Interactive image SMILES CCCCC1=CC(=C(C=C1OC)CCN)OC InChI InChI=1S/C14H23NO2/c1-4-5-6-11-9-14(17-3)12(7-8-15)10-13(11)16-2/h9-10H,4-8,15H2,1-3H3Key:WVGDKSDIKCPRKV-UHFFFAOYSA-N 2C-Bu, also known as 2,5-dimethoxy-4-butylphenethylamine, is a chemical compound of the phenethylamine and 2C families.[1] It has been said by Daniel Trachsel to be completely unknown.[1] 2C-Bu is the 2C analogue of the DOx derivative DOBU, which is active but does not appear to have psychedelic-type effects in either animals or humans.[1][2][3] 2C-Bu has several notable skeletal isomers, including 2C-iBu, 2C-tBu, and 2C-sBu.[1][4] 2C-iBu and 2C-tBu are both active and produce hallucinogen-type effects in animals and/or humans.[5][6][7][4] This is in spite of 2C-tBu being predicted to be inactive[4] and DOTB (the DOx analogue of 2C-tBu) being inactive as a hallucinogen in animals and humans.[2][8] 2C-iBu may have reduced hallucinogenic potency than other 2C drugs and is being developed as a potential anti-inflammatory medication.[6][7] 2C-P

^ a b c d Trachsel D, Lehmann D, Enzensperger C (2013). Phenethylamine: von der Struktur zur Funktion [Phenethylamines: From Structure to Function]. Nachtschatten-Science (in German). Solothurn: Nachtschatten-Verlag. pp. 763–764, 766–767, 771, 901. ISBN 978-3-03788-700-4. OCLC 858805226. Retrieved 29 January 2025. ^ a b Shulgin AT, Shulgin A (1991). "#63 DOBU 2,5-DIMETHOXY-4-(n)-BUTYLAMPHETAMINE". PiHKAL: A Chemical Love Story (1st ed.). Berkeley, CA: Transform Press. ISBN 978-0-9630096-0-9. OCLC 25627628. ^ Seggel MR, Yousif MY, Lyon RA, Titeler M, Roth BL, Suba EA, et al. (March 1990). "A structure-affinity study of the binding of 4-substituted analogues of 1-(2,5-dimethoxyphenyl)-2-aminopropane at 5-HT2 serotonin receptors". Journal of Medicinal Chemistry. 33 (3): 1032–1036. doi:10.1021/jm00165a023. PMID 2308135. ^ a b c Varty GB, Canal CE, Mueller TA, Hartsel JA, Tyagi R, Avery K, et al. (April 2024). "Synthesis and Structure-Activity Relationships of 2,5-Dimethoxy-4-Substituted Phenethylamines and the Discovery of CYB210010: A Potent, Orally Bioavailable and Long-Acting Serotonin 5-HT2 Receptor Agonist". J Med Chem. 67 (8): 6144–6188. doi:10.1021/acs.jmedchem.3c01961. PMID 38593423. The 4-tert-butyl group was considered as a spot for potential hydroxylation by cytochrome P450s to discover analogs with short-lasting effects. However, 2C-t-Bu was a potent agonist at the 5-HT2A receptor (Ki = 9.9 nM, EC50 = 4.2 nM) and elicited a robust HTR (Supporting Information, Table S1), providing in vivo evidence that the tert-butyl group is not rapidly metabolized to an inactive compound in mice, despite predictions. ^ Shulgin A, Manning T, Daley PF (2011). "#60. DOM". The Shulgin Index, Volume One: Psychedelic Phenethylamines and Related Compounds. Vol. 1. Berkeley, CA: Transform Press. pp. 118–129. ISBN 978-0-9630096-3-0. OCLC 709667010. 2C-IB: [...] (15) Synthesis (from 2,5-dimethoxyisobutylbenzene) (Mueller, 2006); although this compound was reported here, a structure-search in Chemical Abstracts does not produce a CAS registry number (16) Threshold activity in humans at 5 mg orally; long duration (about 20 hours; Mueller, 2006). [...] Mueller, M. (2006) Personal communication with A.T. Shulgin. ^ a b WO published 2020210823, Nichols CD, Billac G, Nichols DE, "Compounds and methods for treating inflammatory disorders", published 15 October 2020 ^ a b Raz S (February 2020). Eleusis Drug Development Overview. LSX World Congress 2020. ^ Oberlender RA (May 1989). "Stereoselective aspects of hallucinogenic drug action and drug discrimination studies of entactogens". Purdue e-Pubs. Purdue University. Retrieved 17 February 2025. Table 7. Hallucinogenic potency of 4-alkyl-2,5-dimethoxyamphetamines.a [...] DOTB: [...] Hallucinogenic Potencyb: -c. [...] c this compound has not been established as hallucinogenic. [...] Within this homologous series, optimum activity is straight chain alkyl group, two and three carbons in length 1975). The potency increases by an order of magnitude as associated with a (Shulgin and Dyer, the 4-hydrogen of 2,5-DMA is replaced by a short alkyl chain, then decreases if the chain length exceeds four carbons. In addition, the lack of hallucinogenic activity for the tertiary butyl derivative, DOTB, suggested that branching of the 4-alkyl substituent was not tolerated. [...] In a study employing 5-MeO-DMT as the training drug in rats, DOTB and DOAM were distinguishable from this hallucinogen, while 2,5-DMA and DOM were not (Glennon et al., 1981). This was consistent with the studies described above. Surprisingly, however, stimulus generalization was not observed for DOET, DOPR, and DOBU (Glennon et al., 1981a). [...] Aldous et al. (1974) noted steric restrictions on the 4-substituent in the rabbit hyperthermia model since the 4-isopropyl derivative was more potent than the 4-tert-butyl analogue, DOTB. Additional studies with DOTB, which contains a more highly hindered benzylic carbon, indicate that hallucinogen-like activity may actually be abolished in man (Shulgin and Dyer, 1975) and drastically attenuated in animals (Glennon et al., 1982). 2C-BU - Isomer Design

