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Jodi Pawluski

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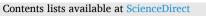
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# The parental brain, perinatal mental illness, and treatment: A review of key structural and functional changes



#### Jodi L. Pawluski

Univ Rennes, Inserm, EHESP, Irset (Institut de Recherche en Santé, Environnement et Travail), UMR\_S 1085, F-35000, Rennes, France

ARTICLE INFO	A B S T R A C T
Keywords: Parenting postpartum Matrescence Perinatal depression Neuroplasticity	The transition to parenthood is perhaps the only time in adult life when the brain changes to such a significant degree in such a short period, particularly in birthing parents. It is also a time when there is an increased risk of developing a mental illness, which may be due, in part, to the increased neuroplasticity. Thus, we must develop interventions and treatments that support parents and promote parental brain health. This review will highlight key findings from current research on how human brain structure and function are modified with 1) the transition to parenthood, 2) parenting stress and perinatal mental illness, and 3) treatments aimed at promoting perinatal mental health. The focus will be on birthing parents and mothers, but brain changes in non-birthing parents will also be discussed. Improvements in our understanding of the parental brain, in health and with illness, will promote the well-being of generations to come.

#### Introduction

Parenting is the only time in adult life when the brain changes a significant degree in such a short period. In recent years an increase in the understanding of the neurobiological changes in the human parental brain has occurred.<sup>1</sup> This research complements what is known in non-human animals showing that the transition to parenthood, particularly in birthing parents, is unique and dynamic.<sup>1-8</sup> With the remarkable plasticity in the parental brain, along with the social and psychological changes that occur in parents-to-be and new parents, it is perhaps not surprising that this is also a time when there is an increased vulnerability to mental illness. Perinatal mental illness can be devastating for the parent, affecting the capacity for them to care for themselves and their child. Recent research points to a unique neurobiology of perinatal mental illness that overlaps with areas of the brain that are important for parenting,<sup>9-11</sup> pointing to an urgency to understand the parental brain in health and with illness. Fortunately, over the past few years, we have seen an increase in our understanding of therapeutic interventions supporting parental brain health.<sup>12,13</sup>

This review will highlight key findings from current research on the ways in which human brain structure (i.e., grey matter volume with magnetic resonance imaging (MRI)) and function (i.e., blood-oxygenlevel-dependent measures with functional MRI (fMRI)) are modified with 1) the transition to parenthood, 2) parenting stress and perinatal mental illness, and 3) treatments aimed at promoting perinatal mental health (Fig. 1). The focus will be on birthing parents and mothers, but brain changes in non-birthing parents will also be discussed.

It should be noted that the terms 'mother' and 'father' will be used throughout, in addition to 'birthing-' and 'non-birthing' parent. This is due, in part, to the fact that the majority of the research to date has been done on those parents who identify as mothers or fathers. It is also important to acknowledge that gender neutrality currently does not exist in parenting roles and we must continue to identify this disparity in research by using sex/gendered terms.<sup>14</sup>

#### Brain changes during the transition to parenthood

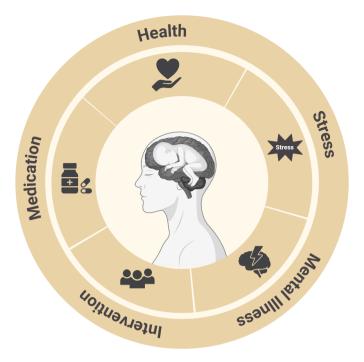
During pregnancy and the postpartum period, there is significant neural plasticity in the structure and function of the adult brain, an adaptation that is essential for the care of the infant<sup>5,15,16</sup>. The 'parental brain network' comprises areas of the brain important for empathy, emotion regulation, decision-making, executive function, threat assessment, motivation, and reward.<sup>17,18</sup> Furthermore, years of research in non-human animals show a complex interaction among many brain networks, neurotransmitters, and the hormones that mediate parenting.<sup>1,19</sup> Much of the recent research on human parents expands and complements what has been shown in non-humans, pointing to many conserved neural networks important for caregiving.<sup>19,20</sup> Below

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<sup>\*</sup> Correspondance author at: University of Rennes, Irset (Institut de Recherche en Santé, Environnement et Travail), UMR\_S 1085, F-35000, Rennes, France. *E-mail address:* j.pawluski@gmail.com.



