**Critical Periods in Brain Development and Behavior**

**PSYC UN3481**

**4 points**

**Spring 2023**

**Where/When**

Thursdays 10:10pm-12pm

In person, location TBD

**Instructor**

Dr. Sarah Canetta ([ses2119@cumc.columbia.edu](mailto:ses2119@cumc.columbia.edu))

**Office Hours**

By appointment

**Prerequisites**

This course is open to advanced undergraduate students who have taken UN1010 (Mind, Brain, & Behavior) or an equivalent introductory course in neuroscience or cognitive psychology. Instructor permission is required prior to registration.

**Bulletin Description**

The majority of our mental capacities—ranging from basic sensory functions to more advanced social, emotional and cognitive capabilities—take many years to develop and are highly influenced by environmental signals encountered during particular developmental ‘critical periods’. In this seminar we will explore examples of these periods across diverse brain systems and behaviors, ranging from vision and audition to social, emotional and cognitive development, by considering each example in the context of human brain function and behavior as well as at the level of more detailed neurobiological mechanisms underlying these changes elucidated by studies using non-human animal systems.

**Course Description**

Unlike many systems of the body, which are largely mature at birth, the human brain continues to undergo massive developmental maturation throughout childhood and adolescence. Likewise, our mental capacities undergo extensive postnatal development and maturation. This is true both for basic senses such as sight, hearing, taste and touch and for advanced social, emotional and cognitive capabilities such as theory of mind, social and emotional regulation, memory, language and abstract reasoning. We now understand that the neural development underlying the acquisition of many of these capabilities is highly regulated by environmental signals that help prepare the brain to respond to the experiences most likely to be encountered later in life. Importantly, we have also learned that the brain is frequently most receptive to these signals during specific developmental windows.

The term ‘critical periods’ has been coined to denote developmental windows in which each brain system is most plastic or malleable, and after which change to the circuitry and the behavior it serves is more difficult, if not impossible. In this course, we will explore this idea of critical periods. We will begin by introducing what they are and why they might exist. We will subsequently explore examples of these periods across diverse brain systems and behaviors, ranging from vision and audition to social, emotional and cognitive development. We will consider each example in the context of human brain function and behavior as well as at the level of more detailed neurobiological mechanisms underlying these changes elucidated by studies using non-human animal systems. We will conclude by examining how our understanding of critical period mechanisms is enabling the possibility of reopening plasticity later in life.

This course is a weekly seminar, with each meeting divided into an introductory lecture followed by a student presentation and discussion of weekly assigned readings. Grading will be based on attendance and general participation (25%), a weekly reading response posted to Courseworks (25%), a presentation of a piece of primary literature required for one session (25%) and an 8-10-page final paper (25%) in which each student is expected to explore one topic from the semester that has peaked their interest in more depth. Details on all of these elements are given below.

**Role in the Psychology Curriculum**

This course is designed to give advanced undergraduates a deeper understanding of the principles and mechanisms underlying critical periods in the development of different facets of behavior and corresponding neural circuitry. It is designed particularly for seniors majoring in Psychology or Neuroscience & Behavior and for students participating in the Post-Baccalaureate Certificate program in Psychology. These students will have priority in registration, followed by junior majors, followed by non-majors. The course fulfills the following degree requirements:

* For the Neuroscience & Behavior major, this course fulfills the fifth Psychology requirement for “one advanced seminar from a list approved by the Psychology Department advisor to the program.”
* For the Psychology major or concentration in Columbia College and in the School of General Studies and for the Psychology Post-Baccalaureate Certificate program, this course meets the Group II (Psychobiology & Neuroscience) distribution requirement.
* For Psychology Post-Baccalaureate students and for Psychology majors, this course will fulfill the seminar requirement.
* For the Barnard Psychology major, this course might fulfill the senior seminar requirement.

**Requirements/Grading**

*Attendance and Participation*: A large portion of each class will be devoted to discussion of the day’s topic and the associated primary literature. Therefore, it is crucial that everyone come prepared having reviewed the required readings PRIOR to class, as well as having considered them in light of the learning objectives I have outlined in the syllabus for that seminar meeting. Attendance and participation are required and will count towards 25% of the final grade. Good participation will reflect both thoughtful listening to other students’ comments as well as consistent contribution to the day’s discussion. Discussion contributions should reflect that the student has reviewed the readings prior to class. *If you have tested positive for COVID or are feeling unwell, please stay home. If possible, please let me know of your absence ahead of class so I can mark it as excused. In person classes will also be available via Zoom for individuals who need to isolate. I will attempt to record our classes as well and post them on the Courseworks website.*

*Weekly Reading Response:* In order to stimulate discussion, a thoughtful response to the weekly readings is required. This response should be between ½ to 1 page in length and submitted prior to the start of class. Thoughtful responses, including those that comment on or critique the week’s primary literature or compare and contrast the topic with another topic from the course, will receive full credit and count towards 25% of the final grade. Feedback will be provided on the first response to help guide students towards what is expected in this regard.

