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REVIEW

Schizophrenia, Bipolar Disorder and Pre-Attentional Inhibitory Deficits

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Abstract: According to recent findings schizophrenia and bipolar disorder as separate disease entities manifest similarities in neuropsychological functioning. Typical disturbances in both disorders are related to sensory gating deficits characterized by decreased inhibitory functions in responses to various insignificant perceptual signals which are experimentally tested by event related potentials (ERP) and measured P50 wave. In this context, recent findings implicate that disrupted binding and disintegration of consciousness in schizophrenia and bipolar disorder that are related to inhibitory deficits reflected in P50 response may explain similarities in psychotic disturbances in both disorders. With this aim, this review summarizes literature about P50 in both schizophrenia and bipolar disorder.

Keywords: bipolar disorder, neural synchrony, event related potentials, inhibition, P50, schizophrenia

Introduction

According to recent findings schizophrenia and bipolar disorder as separate disease entities manifest similarities in neuropsychological functioning profile[1–3] and accumulating evidence also indicates an overlap in various neurobiological changes such as genetic susceptibility, neurochemical markers and other neurophysiological parameters.[1,4–7] Current findings also indicate that significant clinical similarities between both disorders frequently occur.[8–10] For example, frequent manifestations of psychotic symptoms such as hallucinations, delusions and other symptoms of thought disorders were reported in patients with bipolar illness.[10–12] On the other hand in patients with schizophrenia may manifest typical bipolar symptoms.[9,13] Recent findings strongly suggest that both disorders are specifically linked to basic changes in neural correlates of consciousness and integrated cognitive functioning closely related to EEG activities typically presented as synchronous neural oscillations mainly in gamma frequency band which is critical for large-scale integration of distributed neural assemblies.[14,15] These EEG findings are also in agreement with brain imaging studies that reported various structural abnormalities mainly in prefrontal cortex, temporal lobe and limbic structures in schizophrenia as well as bipolar disorder.[16–18]

Recent data indicate that large scale synchronization related to gamma activity is related to global connections of large groups of neurons reflecting activities of interneural excitations in the GABAergic systems.[19–21] These characteristic changes reported in mental disorders such as bipolar disorders or schizophrenia[15,22] link GABA deficits with perceptual and cognitive disturbances.[23–25] GABA systems specifically influence neural networks involved in cognitive and emotional processing and modulates noradrenergic, dopaminergic and serotonergic neural activities.[26] In pathological conditions GABAergic inter-neurons through cortico-limbic connections influence inhibitory processes in cerebral cortex, which are typically disrupted in schizophrenia and bipolar patients.[27–29] In addition connections between both disorders possible might be explained also by reciprocal relationships between GABAergic and dopaminergic systems.[27,30]

These findings also indicate that typical changes in neural oscillations and synchronization are specifically linked to inhibitory deficits that may be measured using event-related potentials (ERP). In addition reported ERP studies of evoked

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responses also show that the P50 inhibitory (suppression) deficits may be specifically related to schizophrenia and bipolar disorder with psychotic symptoms.[31,32]

P50 and Inhibitory Deficits

Recent findings indicate that P50 wave is related to brain processes linked to large scale neural binding mainly in prefrontal and temporo-parietal cortices[33] These processes are reflected by ERPs mainly in early stages of the information processing at about 50 msec after a stimulus presentation[32] in the process of active gating when the S1 stimulus tends to inhibit and "filter out" the response to following identical stimulus (S2).[34–40] For example, Volkov and Galazyuk[39] "in a more general context proposed that synchronous activations of large number of cortical neurons by a short stimulus result in coordinated release of large amount inhibitory transmitters into the synaptic connections, which enables a relatively prolonged hyperpolarization of post-synaptic neurons. As a consequence, repeated stimulus leads to a constant release of a small amount of the transmitter into the synaptic cleft which may explain the process of continued inhibition". These mechanisms enable to distinguish non-identical perceptual signals mainly via processing by different neurons which enable "unhabituated response".[41–43]

Basic role in this inhibitory processes and habituation to repeated stimuli play CA3-CA4 areas of the hippocampus and its cholinergic inputs from the septal nucleus mediated by low-affinity nicotinic receptors affecting CA3-CA4 interneurons and these GABAergic interneurons transiently inhibit pyramidal neurons, and mediate gating of the second stimulus during sensory stimulation usually used in ERP experiments.[27,44–46] These pyramidal neurons of the CA3 region of the hippocampus were therefore identified as sources of brain evoked potentials responding for "habituation" related to repeated perceptual signals processed via cholinergic inhibitory interneurons in the hippocampus. Further findings show that activities of these interneurons may lead to "bursts" activities releasing GABA molecules (gamma aminobutyric acid) which enables to activate presynaptic GABA-B receptors in CA3 pyramidal neurons that block excitatory glutamate release and the CA3 pyramidal neurons are not available for response to the second stimulus.[20,21,47–53]