**Fig. 1.** Key factors that can contribute to parental brain health. A growing body of research is elucidating how stress, perinatal mental illness, psychotherapeutic interventions, and medications are associated with plasticity in the parental brain. In order to promote parental brain health, we need to continue to understand how these factors affect the neuroscience of parenting. Created with BioRender.com.

we will focus on the brain changes in human parents from brain imaging studies.

#### Structural brain changes

Our understanding of how the human brain changes with parenthood has only recently been investigated. Perhaps the most robust findings to date are the extent to which grey matter volumes (consisting of neurons, glial cells, and synapses) of certain brain areas change across pregnancy and the postpartum period in birthing mothers. Recent research shows that from pre-conception to the early weeks postpartum, first-time mothers undergo extensive and highly consistent reductions in grey matter volume at the rate of 1% in brain areas important for aspects of social behaviors.<sup>21,22</sup> The brain areas most affected by pregnancy are those important for the ability to mentalize or cognitively infer the needs of others (theory of mind) and, thus, are critical for caregiving.<sup>21,22</sup> These brain changes are highly consistent, with 92% of mothers showing similar structural adaptations,<sup>22</sup> are related to circulating levels of progesterone in the third trimester,<sup>21</sup> and can persistent for years after birth.<sup>1,23</sup> In addition, recent research shows that these reductions in grey matter volumes may be more significant during late pregnancy and may be affected by the mode of birth in the immediate postpartum (but not months later).<sup>22,24</sup> For example, mothers who had a scheduled C-section (where labor was not initiated) had a larger pregnancy to postpartum increase in cortical volume, thickness and surface area compared to mothers who initiated labor regardless of gestational age, participant age, and other potential confounds. It is only the volume change across time that differed with birth experience but this suggests that the cascade of immune and endocrine adaptations of labor and birth affect the maternal brain. It remains to be determined how this may relate to any aspect of maternal health and wellbeing. It is also unknown whether these structural brain changes are affected differently by pregnancy with multiples or with subsequent pregnancies, but research in laboratory animals suggests that previous pregnancies can also affect the maternal brain.<sup>25</sup>

A reduction in brain volume, however, does not imply a reduction in brain function. The structural brain changes that occur in mothers represent a 'fine tuning' of the parental brain.<sup>1</sup> Less can be more. This 'fine tuning' of the maternal brain can be seen, for example, in associations between structural decreases in grey matter volume and increases in the quality of mother-to-infant bonding, as well as decreases in mothers' hostility toward their newborns in the postpartum period.<sup>23</sup> Thus, these structural brain changes across pregnancy are adaptive and important for the developing mother-child relationship.<sup>1</sup>

Notably, the reductions in grey matter volume observed across pregnancy are remarkably similar to those observed in human adolescence, another transitional life stage characterized by physiological and social changes.<sup>26</sup> This suggests that brain changes with matrescence<sup>27</sup> (the transition to motherhood) and adolescence may be due, in part, to hormonal changes during these life stages. Still, one can't rule out the significant impact of social and experiential factors on brain plasticity throughout life.