*Presentation:* Beginning with the second class period, each week one or more students will present a primary literature article assigned as part of that week’s reading. During the class, the student presentations will follow the mini introductory lecture to the day’s topic given by the instructor. The goal of the presentation will be to provide background and justification for the study, discuss the experimental design (clarifying the methodological details), the results and conclusions, especially with regard to the bigger picture questions being addressed both in the particular class as well as the course as a whole. The student should come prepared with some questions to stimulate discussion on his/her particular article(s) but the instructor will lead the larger class discussion for the day. It is required that all students schedule a time to meet with the instructor at least 2 days prior to their presentation to discuss the article(s). This presentation will count towards 25% of the final grade.

*Final Paper:* Students are asked to pick a topic from the semester to research and write about in more detail. The final paper should be 8-10 pages in length and contain a minimum of 10 primary source citations (not including reviews). In order to assure that you are on the right track, it is required that you come to class on **Thursday, March 31st** with an outline of what you plan to write about. At a minimum, this should include a description of the topic or question of interest and two or three primary source articles you are considering as source material. We will discuss our topics as a group and then there will be an opportunity to meet individually we me if you have more questions afterwards. This paper will count towards 25% of the final grade. To give me sufficient time to grade your papers, they must be submitted by **midnight on Friday, May 6, 2022**.

**Additional Class Policies**

*Conduct:* In the context of Zoom meetings, please keep your video on and mute yourself when you are not participating in the discussion. Whether in the virtual or in-person class environment, students should be attentive to class presentation and work to participate as much as possible in the class discussion.

*Class in the time of COVID*: As mentioned above, if you have COVID or are feeling ill, please stay home. Try your best to let me know ahead of class and I will make every effort to try to provide a Zoom option to participate in class as well as provide a recording that will be posted to Courseworks afterwards.

*Academic Integrity:* Please read and adhere to the policies regarding academic integrity found in Columbia’s Guide to Academic Integrity (<http://www.college.columbia.edu/academics/integrity>). Remember that you are responsible for presenting your own work in assignments and exams and for attributing others’ ideas where appropriate. If you have any questions about these policies and how to correctly adhere to them, please make an appointment to see me.

*Students with Disabilities:* If you have special needs and may require specific accommodations with regard to the classroom or assignments, please 1) Make an appointment to see me during the first week of class and 2) Contact the Office of Disability Services in Lerner Hall before the start of the course to register for these accommodations.

**Schedule**

*The following example schedule gives topics to be covered, with identified learning objectives and example readings (subject to change). Although this course will rely on primary source articles and reviews and there is no official course textbook, I may also post relevant sections of background textbook reading on Courseworks prior to each class period.*

**Week 1. Introduction to Critical Periods, 1/19/2023**

*Learning Objectives:*

* Use early ethological studies (such as Lorenz’s studies of imprinting) to understand the general principles of behavioral critical periods and arrive at a definition of critical periods in the context of brain development and behavior
* Discuss the benefits and drawbacks of critical periods for organism survival
* Understand how critical periods can be understood across multiple timescales
* Understand the concept of neurobiological plasticity and be able to list several ways in which brain plasticity is accomplished

*Readings:*

Cisneros-Franco, J. M., Voss, P., Thomas, M. E. & de Villers-Sidani, E. Critical periods of brain development. *Handb Clin Neurol* **173**, 75-88, doi:10.1016/B978-0-444-64150-2.00009-5 (2020).

Hensch TK. Critical period regulation. Annu Rev Neurosci. 2004;27:549-79. doi: 10.1146/annurev.neuro.27.070203.144327. PubMed PMID: 15217343.