However, other brain regions are also indispensable for the pre-attentional inhibitory deficits, the pulvinar nucleus in the thalamus in particular. Previous studies have shown that the pulvinar nucleus is mutually and extensively connected with the prefrontal cortex, sensory cortex, superior colliculus and amygdala,[54] and plays very important roles in the contextual bottom-up inhibitory multi-sensory gating.[55–57] It is also involved in the cortico cortical synchronization and attention.[58] In addition, the dysfunction of the pulvinar nucleus has been reported to be associated with the sensory and cognitive deficits in schizophrenia.[59,60]

P50 in Schizophrenia

Sensory processing deficits in schizophrenia due to disturbances in attentional filtering of "meaningful" signals[61,62] were reported by studies utilizing "auditory evoked potentials" and mainly reflected by P50 wave[63,64] which might help to explain relationships between clinical symptoms and the brain insufficiency to inhibit "unsignificant" sensory signals.[49,51,65,66] One of the possible consequences of these "sensory gating deficits" reported in schizophrenia may lead to neural hyper-excitability[67,68] reflecting P50 gating disturbances.[69,70]

These findings indicate that schizophrenia patients manifest typical disturbances of dishabituation mechanisms which determine that schizophrenia patients experience "overload" of information.[71,72] In this context, many studies have shown that the P50 sensory gating ratio in a paired click task is higher in patients with schizophrenia compared to healthy control subjects indicating more effective sensory gating.[32] Meta-analysis by Patterson et al[61] shows that the differences between patients and controls in P50 latency were no significant.[61] Based on these findings Patterson et al[61] concluded that their meta-analysis confirms the existence of ERP deficits in schizophrenia with significance similar to the most robust findings reported in neuroimaging studies of schizophrenia. Similar conclusions found also several others meta-analyses or reviews, which have shown that sensory gating impairments in early stages of schizophrenia become more prominent in chronic stages of the disease.[61,63,73] For example, meta-analytical study by Chang et al[73] also confirmed that sensory gating deficits in schizophrenia patients are well-documented and that future studies need to clarify more detailed mechanisms of "gating"- related disturbances and their links to the disease progression[73–75] suggesting that P50 disturbances might reflect deficits in neural connectivity.[76]

P50 in Bipolar Disorder

In schizophrenia typical inhibitory disturbances and deficits in executive functions are linked to information overload in neural processing, on the other hand in bipolar disorder similar inhibitory deficit is related to deficits in action planning that disables coordinated responses which represent typical clinical characteristics of bipolar disorder.[77] In this process impulsivity likely represents a predisposition toward rapid unplanned reactions to internal or external stimuli resulting from impaired neural information processing and executive dysfunctions.[78] Impulsivity mainly is linked to pre-attentional and early attentional neural information processing and impulsive behavior increases probability of action without conscious reflection with excessive spontaneous "context independent" behavior.[79,80] Level of impulsivity may also specifically characterize mania, depression, and anxiety, and recent findings show that these neurophysiological changes associated with impulsivity and attentional deficits related to disturbed executive functions in bipolar disorder are also typically linked to disinhibition of P50 and disturbed sensory gating.[78,80,81]

These findings also show that diminished P50 suppression in bipolar disorder subjects with a history of psychosis might represent a mediating indicator of vulnerability in both trait- and state-like components. In this context several researchers suggest that abnormal P50 sensory gating deficit might represent state markers correlated with symptoms of mood disorders.[82,83] For example, Baker et al[82] found negative relationship between P50 ratios and Brief Psychiatric Rating Scale (BPRS) rating in depressive patients and several studies also found larger P50 ratios in bipolar groups with a history of psychosis.[31,84] Another study[31] focused on associations between psychosis and auditory P50 suppression in bipolar disorder reported that bipolar patients with a history of psychosis manifested significantly decreased P50 suppression in comparison to healthy controls, but significantly higher levels of suppression than patients with schizophrenia. These findings show that bipolar patients without history of psychosis exhibit P50 suppression ratios similar to healthy controls[31] which suggests that vulnerability to psychosis may represent a common psychophysiological mechanism that might connect bipolar disorder and schizophrenia.

