Review

http://dergipark.org.tr/en/pub/anatomy
Received: November 28, 2024; Accepted: February 12, 2025
doi:10.2399/ana.25.1592350

http://dergipark.org.tr/en/pub/anatomy
anatomy
An International Journal of Experimental and Clinical Anatomy

Neurodevelopmental challenges following preterm birth: effects on brain structure and function with a focus on visual perception

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Abstract

Preterm birth is prevalent globally, with approximately 15 million babies born preterm annually. The number of surviving preterm babies has been increasing in recent years due to advancements in medical interventions. This highlights the urgent need to understand the long-term effects of preterm birth, especially on brain development, to minimize the potential negative impacts and to develop effective rehabilitative strategies. Preterm birth disrupts brain development, leaves the infant exposed to environmental stimuli that they are not ready to process, and often leads to brain damage. Two crucial stages of structural and functional brain development are thought to be significantly disrupted due to preterm birth: myelination and synaptic pruning. As a result, preterm birth often coexists with neurodevelopmental disorders affecting motor and cognitive, perceptual systems. The impairments in visual abilities, especially in perceptual domain, are of particular interest, as these issues often go unnoticed and negatively impact academic performance. Notably, these effects can be observed even in the absence of significant brain damage and frequently persist into adulthood. Therefore, this review aims to emphasize the urgent need to address this critical public health concern by comprehensively characterizing the effects of preterm birth on visual functioning and investigating the underlying neural mechanisms. Two hypotheses have been proposed in the literature to explain the neural basis of visual deficits associated with preterm birth. The first posits that preterm birth mainly disrupts the functioning of the dorsal visual pathway, resulting in poorer performance on visuospatial tasks. The second hypothesis suggests that compensatory mechanisms may be involved, where non-visual brain areas compensate for impairments in visual information processing by eliciting higher activations than usual. In this review, inspired by findings from the recent literature on impaired visuospatial processing abilities in early brain-based visual impairments, we propose an alternative hypothesis that preterm birth may be associated with global visual impairment, likely resulting from impaired top-down information processing.

Keywords: brain development; dorsal stream dysfunction; preterm birth; prematurity; top-down processing; visual impairment; visual perception

Anatomy 2025;19(1):41–51 ©2025 Turkish Society of Anatomy and Clinical Anatomy (TSACA)

Introduction

Preterm birth is widespread around the world. Approximately 15 million babies, which is 11% of all babies born alive, are born preterm (before the 37th week of the standard 40-week gestation period) each year. About 15% of these babies are born extremely preterm (before 32 weeks).[1] The survival rate of preterm babies has significantly increased in recent years due to the advancements in medical intervention.[2] Therefore, there is an urgent need to understand the long-term effects of preterm birth on individuals to minimize the potential negative impacts and develop effective rehabilitative strategies.

A common consequence of preterm birth is brain damage, with its severity varying based on both the timing and underlying cause. Typically, the conditions that lead to preterm birth or complications during delivery contribute to brain damage. However, even if no visible brain damage occurs during preterm birth, brain development can still be significantly disrupted due to the

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removal of the infant from an ideal environment for growth and protection, and premature exposure to environmental stimuli and stressors they are not yet equipped to handle.[3,4] Such disruptions or damage during this critical developmental period can lead to lasting cognitive and motor impairments.

This review article explores the effects of preterm birth on brain structure and function. The first section examines how leaving the womb and exposure to environmental stimuli before the brain is fully prepared can impact structural and functional brain development. The second section summarizes current knowledge on the motor and cognitive deficits associated with preterm birth. Following sections focus on the impact of preterm birth on perception, with a particular emphasis on visual perception and visual information processing in the brain.

Impaired visuoperceptual abilities in individuals born preterm suggest that the effects of preterm birth extend beyond obvious motor or cognitive impairments. Even adults born preterm, without evident brain damage or complications, may face perceptual visual challenges. This issue warrants attention for two key reasons. First, it highlights that preterm birth is not solely associated with developmental delays but can have long-lasting perceptual effects into adulthood. Second, in the absence of other noticeable complications, these perceptual difficulties often go unrecognized, despite their significant impact on individuals' abilities, particularly in academic performance. Therefore, understanding how preterm birth affects brain function is crucial for addressing these challenges and developing effective rehabilitative strategies. With this motivation, this article emphasizes findings from studies examining the impact of preterm birth on visuoperceptual abilities, focusing on complications in visual information processing rather than ocular issues.