**Week 2. Critical Periods in Vision – Human and Primate Studies, 1/26/2023**

*Learning Objectives:*

* Understand the basic architecture of the visual system
* Be able to list typical developmental milestones in human vision
* Understand that effects of early perturbations in vision on long-term visual functioning
  + Define amblyopia, identify some of its causes and its long-term consequences for visual functioning and current medical practice for treating it

*Primary Source Readings:*

Birch EE, Stager DR. The critical period for surgical treatment of dense congenital unilateral cataract. Invest Ophthalmol Vis Sci. 1996;37(8):1532-8. PubMed PMID: 8675395.

Harwerth RS, Smith EL, 3rd, Duncan GC, Crawford ML, von Noorden GK. Multiple sensitive periods in the development of the primate visual system. Science. 1986;232(4747):235-8. PubMed PMID: 3952507.

*Reviews:*

Hensch TK, Quinlan EM. Critical periods in amblyopia. Vis Neurosci. 2018;35:E014. Epub 2018/06/16. doi: 10.1017/S0952523817000219. PubMed PMID: 29905116; PMCID: PMC6047524.

Wong AM. New concepts concerning the neural mechanisms of amblyopia and their clinical implications. Can J Ophthalmol. 2012;47(5):399-409. Epub 2012/10/06. doi: 10.1016/j.jcjo.2012.05.002. PubMed PMID: 23036539.

**Week 3. Critical Periods in Vision – Plasticity Mechanisms Drawn from Animal Studies, 2/2/2023**

*Learning Objectives:*

* Review basic architecture of the visual system
* Understand response properties of binocular cells in primary visual cortex
* Use ocular dominance plasticity (ODP) as an example of how the brain and behavior can be shaped by environmental input during critical periods
* Use ODP as an example to understand plasticity mechanisms at work during critical periods

*Primary Source Readings:*

Hubel DH, Wiesel TN. The period of susceptibility to the physiological effects of unilateral eye closure in kittens. J Physiol. 1970;206(2):419-36. PubMed PMID: 5498493; PMCID: PMC1348655.

Wiesel TN, Hubel DH. Single-Cell Responses in Striate Cortex of Kittens Deprived of Vision in One Eye. J Neurophysiol. 1963;26:1003-17. doi: 10.1152/jn.1963.26.6.1003. PubMed PMID: 14084161.

Antonini A, Stryker MP. Rapid remodeling of axonal arbors in the visual cortex. Science. 1993;260(5115):1819-21. PubMed PMID: 8511592.

*Reviews:*

Hooks, B. M. & Chen, C. Circuitry Underlying Experience-Dependent Plasticity in the Mouse Visual System. *Neuron* **107**, 986-987, doi:10.1016/j.neuron.2020.08.004 (2020).

Hensch TK. Critical period mechanisms in developing visual cortex. Curr Top Dev Biol. 2005;69:215-37. doi: 10.1016/S0070-2153(05)69008-4. PubMed PMID: 16243601.

**Week 4. Critical Periods in Vision – Timing Mechanisms Drawn from Animal Studies, 2/9/2023**

*Learning Objectives:*

* Review basic architecture of the visual system
* Use ODP as an example to understand mechanisms that may trigger the opening and closing of critical periods

*Primary Source Readings:*

Fagiolini M, Hensch TK. Inhibitory threshold for critical-period activation in primary visual cortex. Nature. 2000;404(6774):183-6. doi: 10.1038/35004582. PubMed PMID: 10724170.

Kobayashi Y, Ye Z, Hensch TK. Clock genes control cortical critical period timing. Neuron. 2015;86(1):264-75. doi: 10.1016/j.neuron.2015.02.036. PubMed PMID: 25801703; PMCID: PMC4392344.

Spolidoro M, Baroncelli L, Putignano E, Maya-Vetencourt JF, Viegi A, Maffei L. Food restriction enhances visual cortex plasticity in adulthood. Nat Commun. 2011;2:320. Epub 2011/05/19. doi: 10.1038/ncomms1323. PubMed PMID: 21587237.

**Week 5. Critical Periods in Audition – Introduction and Human Studies, 2/16/2023**

*Learning Objectives:*

* Understand the basic architecture of the auditory system
* Be able to list typical developmental milestones in human audition
* Understand that effects of early perturbations in audition on long-term auditory functioning
  + Understand cochlear implant technology, and how the timing of this intervention influences its outcome.
* Define perfect/absolute pitch and describe evidence that this auditory ability may have a critical period

*Primary Source Readings:*

Niparko JK, Tobey EA, Thal DJ, Eisenberg LS, Wang NY, Quittner AL, Fink NE, Team CDI. Spoken language development in children following cochlear implantation. JAMA. 2010;303(15):1498-506. doi: 10.1001/jama.2010.451. PubMed PMID: 20407059; PMCID: PMC3073449.