It is clear that the early postpartum months also are a time of dynamic brain plasticity in parents. Longitudinal studies have observed non-permanent *increases* in grey matter volumes in cortical and subcortical areas in mothers in the first weeks and months of the postpartum period, some of which correspond to brain regions affected by pregnancy.<sup>2</sup> These dynamic brain changes are positively related to feelings of parental efficacy, showing, again, that the structural brain changes with the transition to motherhood are important for the ability to care for a child.<sup>28,29</sup>

In fathers, the research on structural brain changes is steadily growing.<sup>17,30</sup> Research shows that across pregnancy and in early parenthood, the paternal brain decreases in grey matter volume by approximately 1% in cortical brain structures responsible for visual processing, attention, and empathy.<sup>31</sup> The postpartum paternal brain is also a dynamic structure, with research showing that, during the early weeks and months postpartum, fathers, similar to mothers,<sup>32</sup> have increases in grey matter volume in brain areas associated with reward, bonding, and theory of mind such as the amygdala and the striatum.<sup>30</sup> In summary, the experience of pregnancy is associated with a decrease in grey matter volumes in many brain areas in birthing- and non-birthing parents. We know that these decreases can also persist for years postpartum in birthing parents.<sup>33</sup> However, during the early postpartum period there are also non-permanent increases in grey matter volume in the parental brain. We have much more to learn about the structural plasticity of the parental brain but it is clear that it's not just pregnancy that changes the brain - experience parenting is key.

#### Functional brain changes

The effect of pregnancy and parenthood on the brain also involves functional brain changes that are important for responding to the young. These changes in activation of different brain areas are likely driven by a host of neurophysiological mechanisms<sup>16</sup>. Most of this research has focused on postpartum functional brain measurements using functional MRI (fMRI). This research often compares the neural response of parents to an infant cue (their own versus an unknown infant), or compares the neural response of a parent and non-parent to an infant cue. For example, new mothers show higher activation to infant facial expression in brain areas involved in processing and mentalizing networks than non-mothers.<sup>34</sup> In addition, first-time mothers have increased activation of a number of brain areas when they see their own infant's face compared to when they see an unknown infant's face.<sup>35</sup> Others show that mothers compared to non-mothers also have an increase in activation in brain areas involved in parenting when they see an unfamiliar infant's face.<sup>9</sup> This research shows that several neural networks are strongly engaged in a mother's response to cues from her own infant but also that, in general, a mother's (and father's) brain is more active in response to an infant compared to the brain of someone who has not

#### parented.

The brain networks more activated in parents include the brain's reward system, which regulates reward processing and the hedonic value of stimuli and is also known to play a crucial role in maternal motivation in various other mammals.<sup>36–38</sup> The brain's empathy and theory of mind networks are also highly responsive in mothers exposed to cues from their infants,<sup>39–41</sup> with studies showing that mothers have stronger activation to their own versus an unfamiliar infant in certain brain areas of these networks, such as the insula.<sup>42</sup> There is also the role of the brain's networks for processing salience and emotion regulation in mothers in response to their infant,<sup>43</sup> where these networks are activated by one's own versus unfamiliar infant stimuli,<sup>40</sup> especially if the stimulus comprises a negative emotional cue signaling infant distress.<sup>44,45</sup> Prior experience in parenting can also affect neural responses to infants.<sup>46</sup> This shows the importance of subsequent pregnancies and births on the parental brain.

In fathers and non-birthing parents, research points to similarities in functional brain adaptations to those seen in mothers with an enhancement in activation of many brain areas to an infant cue when compared to the neural response to the same cue in a non-parent.<sup>17,47</sup> However, very little research has compared mothers' and fathers' brain activity in the same study, making it challenging to understand how factors such as the time with the child, or pregnancy and lactation, may alter parental brain plasticity.<sup>17,48,49</sup> One study, comparing the brain response to a child in primary caregiver mothers and primary caregiver fathers, shows that primary caregiver mothers and primary caregiver fathers have similar activation levels in the amygdala, a central hub of the parental brain, in response to a video of them interacting with their infant versus a video of an unfamiliar parent interacting with an unfamiliar infant.<sup>50</sup> Furthermore, this amygdala activation is higher in primary caregivers than in secondary caregiver fathers. Interestingly, both groups of fathers (primary or secondary caregivers) showed greater activation in the superior temporal sulcus, an area important for social cognition, compared to mothers, regardless of whether the father was a primary caregiver or not.<sup>50</sup> This shows that time with the child affects brain regions important for parenting, but the question remains how these brain changes are related to the quality or quantity of parenting.