Two hypotheses have been proposed in the literature to explain the neural basis of visual deficits associated with preterm birth. One emphasizes the role of dorsal pathway dysfunction, while the other highlights compensatory mechanisms. In the final section, inspired by research on early brain-based visual impairments, we propose an alternative hypothesis regarding the effect of preterm birth on visual information processing. Specifically, we suggest that preterm birth may be associated with a global impairment in top-down visual information processing, rather than an isolated dysfunction of the dorsal pathway. To date, existing hypotheses lack strong behavioral and neural evidence. Additionally, no studies have yet explored the concept of global visual impairment in preterm individuals. Therefore, the behavioral and neural correlates of preterm birth on visual perception require further investigation.

The Effect of Preterm Birth on Structural and Functional Brain Development

Healthy fetal brain maturation is completed by several complex processes that unfold in overlapping times, such as proliferation, neuronal migration, and differentiation. Preterm birth may disrupt any one of these processes and cause damage at both structural and functional levels, resulting in neurodevelopmental disorders.[5]

Two crucial stages of brain development are thought to be significantly disrupted as a result of preterm birth. The first is myelination, a process in which the myelin membrane wraps around the axons of neurons, speeding up communication between neurons. Myelination begins around the 13th week of pregnancy and continues after birth into adulthood.[4,6] This process and the resulting changes in white matter are critical for numerous brain functions, including information processing and learning.

White matter damage is a common outcome in individuals born preterm and is often associated with disruptions in the myelination process.[7] At 11 years old, preterm children show persistent white matter disturbances and smaller brain size.[8] More subtle forms of white matter damage, such as punctate white matter lesions and diffuse white matter abnormalities are observed more frequently in the preterm population compared to severe forms of brain injuries like periventricular leukomalacia; and pose a neurodevelopmental threat to the infant.[9] Specifically, diffused white matter abnormalities are a predictor of poor motor development and are associated with diminished brain network efficiency; while punctate white matter lesions are predictive of neurodevelopmental deficits such as motor and cognitive delays.[10–13] Abnormalities and reduction in white matter volume are observed even in low-risk preterm groups without a clinical white matter impairment, and this reduction is correlated with poorer performance in processing speed.[14]

The second mechanism that might be affected by preterm birth is synaptic pruning, which begins in the second half of pregnancy and typically continues after birth. During brain development, neurons form connections known as synapses, and this process is crucial for shaping functional neural circuits. In the early stages of brain development, neurons make as many synaptic connections as possible, but not all are necessary. Synaptic pruning is the process of removing extra, unused connections, thereby organizing brain regions so that only essential synapses remain. The removal of unused connections optimizes brain connectivity by reallocating resources to the more frequently used connections, making them stronger and more stable. This process is essential for healthy brain development.[15,16]

A recent study utilizing connectomic analysis found that preterm infants exhibit different brain network connectivity compared to full-term infants. In particular, reduced connectivity strength, and impaired global efficiency have been reported.[17] Additionally, cortical thinning with age, a process driven by synaptic pruning, has been found to be deficient in preterm children.[18] The negative impact of preterm birth on myelination and synaptic pruning persists into adulthood. This suggests that preterm birth not only delays brain development but also causes permanent structural damage.[7,19–21] Consistently, preterm birth has been linked to lifelong neurodevelopmental disorders.[1] Moreover, a recent study exploring resting neural activity in the visual cortex of healthy preterm infants revealed an accelerated functional maturation of the sensory visual cortex.[22] As the authors discussed, this finding may pose a risk to healthy cortical maturation. The earlier maturation of sensory areas, compared to executive functioning and association areas such as the frontal brain areas, could disrupt the typical sequence of functional maturation, potentially leading to life-long changes in brain function.

