Neuroinflammation and cognition across psychiatric conditions

Célia Fourrier,1 Gaurav Singhal,1 and Bernhard T. Baune2*

1 Discipline of Psychiatry, University of Adelaide, Adelaide, Australia
2 Department of Psychiatry, Melbourne Medical School, The University of Melbourne, Melbourne, Australia

Cognitive impairments reported across psychiatric conditions (ie, major depressive disorder, bipolar disorder, schizophrenia, and posttraumatic stress disorder) strongly impair the quality of life of patients and the recovery of those conditions. There is therefore a great need for consideration for cognitive dysfunction in the management of psychiatric disorders. The redundant pattern of cognitive impairments across such conditions suggests possible shared mechanisms potentially leading to their development. Here, we review for the first time the possible role of inflammation in cognitive dysfunctions across psychiatric disorders. Raised inflammatory processes (microglia activation and elevated cytokine levels) across diagnoses could therefore disrupt neurobiological mechanisms regulating cognition, including Hebbian and homeostatic plasticity, neurogenesis, neurotrophic factor, the HPA axis, and the kynurenine pathway. This redundant association between elevated inflammation and cognitive alterations across psychiatric disorders hence suggests that a cross-disorder approach using pharmacological and nonpharmacological (ie, physical activity and nutrition) anti-inflammatory/immunomodulatory strategies should be considered in the management of cognition in psychiatry.

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Introduction

Cognition has been described as “a suite of interrelated conscious (and unconscious) mental activities, including: pre-attentional sensory gating; attention; learning and memory; problem solving, planning, reasoning and judgment; understanding, knowing and representing; creativity, intuition and insight; ’spontaneous’ thought; introspection; as well as mental time travel, self-awareness and meta-cognition (thinking and knowledge about cognition).”1 The range of cognitive impairments reported in psychiatric disorders is wide and redundant across conditions.1 These alterations do not only aggravate the course of the disorders but also strongly compromise patients’ quality of life and recovery. For example, cognitive symptoms (eg, working memory impairments) in bipolar disorder (BD) or schizophrenia (SCZ) predict the development and the severity of psychotic symptoms, suggesting that they may participate in the development of the diseases.2 In addition, symptom severity (ie, intrusive thoughts, nightmares, and flashbacks) in patients with posttraumatic stress disorder (PTSD) is significantly correlated with impairments in attention, learning, memory, executive function, and visuospatial attention.3 Cognitive deficits in attention, verbal learning, and verbal memory predict poorer general and psychosocial functioning in adults with mood disorders or SCZ.4,6–8 There is therefore a great need for consideration for cognitive function in remission and recovery processes in psychiatry, which is emphasized by elevated rates of cognitive impairments after remission7,9,10 representing a risk factor for relapse.11

A better knowledge of the biological mechanisms underlying cognitive dysfunctions in patients suffering from psychiatric disorders is needed, as they would represent potential therapeutic targets in the management of cognition across psychiatric conditions. Numerous studies have implicated inflammation in the...
development of psychiatric disorders. In particular, it has been suggested that inflammation might underlie core symptoms of the disorders, such as somatic symptoms (eg, fatigue, sleep disturbances, appetite disturbances). However, there is less evidence linking elevated inflammation to cognitive deficits across psychiatric disorders. Thus, the purpose of this review is to summarize evidence that supports a role for inflammatory processes in the establishment of cognitive impairments across major depressive disorder (MDD), BD, SCZ, and PTSD.

Biological underpinnings of cognitive function

Various brain areas and mechanisms participate in the regulation of cognitive function in physiological conditions. In particular, these mechanisms have been extensively described in the hippocampus for learning and memory, whereas the mechanisms underlying other cognitive processes remain understudied. Mechanisms underlying learning and memory processes in the hippocampus encompass changes in neurotransmission at the synapse, namely Hebbian synaptic plasticity (including long term potentiation [LTP] and long term depression [LTD]).