A recent study further demonstrates that the experience of parenting, and the ability to actively parent, influences the function of the paternal brain. In this study, fathers who actively responded to an infant cry (either consoling or non-consoling the infant) in a video simulation game, compared to when they passively listened to the cry, showed greater neural activation in brain areas involved in approach motivation and empathy.<sup>51</sup> Taken together these studies show that parenting experience and actively parenting has a significant effect on the paternal brain and influences similar brain areas as in the maternal brain. Thus, the parental brain exists regardless of sex and gender.

#### Brain changes associated with perinatal mental illness

A significant number of parents struggle with increased levels of stress, emotional difficulties, and mental illness during pregnancy and the postpartum period.<sup>11</sup> Baby blues are perhaps the most common experience of birthing mothers in the immediate postpartum period. The 'blues' are characterized by transient changes in mood, physical discomfort, fatigue, anxiety, and uncertainty about the maternal role and typically resolve within two weeks of birth.<sup>52</sup> Perinatal mental illness haves enduring effects on parental health, parent-infant interactions, and child development - in addition to the financial burden to society, which is in the billions each year.<sup>53–55</sup> Despite the prevalence and costs for the mother, parents, and developing child, our understanding of the neurobiological mechanisms mediating perinatal mental illness is limited.<sup>7,10,56–58</sup> As such, the current literature often points to an association between a perinatal mental illness and brain changes in structure and function. It remains to be determined if changes in neuroplasticity predict mental health outcomes or vice versa.

#### Stress and the parental brain

It is well known that various stressors are associated with changes in brain structure and function across the lifespan,<sup>59</sup> including during parenting.<sup>60</sup> When it comes to research on brain changes with parenting, we know that there is a role of parenting stress, which refers to physiological and psychological responses to the demands, stress, and challenges arising from caring for a child.<sup>61</sup> While a certain level of parenting stress is normal, high levels of perceived parenting stress can be associated with perinatal depression and harsh parenting styles.<sup>62</sup>

Research on how parenting stress is related to structural brain changes (such as volume differences) in parents is still needed, as the focus has been on understanding how stressors are associated with the functioning (rather than structure) of the human parental brain.<sup>60,63,64</sup> As early as late pregnancy, there is an association between high levels of perceived stress in mothers and greater brain response to low-distress, but not high-distress, infant cries.<sup>65</sup> This suggests that, even before birth, a parent's stress can begin to alter how the brain processes infant cues.

In the postpartum period, higher levels of parenting stress in birthing mothers (fathers and non-birthing parents were not included) are associated with reduced activity in brain areas important for decision-making and emotion regulation, such as the orbitofrontal gyrus and the amygdala.<sup>66,67</sup> Research also shows that birthing mothers, but not fathers, who feel more stressed in their role as parents have reduced neural synchrony with their children (3-4 years of age) in brain regions important for attention, working memory, and emotion regulation, such as the inferior frontal gyrus and the dorsolateral prefrontal cortex.<sup>68,69</sup>

When looking at physiological measures of stress, mothers who display less reactive circulating cortisol response profiles to the Strange Situation (a commonly used laboratory paradigm for mother-infant dyads that involves a series of brief separations and reunions) show increased brain activation to their infant's cry in brain regions involved in motivation, empathy, and emotion regulation, including the striatum, medial prefrontal cortex, anterior cingulate cortex, and insula.<sup>70</sup> These findings suggest a link between cortisol response trajectories, maternal brain activation, and parenting quality.