Conclusion

According to recent findings recognition process related to stimuli received from the external world in its principle most likely is based on repeated multilevel comparisons of various competitive neural patterns representing possible interpretations of the received information during selective attentional processing and selected interpretation from this competition and its neural pattern represents the output of the recognition process.[85–88] The brain mechanisms that enable multilevel information processing are likely regulated within the framework of contextual understanding which strictly determines what details of the information are important for the whole coherent context.[89–93]

These findings suggest that typical deficits and "mental disintegration" in cognitive processing in schizophrenia and bipolar disorder might be related to executive signals that in the framework of required context determine sensitivity to various details needed for contextual processing the so-called "cognitive bias" which seems to be important for various mental disorders.[94–100] In this sense "mental disintegration" in both schizophrenia and bipolar disorder are linked to disturbances in synchronized oscillations dynamically linking neurons into assemblies through the process of "binding" mainly at gamma frequencies (30–100 Hz) that are closely associated with sensory processing, attentional selection, effective sensory-motor integration and also play an important role in working and long-term memory.[101–106]

According to recent findings disruptions of consciousness and "mental integration" in schizophrenia are related to disturbances of "neural binding"[14,22] and similar disturbances were reported also in bipolar disorders.[27,107,108] In this context, major supportive findings strongly suggest a link between gamma activity and GABAergic postsynaptic excitation.[19–21] In this overall context, disrupted binding and disintegration of consciousness in schizophrenia and bipolar disorder likely are related to inhibitory deficits reflected in P50 response that may explain similarities in psychotic disturbances in both disorder. Nevertheless this review cannot claim that P50 disturbance is really a similarity that is unique to those disorders as it might be a feature that is present also in other disorders that manifest psychotic symptoms (for example PTSD, substance use and others as described diagnostic manuals DSM-V or ICD-10). Similarly, the role of impulsivity in bipolar disorder and its link to P50 may mean that P50 disturbance might not be unique to psychotic symptoms. Furthermore, there are other psychiatric disorders that are associated with high impulsivity (such as ADHD or

borderline personality disorders, please see DSM-V or ICD-10), so the question might be whether these other disorders also share same features as bipolar disorder and schizophrenia. To resolve these limitations needs other detailed analyses of available published findings and further research which could provide more detailed knowledge about neurobiological basis of cognitive-affective processes related to mental disorders.

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Disclosure

The authors declare that there are no conflicts of interest.