Motor and Cognitive Deficits Associated with Preterm Birth

In a study that monitored more than 4000 babies born between 22 and 24 weeks, 43% of surviving infants were reported to have a neurodevelopmental deficit.[2] Neurodevelopmental damage in preterm infants often affects the motor system. For example, preterm birth is the most common known cause of cerebral palsy.[1] Mild motor dysfunction and lack of coordination are also highly prevalent in this population. As these infants grow into childhood and adulthood, they often exhibit motor deficits characterized as developmental coordination disorders including problems with balance, coordination, gross and fine motor control, and visual-motor integration.[23]

Previous studies have reported that preterm birth is also associated with cognitive difficulties.[24] Both preterm and extremely preterm children show lower performance in cognitive skills such as perception, attention, memory, and information processing speed compared to their term peers.[18,25,26] Some studies have also reported lower IQ levels in preterm children compared to their term peers.[25,27] Additionally, children born preterm are more likely to have neurodevelopmental disorders such as attention deficit hyperactivity disorder (ADHD), and autism than their peers born at term.[1,28,29] Moreover, as gestational age decreases, a linear decline is observed in IQ scores and the risk of ADHD increases.[30,31]

Consistent with the persistent structural changes mentioned earlier, studies with preterm adolescents and adults indicate that cognitive deficits and neurobehavioral problems observed in childhood persist into adulthood as well, and lower gestational age is associated with poorer academic and cognitive performance.[32–35] However, these results primarily reflect the impact of extreme preterm birth on cognitive functions, as cognitive outcomes for late preterm births (i.e., between 32 and 37 weeks) are rarely studied. Limited research comparing individuals born extremely and late preterm suggests that cognitive deficits associated with preterm birth persist into adulthood primarily in extremely preterm individuals or those with very low birth weight, while late preterm adults tend to catch up to their peers.[36] However, others argue that while the detrimental effects of preterm birth on cognitive tasks are less pronounced in late preterm individuals, they still perform significantly worse compared to their term-born peers and are more likely to face academic challenges.[37–39] Despite these findings, late preterm infants typically do not receive specialized healthcare, as they are considered low-risk, resulting in very limited studies involving this group.[40] Given that late preterm births constitute a substantial portion of the preterm population, greater attention should be directed toward this group.

Perceptual Deficits Associated with Preterm Birth

Preterm birth is associated with various deficits in the perceptual domain, and preterm children are at higher risk for sensory processing disorder.[41] Deficits in the auditory domain include hearing disabilities, language and speech delays, and atypical speech sound discrimination patterns compared to full-term peers.[42–44] Also, unlike their term peers, preterm infants show no indication of maternal voice recognition.[44] Temporal auditory processing is also affected, as preterm children demonstrate reduced performance in temporal ordering and resolution tasks, as well as atypical neural signaling during these activities.[45] Furthermore, while full-term infants exhibit significantly greater neural responses to forward speech compared to backward speech, preterm infants show no such difference, indicating a deficit in speech discrimination.[46]

Preterm birth is also a risk factor for somatosensory deficits. Preterm infants show heightened tactile sensitivity and a lower threshold for cutaneous withdrawal reflex, suggesting an immature inhibitory system.[47,48]

Multisensory processing is affected by preterm birth as well. Sensory integration problems such as motor coordination and visual-motor integration difficulties are frequently observed in preterm children.[49–51] A neuroimaging study investigating the development of multisensory process with auditory, somatosensory, and combined auditory-somatosensory multisensory stimuli showed atypical patterns of event-related potential (ERP) topographies for multisensory and summed unisensory processes in preterm infants.[52] Another study, using a simple detection task with auditory, visual, and simultaneous auditory-visual stimuli, reported slower and more variable responses in general regardless of the sensory modality, and altered multisensory processes in school-age preterm children compared to full-term peers. This result indicates the long-lasting effects of pre-term birth on various sensory and multisensory processes.[53]

Despite the limited studies in other sensory modalities, vision and visual perception performance accompanying preterm birth has been extensively studied. Challenges in visual perception have been reported to be among the most common neuropsychological deficits in this group.[54,55] Preterm infants are at a higher risk of developing various visual ocular impairments, such as retinopathy of prematurity (retinal damage), nearsightedness or farsightedness due to light refraction defects, strabismus, abnormal ocular motility, nystagmus, decreased contrast sensitivity, visual acuity and visual fields compared to full-term infants.[54,56,57] In addition to these ocular issues, they often perform poorly on visuospatial tasks, suggesting brain-related complications.[58] Consistent with this, preterm birth is one of the most common causes of cerebral visual impairment,[59] a brain-based perceptual impairment that primarily occurs due to perinatal neurological damage and significantly affects visual abilities.[60–65] However, even individuals born preterm without any neurodevelopmental deficit or brain damage have been reported to experience visual problems.[33] Therefore, in this review article, we aim to highlight difficulties in visual perception caused by brain-related issues, as opposed to ophthalmological problems associated with preterm birth because while ophthalmological problems are well-documented in the literature and relatively easier to detect (see Robitaille[59] for a comprehensive review of ophthalmological issues linked to preterm birth), brain-related perceptual difficulties are often overlooked and go unrecognized.