In addition to parenting stress, the association between other life stressors and the functioning of the parental brain has begun to be investigated.<sup>60</sup> For example, mothers who experience elevated exposure to socioeconomic, physical, environmental, and psychosocial stressors, e.g., low income, financial stress, substandard housing, crowding at home, marital dissatisfaction, sociocultural factors, and violence, have modified brain responses to infant cries in brain regions associated with emotion regulation, such as the medial and lateral prefrontal cortex.<sup>63,64,71</sup> Interestingly, mothers with socioeconomic disadvantage (low income-to-needs ratio) show increases in amygdala responses to infant distress images, which are associated with more intrusive parenting behaviors observed during interactions with their own infant.<sup>72</sup> The heightened amygdala response to infant distress may reflect a mother's hypervigilance to protect her infant. However, more research is needed to understand the link between stress, brain function and parenting.

#### Perinatal depression

The majority of research on the neurobiology of perinatal depression has focused on the postpartum period. Postpartum depression is associated with altered structural and functional neuroplasticity in the human maternal brain, which appears to be unique to depression during this period of life.<sup>5,6,73,74</sup> Although very few studies have investigated structural brain changes associated with perinatal depression, the data that do exist show that mothers diagnosed with postpartum depression have modifications in cortical thickness and surface area in brain areas important for empathy, e.g., insula, and sensory function, e.g., parietal lobe.<sup>75</sup> However, the direction of these structural changes is not consistent.<sup>76</sup> This is likely due to the limited research in this area, the

magnitude and type of depressive symptoms, and the timing of these studies during the postpartum period.  $^{76}$ 

The functional brain changes associated with postpartum depressive symptoms have been more commonly investigated. Interestingly, baby blues, which are experienced by a majority of mothers immediately postpartum, are associated with alterations in functional brain activity in brain areas associated with reward and motivation.<sup>77</sup> This suggests that these early postpartum emotional changes are linked to dynamic brain changes. How these changes may be linked to the onset of perinatal mental illness remains to be determined.

Research on the association between perinatal depression and functional brain changes has focused on two areas: 1) investigating brain activity at rest and 2) investigating brain activity in response to a cue or activity. Postpartum depressive symptoms are associated with increases in resting-state activity in the right frontal lobe,<sup>78</sup> and more specifically mothers with postpartum depression (who also have significantly elevated levels of anxiety) show weaker connectivity between the amygdala, anterior cingulate cortex, dorsal lateral prefrontal cortex, and the hippocampus compared to non-depressed postpartum women.<sup>7</sup> Recent research also shows that the changes in functional activity in the dorsal lateral prefrontal cortex are negatively associated with scores on the Edinburgh Postnatal Depression Scale at 4 weeks postpartum.<sup>81</sup> Thus, mothers with perinatal depression have significant alterations in functional brain activity when at rest in brain regions important for self-regulation, empathy, and emotion. It remains to be determined how this is linked to changes in mothering.

Postpartum depression is also associated with altered brain functioning in response to parenting- and non-parenting specific emotional cues.<sup>6</sup> For example, when exposed to an emotional cue, such as a negative word or an adult's angry face, there is a decrease in the activation of the amygdala in women with postpartum depression compared to healthy controls.<sup>82</sup> However, when exposed to an infant's smiling face or infant cry, women with depression compared to women without depression show an increase in the activation of the amygdala.<sup>83</sup> This research underlines the importance of cue type to characterize the association between postpartum depression and the functioning of the maternal brain and shows that brain responses in mothers with postpartum depression are particularly heightened in response to their children. Furthermore, these differences in amygdala response associated with postpartum depression may be contributing to decreases in sensitive and positive caregiving; more research is needed in this area.