1. **Role of neuroinflammation in the dysregulation of neurobiological processes underlying cognition.** The activation of microglia within the brain induces neuroinflammation through the secretion of local pro-inflammatory cytokines and the enhanced expression of chemokine receptors on microglia. Neuroinflammation can then induce dysregulations of neurobiological mechanisms regulating cognitive processes by: (1) changing the expression and activity of AMPAR, therefore impairing homeostatic plasticity; (2) inhibiting LTP and LTD processes and hence impairing Hebbian plasticity; (3) dysregulating the tryptophan-kynurenine pathway, subsequently causing neurodegeneration; (4) impairing neurotrophin metabolism; and (5) dysregulating HPA axis, leading to hypercortisolemia and subsequent neurotoxicity. In addition, the processes (3), (4), and (5) also participate to impairment of neurogenesis and Hebbian plasticity processes.
namely neurogenesis,\(^\text{19,20}\) which also contributes to learning and memory. Indeed, the rate of neurogenesis in rodents was found to be positively correlated to spatial learning and memory performances.\(^\text{21,22}\) In the hippocampus, these key regulatory mechanisms are dependent on the synthesis of neurotrophic factors such as brain-derived neurotrophic factor (BDNF)\(^\text{23–26}\) and the activation of various pathways such as the HPA axis\(^\text{27–31}\) and the kynurenine pathway, which are therefore able to modulate learning and memory.\(^\text{32–36}\)

**Inflammation and cognitive function in physiological conditions: mechanisms**

The relationship between raised levels of inflammation and cognitive changes across inflammation-associated conditions (eg, obesity, rheumatoid arthritis, HIV infection)\(^\text{37–39}\) has suggested a role for inflammation in the regulation of cognition in physiological conditions. The role of peripheral and brain inflammatory mediators (ie, cytokines) in influencing learning and memory was previously reviewed under the name of “cytokine model of cognitive function.”\(^\text{40}\) Microglia, the immune cells of the brain, do not only play a role in brain immune function but are also strong regulators of neurological function\(^\text{41}\) (see Figure 1) and cognition in physiological conditions.

Indeed, microglia depletion or inhibition in mice negatively impairs learning and memory.\(^\text{42}\) Although microglia can directly modulate cognition, it is noteworthy that they can also perform this role by secreting inflammatory mediators such as cytokines. As previously reviewed, inflammatory cytokines (ie, interleukin-1β [IL-1β], IL-6, and tumor necrosis factor-α [TNF-α]) are required for the physiological regulation of memory processes since disrupting their signaling pathway leads to decreased learning and memory.\(^\text{43–46}\) However, the regulatory role of these cytokines on cognition is dose-dependent since overexpression of IL-1β or TNF-α disrupts normal learning and memory in rodents.\(^\text{47,48}\)

Recent evidence suggests that disruption of microglia activation alters hippocampus-dependent neuronal plasticity and learning and memory performance in adulthood.\(^\text{49,50}\) Microglial processes continuously interact with synapses in a glutamate-dependent way,\(^\text{51}\) suggesting a role in learning and memory through their impact on synaptic plasticity. In addition, microglia indirectly modulate synaptic plasticity through the production of inflammatory cytokines.\(^\text{52}\) IL-1β and TNF-α are critical in the establishment of synaptic plasticity since their knockout induces impaired LTP\(^\text{53}\) and LTD,\(^\text{54}\) respectively. Glia-derived TNF-α also strongly regulates homeostatic plasticity by inducing exocytosis of AMPA receptors and inhibiting astrocyte glutamatergic transporters at the synapse.\(^\text{55–57}\) However, the effect of inflammatory cytokines on synaptic plasticity often follows an inverted U-shape since supra-physiological doses of IL-1β, IL-6, and TNF-α disrupts normal LTP,\(^\text{58–60}\) possibly linking raised inflammation to cognitive impairments. Similarly to what has been reported for pro-inflammatory cytokines, anti-inflammatory cytokines, such as IL-10, also participate in the regulation of hippocampal synaptic plasticity in a dose-dependent manner.\(^\text{61–63}\) Microglia and pro- and anti-inflammatory cytokines do not only regulate Hebbian and homeostatic plasticity but can also influence brain function through their effects on neurogenesis. During development, microglia coordinate synaptic pruning, ie, the elimination of weak synapses in order to maintain and strengthen functional synapses.\(^\text{64}\) During adulthood, neurogenesis is then highly dependent on the crosstalk between microglia and neurons through the CX3C chemokine receptor 1/CX3C chemokine ligand 1 (CX3CR1/CX3CL1) pathway.\(^\text{65,66}\) Cytokines such as IL-1β and IL-6 have a dual role on adult neurogenesis in the hippocampus. On one hand, they exert a critical role in the establishment of neurogenesis.\(^\text{67,68}\) On the other hand, their overexpression in the brain negatively affects adult neurogenesis.\(^\text{69,70}\) Similarly, TNF-α may exert a dual role on adult neurogenesis, through a differential effect of its receptors TNF-R1 and TNF-R2,\(^\text{71}\) although the underlying mechanisms remain understudied. Recently, IL-10 was also described as an enhancer of postnatal neurogenesis.\(^\text{72}\)