In a psychophysical experiment, MacKay et al.[66] measured motion coherence thresholds in preterm children between the ages of 5 to 8 years old, to assess their local and global motion perception. In this experiment, participants were shown a group of dots, some moving in the same direction and some moving in different directions completely randomly, and were asked to report the direction in which the dots moved. This task measures the proportion of dots that need to move in the same direction for participants to perceive a global motion. This study showed that the preterm group had a higher motion coherence threshold, meaning that they needed more dots to move in the same direction to perceive global motion. According to the results, 41% of preterm children performed significantly worse on a local or global motion detection task compared to their term peers, and performance was particularly affected when global motion tasks were used. These results were supported by subsequent studies.[67,68] Similarly, Jakobson et al.[69] showed that 49% of preterm children failed the motion-defined form recognition test. Sensitivity to biological motion is also impaired in extremely preterm children.[68] In addition to poor performance in different types of motion perception, impairments in visuospatial working memory, depth perception, and visual attention have also been reported in this group.[69–73] Even after controlling for the effect of low IQ and ocular impairments, preterm children perform worse on visuospatial tasks than their term peers.[74] Additionally, studies have found that preterm infants demonstrated reduced abilities in recognizing faces and did not show a preference for intact faces over distorted ones.[75,76]

Performance on a limited number of visual tasks has been reported to be comparable between preterm and term groups. For instance, behavioral studies with preterm infants have reported no impairment in shape perception, in contrast to motion perception,[77] or that the degree of impairment in shape perception is significantly less severe than that in motion perception.[68] Similarly, preterm children performed poorly on motion and form coherence tests; however, the deficit in form perception disappeared after controlling for IQ and visual acuity.[78] Furthermore, studies investigating visual discrimination, visual closure, and visual working memory have reported similar performance between preterm and term groups.[50,79–80]

It should also be noted that the literature presents mixed findings regarding performance on various visual tasks. For instance, one study found no significant differences in form constancy, visual closure, or figure-ground discrimination performance between 5-year-old preterm children and their term-born peers.[81] However, another study indicated that preterm children perform significantly worse on figure-ground discrimination tasks, and lower birth weight is associated with poorer results in form constancy, visual closure, and figure-ground discrimination.[82] Furthermore, contrary to numerous studies mentioned above, one study reported comparable results in ophthalmological and visual cognitive performance including visual acuity, colour vision, stereopsis, stereoacuity, visual fields, ocular motility, motor fusion, visual-motor, and visual-spatial skills and pattern-reversal visual evoked potentials between preterm children without major neuromotor impairment and their full-term peers.[83] The discrepancy between the findings may be related to the heterogeneity of the preterm group in terms of the timing and cause, and accompanying motor and cognitive conditions.

In addition to lifelong, permanent impairments in brain structure (as discussed in the section “the effect of preterm birth on brain development”), cognitive performance, and motor functioning, adults born preterm have also been shown to perform worse on various visual tasks.[23,33,84] Importantly, structural brain damage is not always necessary for these perceptual impairments to manifest. Visual deficits are often observed in preterm individuals who display no obvious structural brain damage detectable through standard brain imaging,[85,86] suggesting the presence of lasting functional impairments in the brain. Therefore, to gain a deeper understanding of poor behavioral performance, it is crucial to investigate how preterm birth affects the brain’s information-processing mechanisms.