The question of whether neural activation patterns differ in women with postpartum depression and women with depression outside of the postpartum period is a vital topic of discussion and many help us to understand the unique characteristics of perinatal depression, and perinatal mental illness, in general.<sup>9,84</sup> Recent research shows that mothers with postpartum depression have increases in right amygdala activation in response to an infant cue compared to non-mothers with major depression as well as to healthy women both postpartum and not postpartum.<sup>9</sup> Reasons for these differences in brain activation with motherhood remain to be determined, but it is likely that, although postpartum depression and major depression share similar symptomology, they are differentiated by timing of onset, physiological profiles, the presence of an infant, and the excessive worry and/or guilt surrounding parenting abilities that occurs in many women with perinatal depression.<sup>9</sup>

Up to 10% of new fathers will struggle with depression. Yet our understanding of changes in the paternal brain associated with these illnesses is limited. One study points to a link between depression and paternal brain structure by showing that greater increases in grey matter volumes of brain areas important for reward processing and emotion regulation were associated with decreased levels of depressive symptoms in the early postpartum months.<sup>30</sup> The uniqueness of changes in the adult brain associated with perinatal mental illness should direct researchers to consider the importance of the reproductive state when investigating the neurobiology of mental illness.

#### Other perinatal mental illnesses

There are a number of other mental illnesses associated with the perinatal period, but few have been investigated in terms of neurobiology. Following is a review of what we know of brain changes associated with perinatal anxiety and with postpartum psychosis. For parental brain changes associated with childbirth-related PTSD, opioid use disorder, the role of childhood trauma on the parental brain, borderline personality disorder, and pregnancy loss on the maternal brain, see.  $^{10,85-88}$ 

#### Anxiety

The focus of the limited number of studies on perinatal anxiety and associated parental brain changes has been on functional, and not structural, brain changes.<sup>89</sup> A mother's level of anxiety is associated with brain responses to infant cues, often with greater brain activity with higher levels of anxiety. For example, mothers with higher levels of trait anxiety have heightened neural responses in the amygdala to photos of their own and unfamiliar infants exhibiting positive affect (i.e., smiling faces), whereas mothers with lower levels of trait anxiety only show an increase in amygdala response when viewing photos of their own infants.<sup>90</sup> Consistent with this result, mothers with high trait anxiety express lower positive feelings towards their infants. Interestingly, mothers with high trait anxiety show lower amygdala response to infant faces in general, as well as lower functional connectivity in brain areas important for emotion regulation and empathy (i.e., amygdala and insula).<sup>83</sup> This suggests that connectivity between these brain regions may be associated with anxious mothers' caregiving sensitivity.<sup>9</sup> Others have shown that, in the early postpartum period, maternal anxiety levels are associated with reactivity in brain regions involved in emotion regulation (i.e., inferior frontal gyrus and insula) to negative emotional cues that are not specifically infant-related,<sup>39</sup> suggesting a general modification of brain responses to emotional cues with higher levels of anxiety.

#### Postpartum psychosis

A growing body of research is showing that a neural signature of postpartum psychosis may exist.<sup>92</sup> When looking at structural brain changes, mothers with a recent episode of postpartum psychosis have smaller anterior cingulate gyrus, superior temporal gyrus, and parahippocampus gyrus compared to mothers with a history of mental illness but not postpartum psychosis.<sup>93</sup> Functional brain imaging shows that mothers at risk of postpartum psychosis or those who develop an episode have changes in functional connectivity and activation in brain areas important for emotion processes in executive functioning, such as the amygdala and fronto-cingulo-subcortical brain regions.<sup>94</sup> How these changes in neurobiology directly relate to caregiving behaviors remains to be determined.

#### Promoting parental brain health

Parenting and perinatal mental illness are linked to several biological and social factors, including genetics, hormone fluctuations, immune system changes, isolation, relationship distress, and sexism. Effective evidence-based interventions to promote parental mental health are vital to improve outcomes for parents, their children, and society. Given the extensive research based on the Developmental Origins of Health and Disease model (see additional papers in this volume), it is arguably more effective to support and treat parents struggling with parenting or a perinatal mental illness than to combat the multiplicative problems later in life for the mother, child, and family. Interventions and treatments can be, and perhaps should be, multifaceted, focusing on improving perinatal mental health, the co-parenting relationship, parent-child interactions, parental confidence and self-efficacy, and social support. Research shows that simply improving symptoms of mental illness alone does not improve maternal self-efficacy.<sup>95</sup> In turn, interventions that target couples or families have the potential for greater improvements.  $^{96}$ 

Although still in its infancy, there is a growing understanding of how interventions and treatments to support parents and perinatal mental health affect the parental brain.