References

1. Murray RM, Sham P, Van Os J, Zanelli J, Cannon M, McDonald C. A developmental model for similarities and dissimilarities between schizophrenia and bipolar disorder. *Schizophr Res*. 2004;71:405–416. doi:10.1016/j.schres.2004.03.002
2. Addington J, Addington D. Attentional vulnerability indicators in schizophrenia and bipolar disorder. *Schizophr Res*. 1997;23:197–204. doi:10.1016/S0920-9964(96)00105-3
3. Seidman LJ, Kremen WS, Koren D, Faraone SV, Goldstein JM, Tsuang MT. A comparative profile analysis of neuropsychological functioning in patients with schizophrenia and bipolar psychoses. *Schizophr Res*. 2002;53:31–44. doi:10.1016/S0920-9964(01)00162-1
4. Craddock N, O'Donovan MC, Owen MJ. Genes for schizophrenia and bipolar disorder? Implications for psychiatric nosology. *Schizophr Bull*. 2006;32:9–16. doi:10.1093/schbul/sbj033
5. Torrey EF, Barci BM, Webster MJ, Bartko JJ, Meador-Woodruff JH, Knable MB. Neurochemical markers for schizophrenia, bipolar disorder, and major depression in postmortem brains. *Biol Psychiatry*. 2005;57:252–260. doi:10.1016/j.biopsych.2004.10.019
6. Kaymaz N, van Os J. Murray et al. (2004) revisited: is bipolar disorder identical to schizophrenia without developmental impairment? *Acta Psychiatr Scand*. 2009;120:249–252. doi:10.1111/j.1600-0447.2009.01472.x
7. Berrettini WH. Are schizophrenic and bipolar disorders related? A review of family and molecular studies. *Biol Psychiatry*. 2000;48:531–538. doi:10.1016/S0006-3223(00)00883-0
8. Taylor MA. Are schizophrenia and affective disorder related? A selective literature review. *Am J Psychiatry*. 1992;149:22–32.
9. Lapensee MA. A review of schizoaffective disorder: I. Current concepts. *Can J Psychiatry*. 1992;37:335–346. doi:10.1177/070674379203700507
10. Harrow M, MacDonald AW, Sands JR, Silverstein ML. Vulnerability to delusions over time in schizophrenia and affective disorders. *Schizophr Bull*. 1995;21:95–109. doi:10.1093/schbul/21.1.95
11. Grossman LS, Harrow M, Sands JR. Features associated with thought disorder in manic patients at 2–4-year follow-up. *Am J Psychiatry*. 1986;143:306–311.
12. Ketter TA, Wang PW, Becker OV, Nowakowska C, Yang Y. Psychotic bipolar disorders: dimensionally similar to or categorically different from schizophrenia? *J Psychiatr Res*. 2004;38:47–61. doi:10.1016/S0022-3956(03)00099-2
13. Cheniaux E, Landeira-Fernandez J, Lessa Telles L, et al. Does schizoaffective disorder really exist? A systematic review of the studies that compared schizoaffective disorder with schizophrenia or mood disorders. *J Affect Disord*. 2008;106:209–217. doi:10.1016/j.jad.2007.07.009
14. Lee KH, Williams LM, Breakspear M, Gordon E. Synchronous gamma activity: a review and contribution to an integrative neuroscience model of schizophrenia. *Brain Res Brain Res Rev*. 2003;41:57–78. doi:10.1016/S0165-0173(02)00220-5
15. Ozerdem A, Guntekin B, Saatci E, Tunca Z, Basar E. Disturbance in long distance gamma coherence in bipolar disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2010;34:861–865. doi:10.1016/j.pnpbp.2010.04.001
16. Kasai K, Iwanami A, Yamasue H, Kuroki N, Nakagome K, Fukuda M. Neuroanatomy and neurophysiology in schizophrenia. *Neurosci Res*. 2002;43:93–110. doi:10.1016/S0168-0102(02)00023-8
17. Whalley HC, Papmeyer M, Sprooten E, Lawrie SM, Sussmann JE, McIntosh AM. Review of functional magnetic resonance imaging studies comparing bipolar disorder and schizophrenia. *Bipolar Disord*. 2012;14:411–431. doi:10.1111/j.1399-5618.2012.01016.x
18. Strakowski SM, Adler CM, Almeida J, et al. The functional neuroanatomy of bipolar disorder: a consensus model. *Bipolar Disord*. 2012;14:313–325. doi:10.1111/j.1399-5618.2012.01022.x
19. Fuchs EC, Doheny H, Faulkner H, et al. Genetically altered AMPA-type glutamate receptor kinetics in interneurons disrupt long-range synchrony of gamma oscillation. *Proc Natl Acad Sci U S A*. 2001;98:3571–3576. doi:10.1073/pnas.051631898
20. Moxon KA, Gerhardt GA, Gulinello M, Adler LE. Inhibitory control of sensory gating in a computer model of the CA3 region of the hippocampus. *Biol Cybern*. 2003;88:247–264. doi:10.1007/s00422-002-0373-7
21. Klausberger T, Somogyi P. Neuronal diversity and temporal dynamics: the unity of hippocampal circuit operations. *Science*. 2008;321:53–57. doi:10.1126/science.1149381
22. Uhlhaas PJ, Singer W. Abnormal neural oscillations and synchrony in schizophrenia. *Nat Rev Neurosci*. 2010;11:100–113. doi:10.1038/nrn2774
23. Lewis DA, Curley AA, Glausier JR, Volk DW. Cortical parvalbumin interneurons and cognitive dysfunction in schizophrenia. *Trends Neurosci*. 2012;35:57–67. doi:10.1016/j.tins.2011.10.004
24. Petty F. GABA and mood disorders: a brief review and hypothesis. *J Affect Disord*. 1995;34:275–281. doi:10.1016/0165-0327(95)00025-I
25. Kim DJ, Bolbecker AR, Howell J, et al. Disturbed resting state EEG synchronization in bipolar disorder: a graph-theoretic analysis. *NeuroImage Clin*. 2013;2:414–423. doi:10.1016/j.nicl.2013.03.007