Effect of Preterm Birth on Visual Information Processing

There is limited information on how preterm birth affects visual information processing. Two explanations have been proposed in the literature so far to account for how visual information processing might be affected by preterm birth. Some researchers suggest that preterm birth may exclusively impair information processing along the dorsal pathway. In the classical two-stream organization of visual information processing,[87,88] spatial features of visual information such as location, direction, and motion are processed in the dorsal pathway, while stimulus-related features like color, shape, and size are processed in the ventral pathway. Previous studies have shown that the dorsal pathway is more vulnerable to damage than the ventral pathway due to physiological reasons during brain development.[89,90] As a result, it has been suggested that brain damage in the early stages of life more frequently affects the dorsal pathway. This view is supported by clinical reports indicating that tasks associated with the dorsal pathway are more commonly impaired in individuals with brain damage. Consistently, visual impairments in preterm individuals are also often linked to dysfunctions in the dorsal pathway, suggesting that preterm birth may lead to dorsal stream dysfunction. Furthermore, studies showing comparable shape and form perception,[68,77,78] in contrast to motion perception, support the view that preterm birth leads to a specific deficit in the dorsal stream. Consistently, a meta-analysis[50] has shown that while preterm individuals exhibit poorer visuospatial perceptual abilities, their performance on visual closure tasks is comparable to that of term groups. However, despite behavioral evidence supporting this hypothesis, neural evidence remains lacking.

Another line of research suggests the existence of compensatory neural mechanisms, where activations in both visual and non-visual brain areas may compensate for impairments in visual processing regions in preterm individuals. In one of the few functional brain imaging studies on visual processing in preterm children, researchers first tested nonverbal skills at age five on preterm children without visual or other neurodevelopmental impairments using standard intelligence tests for preschool children. At age twelve, the same children’s brain activity was assessed using functional magnetic resonance imaging (fMRI) during visual discrimination and visual closure tasks from the Motor-Free Visual Perception Test.[91] Five-year-old preterm children performed significantly worse than their term peers on nonverbal intelligence tests. However, while no differences in visual performance were observed between the two groups at age twelve (notably, visual functions were not assessed at age five), preterm children who outperformed their preterm peers at age five on nonverbal intelligence tests demonstrated stronger neural activation in various regions of the posterior cortex, a critical area for visual tasks and cognitive functions. Also, there was no such association in the control group.[79] The same research group found similar results in a study involving adolescents on visual closure, deviating figure and figure-ground discrimination tasks. Their results demonstrated an increased neural activity in brain regions not directly associated with visual tasks (e.g., frontal, anterior cingulate, temporal, and posterior medial parietal/cingulate cortices, as well as parts of the cerebellum, thalamus, and caudate nucleus) in the extremely preterm group.[80] In the first study, the visual tasks primarily required ventral stream processing, yet increased activity was observed in the dorsal stream areas.[79] In the second study, increased neural activity was mainly observed in non-visual areas.[80] Therefore, the researchers suggested that the similar perceptual performance between preterm and full-term groups, alongside increased neural activity in either non-critical visual areas for the executed visual task or non-visual regions, may indicate a compensatory mechanism in the preterm group.

The compensation hypothesis has been explored by other studies. For example, Narberhaus et al.[92] found that while behavioral performance in a visuo-spatial memory task was similar, a distinct neural network emerged in the very preterm group during visuo-perceptual learning processing. Specifically, during encoding, increased fMRI signals were observed in the occipital and parietal cortex, along with certain subcortical regions, while the frontal cortex showed decreased signal. During recognition, very preterm adults exhibited increased signals in the right cerebellum and bilateral anterior cingulate gyrus. These findings were interpreted as evidence of neural compensation. In support of these findings, other studies also demonstrated altered fMRI activity in multiple brain regions, including the frontal and parietal cortices, in very preterm groups compared to their term peers during visual memory or learning tasks involving encoding and recognition.[93,94] In another study on visuospatial working memory in very preterm and term children, researchers found that younger and low-performing preterm children exhibited an atypical working memory network, particularly within the frontal brain areas. In contrast, older and high-performing preterm children displayed a typical neural network, similar to that of controls, again, suggesting a compensatory mechanism.[95]

A New Proposal for the Effect of Preterm Birth on Visual Information Processing

So far, two hypotheses have been proposed in the literature regarding the neural basis of visual problems associated with preterm birth. The first hypothesis suggests that preterm birth disrupts information processing in the dorsal pathway, leading to impaired behavioral performance on tasks linked to this pathway. The second hypothesis posits that, in cases where visual performance is unaffected, regions of the brain not directly involved in visual information processing may take over during visual tasks, serving as a compensatory mechanism for the damage caused by preterm birth.