Retrieved from " 5 Pharmaceutical compound 2C-tBuClinical dataOther names2,5-Dimethoxy-4-tert-butylphenethylamine; 4-tert-Butyl-2,5-dimethoxyphenethylamine; 2C-TBU; 2C-t-BuDrug classSerotonin receptor agonist; Serotonergic psychedelic; HallucinogenIdentifiers IUPAC name 2-(4-tert-butyl-2,5-dimethoxyphenyl)ethanamine PubChem CID117347542ChemSpider76370331Chemical and physical dataFormulaC14H23NO2Molar mass237.343 g·mol−13D model (JSmol)Interactive image SMILES CC(C)(C)C1=C(C=C(C(=C1)OC)CCN)OC InChI InChI=1S/C14H23NO2/c1-14(2,3)11-9-12(16-4)10(6-7-15)8-13(11)17-5/h8-9H,6-7,15H2,1-5H3Key:MHNFTGKRRUDUST-UHFFFAOYSA-N 2C-tBu, or 2C-t-Bu, also known as 4-tert-butyl-2,5-dimethoxyphenethylamine, is a serotonin receptor agonist and putative serotonergic psychedelic of the phenethylamine and 2C families.[1][2] It is a potent serotonin 5-HT2A receptor agonist (Ki = 9.9–35 nM, EC50Tooltip half-maximal effective concentration = 4.2 nM) and also binds to the serotonin 5-HT2C receptor (Ki = 7–24 nM).[1][2] The drug produces a robust head-twitch response, a behavioral proxy of psychedelic effects, in rodents.[2] It also produces hyperlocomotion in rodents.[2] The active dosage in humans is >5 mg per Daniel Trachsel and its duration is unknown.[1] Initial tests with 7 mg and with 10 mg (as 5 mg plus 5 mg 2 hours apart) produced no psychedelic effects in humans, but instead induced a pronounced and long-lasting tiredness.[1] It was hypothesized that 2C-tBu might be a serotonin 5-HT2A receptor antagonist and might thereby be hypnotic,[1] but it was instead shown to be an agonist in subsequent studies.[2] 2C-Bu 2C-iBu DOTB

^ a b c d e Trachsel D, Lehmann D, Enzensperger C (2013). Phenethylamine: von der Struktur zur Funktion [Phenethylamines: From Structure to Function]. Nachtschatten-Science (in German). Solothurn: Nachtschatten-Verlag. pp. 766–767, 771, 901. ISBN 978-3-03788-700-4. OCLC 858805226. Retrieved 29 January 2025. ^ a b c d e Varty GB, Canal CE, Mueller TA, Hartsel JA, Tyagi R, Avery K, et al. (April 2024). "Synthesis and Structure-Activity Relationships of 2,5-Dimethoxy-4-Substituted Phenethylamines and the Discovery of CYB210010: A Potent, Orally Bioavailable and Long-Acting Serotonin 5-HT2 Receptor Agonist". Journal of Medicinal Chemistry. 67 (8): 6144–6188. doi:10.1021/acs.jmedchem.3c01961. PMID 38593423. The 4-tert-butyl group was considered as a spot for potential hydroxylation by cytochrome P450s to discover analogs with short-lasting effects. However, 2C-t-Bu was a potent agonist at the 5-HT2A receptor (Ki = 9.9 nM, EC50 = 4.2 nM) and elicited a robust HTR (Supporting Information, Table S1), providing in vivo evidence that the tert-butyl group is not rapidly metabolized to an inactive compound in mice, despite predictions. 2C-TBU - Isomer Design

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