Russo FA, Windell DL, Cuddy LL. Learning the "special note": Evidence for a critical period for absolute pitch acquisition. Music Percept. 2003;21(1):119-27. doi: DOI 10.1525/mp.2003.21.1.119. PubMed PMID: WOS:000185341900008.

Gervain J, Vines BW, Chen LM, Seo RJ, Hensch TK, Werker JF, Young AH. Valproate reopens critical-period learning of absolute pitch. Front Syst Neurosci. 2013;7:102. Epub 2013/12/19. doi: 10.3389/fnsys.2013.00102. PubMed PMID: 24348349; PMCID: PMC3848041.

*Reviews:*

Whitton JP & Polley DB. Evaluating the Perceptual and Pathophysiological Consequences of Auditory Deprivation in Early Postnatal Life. JARO.

**Week 6. No class**

**Week 7. Critical Periods for Cross-modal Plasticity During Development – Human and Animal Studies, 3/2/2022**

*Learning Objectives:*

* Understand what is meant by cross-modal plasticity
* Understand how this cross-modal plasticity evolves during development
* Examine evidence for a critical period for cross modal plasticity in humans

*Primary Source Readings:*

Cohen LG, Celnik P, Pascual-Leone A, Corwell B, Falz L, Dambrosia J, Honda M, Sadato N, Gerloff C, Catala MD, Hallett M. Functional relevance of cross-modal plasticity in blind humans. Nature. 1997;389(6647):180-3. doi: 10.1038/38278. PubMed PMID: 9296495.

Bedny M, Richardson H, Saxe R. "Visual" Cortex Responds to Spoken Language in Blind Children. J Neurosci. 2015;35(33):11674-81. doi: 10.1523/JNEUROSCI.0634-15.2015. PubMed PMID: 26290244.

Kanjlia S, Pant R, Bedny M. Sensitive Period for Cognitive Repurposing of Human Visual Cortex. Cereb Cortex. 2019;29(9):3993-4005. Epub 2018/11/13. doi: 10.1093/cercor/bhy280. PubMed PMID: 30418533; PMCID: PMC6686750.

**Week 8. Critical Periods for Language – Human Studies, 3/9/2023**

*Learning Objectives:*

* Understand basic neural circuitry contributing to language perception and production
* Be able to describe typical development of the human language system
* Be able to provide evidence for critical periods for acquisition of language phonology and syntax

*Primary Source Readings:*

Werker JF, Gilbert JH, Humphrey K, Tees RC. Developmental aspects of cross-language speech perception. Child Dev. 1981;52(1):349-55. Epub 1981/03/01. PubMed PMID: 7238150.

Johnson JS, Newport EL. Critical period effects in second language learning: the influence of maturational state on the acquisition of English as a second language. Cogn Psychol. 1989;21(1):60-99. PubMed PMID: 2920538.

Hartshorne, J. K., Tenenbaum, J. B. & Pinker, S. A critical period for second language acquisition: Evidence from 2/3 million English speakers. *Cognition* **177**, 263-277, doi:10.1016/j.cognition.2018.04.007 (2018).

*Reviews:*

Werker JF, Hensch TK. Critical periods in speech perception: new directions. Annu Rev Psychol. 2015;66:173-96. doi: 10.1146/annurev-psych-010814-015104. PubMed PMID: 25251488.

Friedmann, N. & Rusou, D. Critical period for first language: the crucial role of language input during the first year of life. *Curr Opin Neurobiol* **35**, 27-34, doi:10.1016/j.conb.2015.06.003 (2015).

**Week 9. \*\*\*Spring Break\*\*\***

**Week 10. Critical Periods for Social and Emotional Development – Human Studies, 3/23/2023**

*Learning Objectives:*

* Understand basic brain systems involved in social and emotional behavior
* Be able to describe typical milestones in human social and emotional development
* Using the Romanian Foster Care studies, describe evidence for a critical period for social and emotional development

*Primary Source Readings:*

Nelson CA, 3rd, Zeanah CH, Fox NA, Marshall PJ, Smyke AT, Guthrie D. Cognitive recovery in socially deprived young children: the Bucharest Early Intervention Project. Science. 2007;318(5858):1937-40. doi: 10.1126/science.1143921. PubMed PMID: 18096809.