26. Carlsson A, Waters N, Holm-Waters S, Tedroff J, Nilsson M, Carlsson ML. Interactions between monoamines, glutamate, and GABA in schizophrenia: new evidence. *Annu Rev Pharmacol Toxicol*. 2001;41:237–260. doi:10.1146/annurev.pharmtox.41.1.237
27. Benes FM, Berretta S. GABAergic interneurons: implications for understanding schizophrenia and bipolar disorder. *Neuropsychopharmacology*. 2001;25:1–27. doi:10.1016/S0893-133X(01)00225-1
28. Nakazawa K, Zsiros V, Jiang Z, et al. GABAergic interneuron origin of schizophrenia pathophysiology. *Neuropharmacology*. 2012;62:1574–1583. doi:10.1016/j.neuropharm.2011.01.022
29. Levinson AJ, Young LT, Fitzgerald PB, Daskalakis ZJ. Cortical inhibitory dysfunction in bipolar disorder: a study using transcranial magnetic stimulation. *J Clin Psychopharmacol*. 2007;27:493–497. doi:10.1097/jcp.0b013e31814ce524
30. Kalkman HO, Loetscher E. GAD(67): the link between the GABA-deficit hypothesis and the dopaminergic- and glutamatergic theories of psychosis. *J Neural Transm*. 2003;110:803–812. doi:10.1007/s00702-003-0826-8
31. Olincy A, Martin L. Diminished suppression of the P50 auditory evoked potential in bipolar disorder subjects with a history of psychosis. *Am J Psychiatry*. 2005;162:43–49. doi:10.1176/appi.ajp.162.1.43
32. de Wilde OM, Bour LJ, Dingemans PM, Koelman JH, Linszen DH. A meta-analysis of P50 studies in patients with schizophrenia and relatives: differences in methodology between research groups. *Schizophr Res*. 2007;97:137–151. doi:10.1016/j.schres.2007.04.028
33. Boutros NN, Gjini K, Eickhoff SB, Urbach H, Pflieger ME. Mapping repetition suppression of the P50 evoked response to the human cerebral cortex. *Clin Neurophysiol*. 2013;124:675–685. doi:10.1016/j.clinph.2012.10.007
34. Boutros NN, Belger A. Midlatency evoked potentials attenuation and augmentation reflect different aspects of sensory gating. *Biol Psychiatry*. 1999;45:917–922. doi:10.1016/S0006-3223(98)00253-4
35. Galazyuk AV, Feng AS. Encoding of sound duration by neurons in the auditory cortex of the little brown bat, Myotis lucifugus. *J Comp Physiol A*. 1997;180:301–311. doi:10.1007/s003590050050
36. Tan AY, Zhang LI, Merzenich MM, Schreiner CE. Tone-evoked excitatory and inhibitory synaptic conductances of primary auditory cortex neurons. *J Neurophysiol*. 2004;92:630–643. doi:10.1152/jn.01020.2003
37. Miller CL, Freedman R. The activity of hippocampal interneurons and pyramidal cells during the response of the hippocampus to repeated auditory stimuli. *Neuroscience*. 1995;69:371–381. doi:10.1016/0306-4522(95)00249-I
38. Mears RP, Klein AC, Cromwell HC. Auditory inhibitory gating in medial prefrontal cortex: single unit and local field potential analysis. *Neuroscience*. 2006;141:47–65. doi:10.1016/j.neuroscience.2006.03.040
39. Volkov IO, Galazyuk AV. Peculiarities of inhibition in cat auditory cortex neurons evoked by tonal stimuli of various durations. *Exp Brain Res*. 1992;91:115–120. doi:10.1007/BF00230019
40. Wehr M, Zador AM. Balanced inhibition underlies tuning and sharpens spike timing in auditory cortex. *Nature*. 2003;426:442–446. doi:10.1038/nature02116
41. Boutros NN, Belger A, Campbell D, D'Souza C, Krystal J. Comparison of four components of sensory gating in schizophrenia and normal subjects: a preliminary report. *Psychiatry Res*. 1999;88:119–130. doi:10.1016/S0165-1781(99)00074-8
42. Korzyukov O, Pflieger ME, Wagner M, et al. Generators of the intracranial P50 response in auditory sensory gating. *Neuroimage*. 2007;35:814–826. doi:10.1016/j.neuroimage.2006.12.011
43. Sakai M, Chimoto S, Qin L, Sato Y. Neural mechanisms of interstimulus interval-dependent responses in the primary auditory cortex of awake cats. *BMC Neurosci*. 2009;10:10. doi:10.1186/1471-2202-10-10
44. Freedman R, Adams CE, Leonard S. The alpha7-nicotinic acetylcholine receptor and the pathology of hippocampal interneurons in schizophrenia. *J Chem Neuroanat*. 2000;20:299–306. doi:10.1016/S0891-0618(00)00109-5
45. Bickford-Wimer PC, Nagamoto H, Johnson R, et al. Auditory sensory gating in hippocampal neurons: a model system in the rat. *Biol Psychiatry*. 1990;27:183–192. doi:10.1016/0006-3223(90)90648-L
46. Miller CL, Freedman R. Medial septal neuron activity in relation to an auditory sensory gating paradigm. *Neuroscience*. 1993;55:373–380. doi:10.1016/0306-4522(93)90506-B
47. Homayoun H, Moghaddam B. NMDA receptor hypofunction produces opposite effects on prefrontal cortex interneurons and pyramidal neurons. *J Neurosci*. 2007;27:11496–11500. doi:10.1523/JNEUROSCI.2213-07.2007
48. Luntz-Leybman V, Bickford PC, Freedman R. Cholinergic gating of response to auditory stimuli in rat hippocampus. *Brain Res*. 1992;587:130–136. doi:10.1016/0006-8993(92)91437-J
49. Adler LE, Olincy A, Waldo M, et al. Schizophrenia, sensory gating, and nicotinic receptors. *Schizophr Bull*. 1998;24:189–202. doi:10.1093/oxfordjournals.schbul.a033320
50. Brinkman MJ, Stauder JE. Development and gender in the P50 paradigm. *Clin Neurophysiol*. 2007;118:1517–1524. doi:10.1016/j.clinph.2007.04.002
51. Freedman R, Olincy A, Ross RG, et al. The genetics of sensory gating deficits in schizophrenia. *Curr Psychiatry Rep*. 2003;5:155–161. doi:10.1007/s11920-003-0032-2
52. Adler LE, Hoffer L, Nagamoto HT, Waldo MC, Kisley MA, Giffith JM. Yohimbine impairs P50 auditory sensory gating in normal subjects. *Neuropsychopharmacology*. 1994;10:249–257. doi:10.1038/npp.1994.28
53. Oranje B, Glenthoj BY. Clonidine normalizes levels of P50 gating in patients with schizophrenia on stable medication. *Schizophr Bull*. 2013;39:684–691. doi:10.1093/schbul/sbs071
54. Zhou N, Masterson SP, Damron JK, Guido W, Bickford ME. The mouse pulvinar nucleus links the lateral extrastriate cortex, striatum, and amygdala. *J Neurosci*. 2018;38:347–362. doi:10.1523/JNEUROSCI.1279-17.2017
55. Chou XL, Fang Q, Yan L, et al. Contextual and cross-modality modulation of auditory cortical processing through pulvinar mediated suppression. *Elife*. 2020;9. doi:10.7554/eLife.54157
56. Fang Q, Chou XL, Peng B, Zhong W, Zhang LI, Tao HW. A differential circuit via retino-colliculo-pulvinar pathway enhances feature selectivity in visual cortex through surround suppression. *Neuron*. 2020;105:355–69 e6. doi:10.1016/j.neuron.2019.10.027
57. Ibrahim LA, Mesik L, Ji XY, et al. Cross-modality sharpening of visual cortical processing through layer-1-mediated inhibition and disinhibition. *Neuron*. 2016;89:1031–1045. doi:10.1016/j.neuron.2016.01.027
58. Saalmann YB, Pinsk MA, Wang L, Li X, Kastner S. The pulvinar regulates information transmission between cortical areas based on attention demands. *Science*. 2012;337:753–756. doi:10.1126/science.1223082