Microglia and inflammatory mediators may also have an indirect effect on cognition-associated biological mechanisms through modulation of neurotrophic factors levels and signaling pathway activation. Although the link between inflammation, cognition, and neurotrophic factors needs further consideration, there is evidence that cytokines can modulate BDNF levels and activity.\(^\text{73}\) In particular, immune stimulation decreases brain BDNF expression and activity.\(^\text{74,75}\) therefore altering synaptic plasticity in the hippocampus.\(^\text{75}\) In mice, BDNF removal from microglia revealed that these cells regulate memory by promoting synapse formation through BDNF signaling.\(^\text{76}\) Along with altering neurotrophic factor activity, cytokine signaling pathways can interact with GC receptor signaling and therefore change GC action.\(^\text{77}\) Inflammatory cytokines can indeed influence the production of all the hormones produced along the hypothalamic–pituitary–adrenal (HPA) axis\(^\text{78}\) and modulate GR function at multiple levels, from expression to translocation and associated signaling pathways.\(^\text{79}\) In addition to their effects on neurotrophic factors and the HPA axis, inflammatory processes can influence kynurenine pathway activation. Pro-inflammatory cytokines induce hippocampal activation of the kynurenine-producing enzyme indoleamine 2,3-dioxygenase (IDO),\(^\text{80,81}\) which participates in the regulation of learning and memory.\(^\text{35,82}\)
Inflammation and Cognition Across Psychiatric Conditions

The key role that inflammatory processes play in the regulation of the neurobiological processes underlying cognition in physiological conditions suggests that dysregulations of the immune system could participate in cognitive alterations reported across psychiatric diseases. In agreement with this hypothesis, alterations of neurobiological mechanisms regulating cognition are redundant across disorders (see Table 1). Here, we review the evidence suggesting that inflammatory processes, in particular activated microglia and inflammatory cytokines, play a role in impaired cognitive performance associated with psychiatric disorders through the regulation of the neurobiological processes underlying cognitive function (see Figure 1).

Inflammation and cognition in major depressive disorder

Levels of inflammatory markers have been found to be associated with cognitive performance in MDD. In patients with MDD, elevated serum levels of TNF-α, TNF-R1, and TNF-R2 negatively correlate with performance in executive functioning, attention, learning, working, and declarative memories. Similarly, elevated plasma levels of C-reactive protein (CRP) and IL-6 are associated with impaired cognitive performance in the domains of attention and executive function and of verbal memory and psychomotor speed, respectively. It is noteworthy that CRP and IL-6 levels are not only associated with cognitive symptoms of depression at baseline but also predict those symptoms at 12 years follow-up, suggesting that inflammation contributes to the progression of MDD rather than to the later stages of the disease. This relationship appears to be unilateral since cognitive symptoms of depression at baseline are not predictive of inflammatory status at follow-up. Although double-blind, randomized, placebo-controlled trials with anti-inflammatory agents are necessary to establish a causal link between inflammation and cognition in MDD, acute treatment with the cyclooxygenase (COX)-2 inhibitor Celecoxib has been reported to improve cognitive function in an elderly depressed woman with recurrent MDD.

It is noteworthy that individuals with MDD display dysregulations of the kynurenine (KYNA) pathway, which could mediate the relationship between elevated levels of inflammatory markers and cognitive function through its effects on brain plasticity. Elevated levels of inflammatory markers were found to be associated with decreased urinary KYNA in MDD patients. Interestingly, KYNA/3-hydroxykynurenine (3-HK) was also reported to negatively correlate with hippocampal activity during memory recall, and KYNA/quinolinic acid (QA) correlated with negative specific memory recall and with hippocampal and amygdala volume in MDD patients. It might be hypothesized that the kynurenine pathway could participate in the impairment of cognitive functions observed in MDD by influencing glutamatergic transmission in brain structures associated with cognitive processes. Numerous alterations in glutamatergic synaptic plasticity have indeed been reported in animal models of depression. Inhibition of microglia activation prevents impairments of both spatial memory and hippocampal LTP in a rodent model of depression. This effect is likely to involve a role of GluR1 phosphorylation. BDNF is also likely to be a mediator of inflammation-associated cognitive impairments in MDD. In cancer patients with depression, plasma IL-6 levels predict serum BDNF levels, which are significantly associated with short-term memory performance. In addition, inhibiting TNF-α in a rat model of depression prevents stress-induced cognitive impairments as well as the associated reduction of hippocampal BDNF expression.