A recent functional brain imaging study on patients with cerebral visual impairment suggested that increased activation in visual areas that are not directly related to task demands may be linked to difficulty in suppressing irrelevant visual information, rather than serving as a compensatory mechanism. This finding points to a more global impairment in the visual system, specifically in top-down information processing, through which limited neuronal resources are allocated based on task demands or the observer's expectations and goals.[62] Furthermore, before this discovery, the prevailing view in the literature was that cerebral visual impairment was primarily associated with dorsal pathway dysfunction based on the behavioral results and clinical reports.

Although the visual problems associated with preterm birth are not as severe as those seen in cerebral visual impairment, the underlying causes and consequences of both conditions are quite similar. In fact, for a considerable number of individuals with cerebral visual impairment, preterm birth is the primary factor in the medical history related to impaired vision.[65] Therefore, underlying neural mechanisms may be similar in both conditions. If this is the case, increased neural activity in either visual areas that are not directly related to task demands or non-visual brain areas may not be directly related to compensatory neural mechanisms, and preterm birth may not cause only dorsal pathway dysfunction, but a global impairment in the top-down visual information processing as in the case of cerebral visual impairment. This impairment may hinder the system's ability to effectively prioritize relevant visual information while suppressing the irrelevant information, due to an inefficient allocation of limited neural resources. Supporting this view, a recent behavioral study reported that preterm children had more difficulty than full-term children in suppressing distractors in a visual search task especially when visual distractors were increased.[96] Additionally, Morcom and Henson[97] investigated compensatory mechanisms through increased frontal activity in healthy aging. They suggested that the increased prefrontal activity is associated with reduced efficiency or specificity rather than compensation. Considering the altered neural networks, particularly in the frontal areas, observed in the very preterm group in the studies mentioned in the previous section,[93,94] the compensation hypothesis alone may not fully explain the changes in brain functioning in this group, and altered neural activity in frontal brain regions may be associated with impairments in top-down processing.

Concluding Remarks

Preterm birth is a neurodevelopmental risk factor with lasting negative effects into adulthood. Disruption of normal brain development due to preterm birth can result in varying degrees of brain damage.[7,19,20] Even without significant brain damage, preterm birth is linked to a range of persistent developmental disorders. Behavioral studies have identified notable differences in motor, cognitive, and visual-perceptual functions, though the neural basis for these differences remains unclear. Beyond current hypotheses on potential neural mechanisms affecting visual perception, this review proposes that a global impairment in top-down information processing may underlie the visual processing deficits associated with preterm birth. Comprehensive behavioral and neuroimaging studies are needed to investigate these potential mechanisms.

In this review, we aim to highlight the potential neural mechanisms affected by preterm birth, including the two already identified in the preterm literature, as well as recent findings on early brain-based visual impairments in cerebral visual impairment, to emphasize the need for further research. Understanding the visual perception deficits associated with preterm birth, along with their underlying neural mechanisms, is crucial, as these deficits are also linked to impaired academic performance, including challenges in math and reading.[82] Identifying both the behavioral and neural effects of preterm birth could enable early intervention through targeted neuropsychological rehabilitation or occupational therapy for preterm children. As Lind et al.[79] pointed out that while programs exist to support the cognitive and motor development of preterm infants, no programs specifically aim to improve their visual abilities. To bridge this gap, it is critical to investigate preterm birth-related visual impairments and their neural underpinnings. In particular, long-term studies on healthy adults born preterm, without known neurodevelopmental disorders or brain pathology, are necessary. Focusing on this population would help distinguish the effects of preterm birth on information processing mechanisms from those caused by brain damage or other complications, providing a clearer understanding of the behavioral and neural challenges linked specifically to preterm birth.

Conflict of Interest

We declare no conflict of interest related to this work.

Author Contributions

FHÇ: investigation, writing: original draft, writing: reviewing and editing; ZP: conceptualization, methodology, investigation, writing: original draft, writing: reviewing and editing.

Ethics Approval

Not applicable.

Funding

No financial support was received for this article; however, the author ZP holds a TÜBİTAK grant (1001, Project Number: 124K976) to investigate neural mechanisms affected by preterm birth.

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Conflict of interest statement: No conflicts declared.

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