Humphreys KL, Gleason MM, Drury SS, Miron D, Nelson CA, 3rd, Fox NA, Zeanah CH. Effects of institutional rearing and foster care on psychopathology at age 12 years in Romania: follow-up of an open, randomised controlled trial. Lancet Psychiatry. 2015;2(7):625-34. doi: 10.1016/S2215-0366(15)00095-4. PubMed PMID: 26303560; PMCID: PMC4550037.

McLaughlin KA, Sheridan MA, Tibu F, Fox NA, Zeanah CH, Nelson CA, 3rd. Causal effects of the early caregiving environment on development of stress response systems in children. Proc Natl Acad Sci U S A. 2015;112(18):5637-42. doi: 10.1073/pnas.1423363112. PubMed PMID: 25902515; PMCID: PMC4426436.

*Review*:

Bick J, Nelson CA. Early Adverse Experiences and the Developing Brain. Neuropsychopharmacology. 2016;41(1):177-96. Epub 2015/09/04. doi: 10.1038/npp.2015.252. PubMed PMID: 26334107; PMCID: PMC4677140.

**Week 11. Critical Periods for Social and Emotional Development – Mechanisms and Factors Drawn from Animal Studies, 3/30/2023**

*Learning Objectives:*

* Review brain systems involved in social and emotional development
* Using primate studies, describe evidence for some of the environmental factors regulating social and emotional development during critical periods
* Using rodent studies, describe some neurobiological mechanisms by which these early environmental factors may influence brain circuits relating to social and emotional behavior

*Primary Source Readings (Please select three):*

Harlow HF. Total Social Isolation: Effects on Macaque Monkey Behavior. Science. 1965;148(3670):666. doi: 10.1126/science.148.3670.666-a. PubMed PMID: 17801949.

Harlow HF, Zimmermann RR. Affectional responses in the infant monkey; orphaned baby monkeys develop a strong and persistent attachment to inanimate surrogate mothers. Science. 1959;130(3373):421-32. PubMed PMID: 13675765.

Pena CJ, Kronman HG, Walker DM, Cates HM, Bagot RC, Purushothaman I, Issler O, Loh YE, Leong T, Kiraly DD, Goodman E, Neve RL, Shen L, Nestler EJ. Early life stress confers lifelong stress susceptibility in mice via ventral tegmental area OTX2. Science. 2017;356(6343):1185-8. doi: 10.1126/science.aan4491. PubMed PMID: 28619944; PMCID: PMC5539403.

**Week 12. Discussion of Paper Topics, 4/6/2023**

**Week 13. Critical Periods for Exposure to Neuromodulators, 4/13/2023**

*Learning Objectives:*

* Using the example of seratonin and dopamine, explore how neuromodulator levels influence the development of brain circuitry
* Use the concept of critical periods to understand the paradox of SSRI exposure in terms of conflicting outcomes on emotional behaviors during development versus adulthood
* Consider the implications of developmental changes in serotonin and dopamine for the development of psychopathology in adulthood

*Primary Source Readings:*

Ansorge MS, Zhou M, Lira A, Hen R, Gingrich JA. Early-life blockade of the 5-HT transporter alters emotional behavior in adult mice. Science. 2004;306(5697):879-81. doi: 10.1126/science.1101678. PubMed PMID: 15514160.

Malm H, Brown AS, Gissler M, Gyllenberg D, Hinkka-Yli-Salomaki S, McKeague IW, Weissman M, Wickramaratne P, Artama M, Gingrich JA, Sourander A. Gestational Exposure to Selective Serotonin Reuptake Inhibitors and Offspring Psychiatric Disorders: A National Register-Based Study. J Am Acad Child Adolesc Psychiatry. 2016;55(5):359-66. doi: 10.1016/j.jaac.2016.02.013. PubMed PMID: 27126849; PMCID: PMC4851729.

Yu Q, Teixeira CM, Mahadevia D, Huang Y, Balsam D, Mann JJ, Gingrich JA, Ansorge MS. Dopamine and serotonin signaling during two sensitive developmental periods differentially impact adult aggressive and affective behaviors in mice. Mol Psychiatry. 2014;19(6):688-98. Epub 2014/03/05. doi: 10.1038/mp.2014.10. PubMed PMID: 24589889; PMCID: PMC4311886.