Inflammation and cognition in bipolar disorder

Currently, few studies have reported associations between inflammatory processes and cognitive performances in BD. In individuals with BD, plasma CRP levels are negatively correlated with immediate memory, language, and attention. Similarly, elevated levels of

| TABLE 1. Main biological mechanisms impairments across psychiatric conditions |
|---------------------------------|----------------|----------------|----------------|----------------|
|                                | MDD            | BD             | SKZ            | PTSD           |
| Impaired Hebbian plasticity    | + (89)         | ?              | ++ (148, 149)  | 0/+ (154–156) |
| Impaired homeostatic plasticity| + (143)        | ?              | ?              | ?              |
| Impaired neurogenesis          | + (90, 91)     | 0/+ (100)      | 0/+ (151)      | ?              |
| Decreased peripheral BDNF levels| +/+ (94, 147)  | +/+ (101, 102) | +/+ (152, 153) | + (163, 164)  |
| Impaired HPA axis activation   | +/+ (148, 149) | +/+ (101, 144) | +/+ (152, 147) | + (163, 148)  |
| Increased KYNA levels          | ++ (95–97)     | +/+ (103)      | +/+ (115)      | ?              |

0: essentially absent; 0/+: anecdotal, poorly documented, ambiguous; +: preclinical; ++: clinical; +++: clinical, consistent; ?: not clearly evaluated. Reference numbers are in parentheses.
IL-1α and TNF-α are associated with worse memory performances, even during euthymic states. Elevated plasma levels of soluble TNF (sTNF)-RI were also found to be associated with impaired declarative memory in patients with BD. The only study assessing the relationship between cerebrospinal fluid (CSF) inflammatory markers and cognition in BD reported a negative association between CSF concentration of the inflammatory biomarker YLK-40 and executive function in those patients. It is noteworthy that in addition to elevated peripheral inflammation reported in BD patients with cognitive impairments, increased microglial activation was reported in the right hippocampus of BD patients in comparison to healthy controls. Hence, these studies provide evidence that elevated inflammatory profile is negatively associated with cognitive function in BD.

Various neurobiological systems have been reported to potentially participate in inflammation-associated cognitive impairments in BD. A recent study reported that pro-inflammatory cytokines such as TNF-α decrease white matter integrity in BD individuals, which could be mediated by alterations in neurogenesis. Cytokines may also alter cognition by influencing the activity of the HPA axis, subsequently leading to impaired neuroplasticity. Indeed, HPA axis alterations are associated with impaired cognition in individuals with BD. GR insensitivity was reported in BD and mifepristone (GR antagonist) treatment for 1 week improves spatial working memory performance in BD. In addition, a very recent study showed that adult males with BD display elevated plasma 3-HK/KYNA ratio, which is significantly associated with poorer declarative memory performances. Given the role that inflammatory cytokines play in the regulation of the IDO pathway, inflammation may dysregulate this pathway, leading to an imbalance between neuroprotective and neurotoxic metabolites and to a subsequent cognitive impairment in BD patients. Finally, it is worth mentioning that peripheral BDNF levels, which can also be regulated by inflammation, predict cognitive function in BD. Moreover, the BDNF val66met polymorphism could be a risk factor for cognitive impairment in this disease, further reinforcing the possible role of BDNF in mediating the effects of inflammation on cognition in BD.