59. Shen L, Liu D, Huang Y. Hypothesis of subcortical visual pathway impairment in schizophrenia. *Med Hypotheses*. 2021;156:110686. doi:10.1016/j.mehy.2021.110686
60. Zhuo C, Tian H, Fang T, et al. Neural mechanisms underlying visual and auditory processing impairments in schizophrenia: insight into the etiology and implications for tailoring preventive and therapeutic interventions. *Am J Transl Res*. 2020;12:7657–7669.
61. Patterson JV, Hetrick WP, Boutros NN, et al. P50 sensory gating ratios in schizophrenics and controls: a review and data analysis. *Psychiatry Res*. 2008;158:226–247. doi:10.1016/j.psychres.2007.02.009
62. Olincy A, Braff DL, Adler LE, et al. Inhibition of the P50 cerebral evoked response to repeated auditory stimuli: results from the Consortium on Genetics of Schizophrenia. *Schizophr Res*. 2010;119:175–182. doi:10.1016/j.schres.2010.03.004
63. Bramon E, Rabe-Hesketh S, Sham P, Murray RM, Frangou S. Meta-analysis of the P300 and P50 waveforms in schizophrenia. *Schizophr Res*. 2004;70:315–329. doi:10.1016/j.schres.2004.01.004
64. Onitsuka T, Oribe N, Nakamura I, Kanba S. Review of neurophysiological findings in patients with schizophrenia. *Psychiatry Clin Neurosci*. 2013;67:461–470. doi:10.1111/pcn.12090
65. Rajji TK, Miranda D, Mulsant BH. Cognition, function, and disability in patients with schizophrenia: a review of longitudinal studies. *Can J Psychiatry*. 2014;59:13–17. doi:10.1177/070674371405900104
66. Hetrick WP, Erickson MA, Smith DA. Phenomenological dimensions of sensory gating. *Schizophr Bull*. 2012;38:178–191. doi:10.1093/schbul/sbq054
67. Adler LE, Pachtman E, Franks RD, Pecevich M, Waldo MC, Freedman R. Neurophysiological evidence for a defect in neuronal mechanisms involved in sensory gating in schizophrenia. *Biol Psychiatry*. 1982;17:639–654.
68. Freedman R, Waldo M, Bickford-Wimer P, Nagamoto H. Elementary neuronal dysfunctions in schizophrenia. *Schizophr Res*. 1991;4:233–243. doi:10.1016/0920-9964(91)90035-P
69. Martin LF, Freedman R. Schizophrenia and the alpha7 nicotinic acetylcholine receptor. *Int Rev Neurobiol*. 2007;78:225–246.
70. Zhang XY, Liu L, Liu S, et al. Short-term tropisetron treatment and cognitive and P50 auditory gating deficits in schizophrenia. *Am J Psychiatry*. 2012;169:974–981. doi:10.1176/appi.ajp.2012.11081289
71. Javitt DC. When doors of perception close: bottom-up models of disrupted cognition in schizophrenia. *Annu Rev Clin Psychol*. 2009;5:249–275. doi:10.1146/annurev.clinpsy.032408.153502
72. Williams LE, Blackford JU, Luksik A, Gauthier I, Heckers S. Reduced habituation in patients with schizophrenia. *Schizophr Res*. 2013;151:124–132. doi:10.1016/j.schres.2013.10.017
73. Chang WP, Arfken CL, Sangal MP, Boutros NN. Probing the relative contribution of the first and second responses to sensory gating indices: a meta-analysis. *Psychophysiology*. 2011;48:980–992. doi:10.1111/j.1469-8986.2010.01168.x
74. Brockhaus-Dumke A, Schultze-Lutter F, Mueller R, et al. Sensory gating in schizophrenia: P50 and N100 gating in antipsychotic-free subjects at risk, first-episode, and chronic patients. *Biol Psychiatry*. 2008;64:376–384. doi:10.1016/j.biopsych.2008.02.006
75. Sanchez-Morla EM, Garcia-Jimenez MA, Barabash A, et al. P50 sensory gating deficit is a common marker of vulnerability to bipolar disorder and schizophrenia. *Acta Psychiatr Scand*. 2008;117:313–318. doi:10.1111/j.1600-0447.2007.01141.x