**Week 14. Critical Period Disruption in Psychiatric Disorders Focusing on Schizophrenia, 4/20/2023**

*Learning Objectives:*

* Be able to describe key defining behavioral symptoms of schizophrenia and associated proxy behaviors in mice
* Discuss the evidence that developmental disruption may play a role in changes in brain circuitry related to schizophrenia

*Primary Source Readings:*

Benoit LJ, Holt ES, Posani L, Fusi S, Harris AZ, Canetta S, Kellendonk C. Adolescent thalamic inhibition leads to long-lasting impairments in prefrontal cortex function. Nat Neurosci. 2022;25(6):714-25. Epub 2022/05/20. doi: 10.1038/s41593-022-01072-y. PubMed PMID: 35590075; PMCID: PMC9202412.

Anticevic A, Haut K, Murray JD, Repovs G, Yang GJ, Diehl C, McEwen SC, Bearden CE, Addington J, Goodyear B, Cadenhead KS, Mirzakhanian H, Cornblatt BA, Olvet D, Mathalon DH, McGlashan TH, Perkins DO, Belger A, Seidman LJ, Tsuang MT, van Erp TG, Walker EF, Hamann S, Woods SW, Qiu M, Cannon TD. Association of Thalamic Dysconnectivity and Conversion to Psychosis in Youth and Young Adults at Elevated Clinical Risk. JAMA Psychiatry. 2015;72(9):882-91. Epub 2015/08/13. doi: 10.1001/jamapsychiatry.2015.0566. PubMed PMID: 26267151; PMCID: PMC4892891.

*Reviews:*

Benoit LJ, Canetta S, Kellendonk C. Thalamocortical Development: A Neurodevelopmental Framework for Schizophrenia. Biol Psychiatry. 2022;92(6):491-500. Epub 2022/05/14. doi: 10.1016/j.biopsych.2022.03.004. PubMed PMID: 35550792.

**Week 15. Reopening Adult Plasticity – Possibilities and Pitfalls, 4/27/2022**

*Learning Objectives:*

* Compare and contrast brain plasticity during development and in adulthood
* Discuss principles for opening critical periods during development and how they can be applied for the reopening of critical periods in adulthood
* Discuss the possibilities and pitfalls of reopening critical periods in adulthood

*Primary Source Readings:*

Clarkson AN, Huang BS, Macisaac SE, Mody I, Carmichael ST. Reducing excessive GABA-mediated tonic inhibition promotes functional recovery after stroke. Nature. 2010;468(7321):305-9. doi: 10.1038/nature09511. PubMed PMID: 21048709; PMCID: PMC3058798.

Yang WZ, Liu TT, Cao JW, Chen XF, Liu X, Wang M, Su X, Zhang SQ, Qiu BL, Hu WX, Liu LY, Ma L, Yu YC. Fear Erasure Facilitated by Immature Inhibitory Neuron Transplantation. Neuron. 2016;92(6):1352-67. Epub 2016/12/13. doi: 10.1016/j.neuron.2016.11.018. PubMed PMID: 27939579.

Mitchell JM, Bogenschutz M, Lilienstein A, Harrison C, Kleiman S, Parker-Guilbert K, Ot'alora GM, Garas W, Paleos C, Gorman I, Nicholas C, Mithoefer M, Carlin S, Poulter B, Mithoefer A, Quevedo S, Wells G, Klaire SS, van der Kolk B, Tzarfaty K, Amiaz R, Worthy R, Shannon S, Woolley JD, Marta C, Gelfand Y, Hapke E, Amar S, Wallach Y, Brown R, Hamilton S, Wang JB, Coker A, Matthews R, de Boer A, Yazar-Klosinski B, Emerson A, Doblin R. MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study. Nat Med. 2021;27(6):1025-33. Epub 2021/05/12. doi: 10.1038/s41591-021-01336-3. PubMed PMID: 33972795; PMCID: PMC8205851.

*Reviews:*

Hensch TK, Bilimoria PM. Re-opening Windows: Manipulating Critical Periods for Brain Development. Cerebrum. 2012;2012:11. PubMed PMID: 23447797; PMCID: PMC3574806.

Lepow L, Morishita H, Yehuda R. Critical Period Plasticity as a Framework for Psychedelic-Assisted Psychotherapy. Front Neurosci. 2021;15:710004. Epub 2021/10/08. doi: 10.3389/fnins.2021.710004. PubMed PMID: 34616272; PMCID: PMC8488335.