**Inflammation and cognition in schizophrenia**

Inflammation has also been extensively reported to be a potential player in the etiology and pathophysiology of SCZ. Epidemiological studies have reported elevated risk of schizophrenia following prenatal or childhood exposure to infection. Infection then mediates peripheral and central inflammatory responses which in turn alter brain development (for a review, see Meyer). Similarly to what has been reported in other psychiatric conditions, cognitive impairments associated with schizophrenia are correlated with raised peripheral inflammation. A recent systemic review conducted on SCZ patients reported an association between plasma CRP levels and worse cognitive performance including in the domains of attention, memory, and learning abilities. Similarly, significant negative associations have been reported between general cognitive function and serum IL-6, sTNF-R1, and IL-1ra levels, and elevated peripheral IL-1β mRNA levels are associated with both impairments in verbal fluency and brain volume reduction in a subgroup of patients with SCZ. It is noteworthy that an association has also been reported between cognitive impairments and anti-inflammatory cytokines in SCZ, since serum IL-10 levels negatively correlate with cognitive factor (made up of 3 items of the Positive and Negative Syndrome Scale). Particularly, patients who carry the AA allele of the IL10-592 A/C polymorphism perform worse in attention, suggesting that this IL-10 allele could contribute to cognitive impairments in SCZ. Moreover, inflammatory pathways are enriched in mutations associated with cognitive impairments in SCZ patients. In addition to these studies showing association between inflammation and cognition in SCZ, Müller et al reported that decreasing inflammation through anti-inflammatory add-on to risperidone treatment for 5 weeks trends to improve cognition factor in SCZ patients (F1,47 = 3.64; p = 0.06).

A longitudinal, double-blind, randomized, placebo-controlled study showed that minocycline add-on to atypical antipsychotic treatment has a beneficial effect on executive functioning (such as working memory, cognitive shifting, and cognitive planning), suggesting that inhibiting microglia activation in patients with SCZ could be a strategy to decrease SCZ-associated cognitive impairments. This is in agreement with the microglia hypothesis of SCZ, which states that the neuropathology of SCZ is closely associated with elevated microglia activation. Indeed, inflammatory cytokines and free radicals produced by activated microglia in animal models of SCZ lead to decreased neurogenesis, white matter abnormalities, and neuronal degeneration, which may participate in the pathophysiology of the disease.

Similarly to what has been suggested for MDD and BD, inflammation-mediated kynurenine pathway dysfunctions could also participate in cognitive alterations in SCZ, since patients display raised levels of KYNA in the CSF. This effect could be mediated by changes in glutamatergic neurotransmission. Müller suggested that elevated inflammation in SCZ may promote the production of the NMDA antagonist KYNA, therefore resulting in a glutamatergic imbalance. The glutamate hypothesis of SCZ suggests that a deficit in glutamatergic transmission in the brain of SCZ patients may lead to...
dopaminergic system dysfunction, which may in turn exacerbate glutamatergic transmission impairments, eventually leading to psychotic and cognitive symptoms. Decreased glutamatergic neurotransmission may be associated with alterations in synaptic vesicles transportation, which is linked to IL-10 levels in the brain of SCZ patients.

Inflammation and cognition in PTSD

Currently, the link between inflammatory processes and cognitive impairments remains understudied in the context of PTSD. However, a few recent studies reported elevated levels of inflammatory markers (such as CRP, TNF-α, IL-6, and IL-1β) in the plasma of individuals with a diagnosis of PTSD. In a rat model of PTSD, chronic consumption of curcumin, a component with anti-inflammatory properties, impairs the consolidation and reconsolidation of fear memories, suggesting a possible role for inflammation in memory processes. Interestingly, plasma levels of sTNF-RII are associated with reduced hippocampal volume in Gulf War veterans with current and past PTSD. Hence, one can hypothesize that inflammation could impair cognition by reducing hippocampal volume via its deleterious effect on neurogenesis or HPA axis activation. In agreement with this last assumption, the GC receptor antagonist mifepristone improves cognition in Gulf War veterans with PTSD.

Future Directions

Anti-inflammatory strategies to improve cognition across psychiatric conditions

The redundant association between inflammatory alterations and cognitive processes across psychiatric disorders suggests that deconstructing psychiatric disorders to account for the heterogeneity across individuals and consider patients’ endophenotypes may be promising in the development of novel strategies in the management of cognitive alterations in psychiatry. A cross-disorder approach is in agreement with the Research Domain Criteria (RDoC) initiative led by the National Institute of Mental Health (NIH), which is aimed at developing new ways of classifying mental disorders based on dimensions of both observable behavior and neurobiological measures, in order to develop new and individualized treatments. The evidence reviewed here suggests that the use of anti-inflammatory strategies as adjunctive

![FIGURE 2](https://doi.org/10.1017/S1092852918001499) Published online by Cambridge University Press