76. Magnee MJ, Oranje B, van Engeland H, Kahn RS, Kemner C. Cross-sensory gating in schizophrenia and autism spectrum disorder: EEG evidence for impaired brain connectivity? *Neuropsychologia*. 2009;47:1728–1732. doi:10.1016/j.neuropsychologia.2009.02.012
77. Najt P, Perez J, Sanches M, Peluso MA, Glahn D, Soares JC. Impulsivity and bipolar disorder. *Eur Neuropsychopharmacol*. 2007;17:313–320. doi:10.1016/j.euroneuro.2006.10.002
78. Barratt ES. Impulsivity: integrating cognitive, behavioral, biological, and environmental data. 1993.
79. Swann AC, Steinberg JL, Lijffijt M, Moeller FG. Impulsivity: differential relationship to depression and mania in bipolar disorder. *J Affect Disord*. 2008;106:241–248. doi:10.1016/j.jad.2007.07.011
80. Swann AC, Lijffijt M, Lane SD, et al. Pre-attentive information processing and impulsivity in bipolar disorder. *J Psychiatr Res*. 2013;47:1917–1924. doi:10.1016/j.jpsychires.2013.08.018
81. Lijffijt M, Moeller FG, Boutros NN, et al. Diminished P50, N100 and P200 auditory sensory gating in bipolar I disorder. *Psychiatry Res*. 2009;167:191–201. doi:10.1016/j.psychres.2008.04.001
82. Baker N, Adler LE, Franks RD, et al. Neurophysiological assessment of sensory gating in psychiatric inpatients: comparison between schizophrenia and other diagnoses. *Biol Psychiatry*. 1987;22:603–617. doi:10.1016/0006-3223(87)90188-0
83. Adler LE, Gerhardt GA, Franks R, et al. Sensory physiology and catecholamines in schizophrenia and mania. *Psychiatry Res*. 1990;31:297–309. doi:10.1016/0165-1781(90)90099-Q
84. Schulze KK, Hall MH, McDonald C, et al. P50 auditory evoked potential suppression in bipolar disorder patients with psychotic features and their unaffected relatives. *Biol Psychiatry*. 2007;62:121–128. doi:10.1016/j.biopsych.2006.08.006
85. Baars BJ. *A Cognitive Theory of Consciousness*. Cambridge University Press; 1993.
86. Baars BJ. The conscious access hypothesis: origins and recent evidence. *Trends Cogn Sci*. 2002;6:47–52. doi:10.1016/S1364-6613(00)01819-2
87. Desimone R, Duncan J. Neural mechanisms of selective visual attention. *Annu Rev Neurosci*. 1995;18:193–222. doi:10.1146/annurev.ne.18.030195.001205
88. Kanwisher N. Neural events and perceptual awareness. *Cognition*. 2001;79:89–113. doi:10.1016/S0010-0277(00)00125-6
89. Felleman DJ, Van Essen DC. Distributed hierarchical processing in the primate cerebral cortex. *Cereb Cortex*. 1991;1:1–47. doi:10.1093/cercor/1.1.1
90. Mesulam MM. From sensation to cognition. *Brain*. 1998;121(Pt 6):1013–1052. doi:10.1093/brain/121.6.1013
91. Nadel L, Jacobs WJ. Traumatic memory is special. *Curr Dir Psychol Sci*. 1998;7:154–157. doi:10.1111/1467-8721.ep10836842
92. Lavenex P, Amaral DG. Hippocampal-neocortical interaction: a hierarchy of associativity. *Hippocampus*. 2000;10:420–430. doi:10.1002/1098-1063(2000)10:4<420::AID-HIPO8>3.0.CO;2-5
93. Bob P. *Brain, Mind and Consciousness: Advances in Neuroscience Research*. Springer; 2011.
94. Gilbert CD, Wiesel TN. The influence of contextual stimuli on the orientation selectivity of cells in primary visual cortex of the cat. *Vision Res*. 1990;30:1689–1701. doi:10.1016/0042-6989(90)90153-C
95. Francis G, Grossberg S, Mingolla E. Cortical dynamics of feature binding and reset: control of visual persistence. *Vision Res*. 1994;34:1089–1104. doi:10.1016/0042-6989(94)90012-4

96. Grossberg S, Grunewald A. Cortical synchronization and perceptual framing. *J Cogn Neurosci*. 1997;9:117–132. doi:10.1162/jocn.1997.9.1.117
97. Gray CM. The temporal correlation hypothesis of visual feature integration: still alive and well. *Neuron*. 1999;24:31–47, 111–125. doi:10.1016/s0896-6273(00)80820-x
98. Ito M, Gilbert CD. Attention modulates contextual influences in the primary visual cortex of alert monkeys. *Neuron*. 1999;22:593–604. doi:10.1016/S0896-6273(00)80713-8
99. Raizada RD, Grossberg S. Context-sensitive binding by the laminar circuits of V1 and V2: a unified model of perceptual grouping, attention, and orientation contrast. *Vis cogn*. 2001;8:431–466. doi:10.1080/13506280143000070
100. Kang K, Williams LM, Hermens D, Gordon E. Neurophysiological markers of contextual processing: the relationship between P3b and Gamma synchrony and their modulation by arousal, performance and individual differences. *Brain Res Cogn Brain Res*. 2005;25:472–483. doi:10.1016/j.cogbrainres.2005.07.008
101. Singer W. Consciousness and the binding problem. *Ann N Y Acad Sci*. 2001;929:123–146. doi:10.1111/j.1749-6632.2001.tb05712.x
102. Varela F, Lachaux JP, Rodriguez E, Martinerie J. The brainweb: phase synchronization and large-scale integration. *Nat Rev Neurosci*. 2001;2:229–239. doi:10.1038/35067550
103. Fell J, Fernandez G, Klaver P, Elger CE, Fries P. Is synchronized neuronal gamma activity relevant for selective attention? *Brain Res Brain Res Rev*. 2003;42:265–272. doi:10.1016/S0165-0173(03)00178-4
104. Womelsdorf T, Fries P. The role of neuronal synchronization in selective attention. *Curr Opin Neurobiol*. 2007;17:154–160. doi:10.1016/j.conb.2007.02.002
105. Jensen O, Kaiser J, Lachaux JP. Human gamma-frequency oscillations associated with attention and memory. *Trends Neurosci*. 2007;30:317–324. doi:10.1016/j.tins.2007.05.001
106. Fries P. Neuronal gamma-band synchronization as a fundamental process in cortical computation. *Annu Rev Neurosci*. 2009;32:209–224. doi:10.1146/annurev.neuro.051508.135603
107. Guidotti A, Pesold C, Costa E. New neurochemical markers for psychosis: a working hypothesis of their operation. *Neurochem Res*. 2000;25:1207–1218. doi:10.1023/A:1007635927069
108. Basar E. Brain oscillations in neuropsychiatric disease. *Dialogues Clin Neurosci*. 2013;15:291–300.