Role of neuroinflammation in the cognitive alterations and disease outcomes across psychiatric conditions. The detection of damage-associated molecular patterns (DAMPs) or pathogen-associated molecular patterns (PAMPs) by the immune system following psychological stress, infections or injury induces a switch of the microglia phenotype from a quiescent M2 phenotype to an activated or reactive M1 phenotype. As described in Figure 1, this induces neuroinflammation, therefore dysregulating neurobiological processes underlying cognition. The cognitive alterations resulting from this inflammatory state are redundant across psychiatric conditions and encompass impaired episodic memory, processing speed, social cognition, fear-extinction learning, attention, executive function, and declarative learning and memory. Importantly, this common pattern of cognitive alterations in psychiatric disorders increases the severity of symptoms, decreases the quality of life and workplace and psychosocial functioning of patients, has a negative effect on remission and recovery processes, and increases the risk of relapse.
therapies across diagnoses could improve the management of cognitive impairments in psychiatry.

**Pharmacological approaches**

Nonsteroidal anti-inflammatory drugs (NSAIDs) such as celecoxib (COX-2 inhibitor) are widely used in the treatment of inflammatory conditions (eg, arthritis, multiple sclerosis). In the last decades, they have also been used as effective additional therapies to antidepressant and antipsychotic treatments across psychiatric conditions. However, only a few preliminary data suggest a possible enhancing effect of the anti-inflammatory medication celecoxib on cognition in psychiatric disorders. Interestingly, NSAIDs were shown to improve memory in mouse models of neurotoxicity and Parkinson’s disease, suggesting that their impact on cognition across psychiatric conditions requires further examination.

**Nutritional interventions**

Numerous research efforts have reported a beneficial effect of nutrients such as n-3 polyunsaturated fatty acids (n-3 PUFAs) and flavonoids on inflammatory processes underlying cognitive dysfunctions. Indeed, these nutrients and their metabolites have been extensively described to potently reduce microglia activation and cytokine production in inflammatory conditions and improve associated alterations in HPA axis activation, synaptic plasticity, and BDNF production. It is noteworthy that polyphenols (such as flavonoids) and n-3 PUFAs can alleviate cognitive impairments in inflammation-associated conditions such as aging and disorders such as Parkinson’s disease and Alzheimer’s disease. There is also evidence that they have a beneficial effect on psychiatric disorders, although it is unclear whether those cognitive improvements are mediated by inflammatory changes.

**Physical activity**

Physical activity has been reported to decrease inflammation in both preclinical and clinical models of psychiatric conditions such as MDD. In rodents, exercise does not only enhance anti-inflammatory processes at the cellular level, by changing microglial phenotype, but also at the molecular level by increasing the production of anti-inflammatory cytokines in the brain. This anti-inflammatory effect of exercise positively influences the activity of the HPA axis as well as neuronal proliferation, neurotrophic factor levels, and the activation of the kynurenine pathway which suggests that it could positively impact cognition across psychiatric conditions. In agreement with this hypothesis, moderate physical activity has a beneficial effect on cognition in patients with psychiatric conditions.

**Conclusion**

The numerous cognitive impairments across major psychiatric disorders highlight a strong need for consideration since they not only affect the quality of life but also the treatment and recovery of patients. However, the mechanisms underlying these deficits are still understudied and must be addressed to allow a better management of the disorders. The common pattern of cognitive impairments across psychiatric conditions suggests shared mechanisms potentially leading to their causation. As described in this review, inflammation could be a shared mechanism underlying the development of cognitive impairments in MDD, BD, SCZ, and PTSD. Indeed, raised inflammatory processes (ie, activated microglia and elevated levels of inflammatory cytokines) can disrupt neurobiological mechanisms regulating cognitive processes (see Figure 2). However, although most studies report associations or correlations between inflammatory biomarkers, cognitive-related biological mechanisms, and cognitive performance, causal evidence is still strongly lacking. Few studies have evaluated the role of inflammation in cognitive alterations in other psychiatric conditions such as autism or attention deficit hyperactivity disorder, but one may hypothesize that the underlying mechanisms could be similar given the shared pattern of cognitive alteration across psychiatric conditions.

**Disclosures**

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**REFERENCES:**


60. Camissey D, Butler MP, Moynagh PN, O’Connor JJ. Evidence for a role in the group I metabotropic glutamate receptor in the inhibitory effect of tumor necrosis factor-alpha on long-term potentiation. Brain Res. 2007; 1136(1): 13–19.


114. Fischer EK, Drago A. A molecular pathway analysis stresses the role of inflammation and oxidative stress towards cognition in schizophrenia. *J Neural Transm (Vienna).* 2017; 124(7): 765–774.