#### Psychotherapies and the parental brain

There are a growing number of evidence-based psychotherapeutic interventions for perinatal mental illness, but further research is needed to understand how they are linked to changes in the parental brain. For example, we know that Interpersonal Therapy (IPT) as well as Cognitive Behavioral Therapy (CBT) are effective in reducing symptoms of perinatal depression.<sup>97</sup> Recent research also suggests that eye movement desensitization and reprocessing (EMDR) is an effective treatment for posttraumatic stress following a traumatic birth.<sup>98</sup> The effectiveness of these treatments is likely related to changes in the parental brain, as both IPT and CBT can alter activity in brain regions important for emotion regulation in non-parents.<sup>99,100</sup>

The most well-studied psychotherapy in terms of neurobiological changes is *Mom Power*. This 13-session parenting and self-care skills group, which is client-led, focuses on enhancing a parent's mental health, parenting competence, and engagement in treatment. This intervention reduces perinatal depression, posttraumatic stress, and caregiving helplessness.<sup>101</sup> In addition, the affect of *Mom Power* can be seen in improvements in neural activity in parental brain areas related to 'over mentalizing', e.g., misattributing the child's behavior, and 'undercoupling', e.g., the parent is disengaged from observing how their physical or verbal actions make their child feel.<sup>102</sup>

Mindfulness interventions also show promise in improving parentchild interactions, and a recent study shows that a mindfulness-based parenting intervention is associated with altered functional activity in the maternal brain. More specifically, modifications in mothers' brain function and connectivity were associated with increased mindful parenting and decreased emotional reactivity during a parentadolescent conflict task.<sup>103</sup> The exact way in which psychotherapeutic interventions affect the neurobiology of parents remains to be determined, but the emerging evidence demonstrates the biological impact of these interventions.

#### Pharmacotherapies and the parental brain

It is assumed that pharmacotherapies directly affect the parental brain due to their mechanisms of action and previous research.<sup>104</sup> However, there is little research on human parents in this area. Perhaps the most widely studied pharmacotherapies with regard to neurobiological mechanisms are the allopregnanolone-based medications brexanolone and zuranolone (for review see<sup>105</sup>). These medications are synthetic neuroactive steroids that alter functional connectivity in the brain via their actions on GABA signaling.<sup>80,106,107</sup> Research shows they are effective in the treatment of postpartum depression, and there is a growing body of research on their neural mechanisms of action in the postpartum brain.<sup>57,108</sup>

Selective serotonin reuptake inhibitor medications (SSRIs) are the most widely used pharmacotherapies for perinatal mood and anxiety disorders, yet our understanding of how they act to modify the parental brain is limited in both humans and animal models (for a review see<sup>109</sup>). One study looking at neural biomarkers shows that SSRIs significantly increase serum brain-derived neurotrophic factor levels in late pregnancy, suggesting an increase in neuroplasticity. This research also shows that there is an association between a biomarker for glial cells (S100 calcium-binding protein B) and depressive symptoms in SSRI-treated women.<sup>110</sup> This suggests that neural cell types are differentially involved in the functions of SSRIs on depressive symptoms in birthing parents.

received tDCS during pregnancy remitted at 4 weeks postpartum,

compared to just 12.5% of women in the sham group<sup>114</sup>. The neural mechanisms behind these effects on the parental brain remain to be determined, but these therapies show promise in the treatment of perinatal mental illness.

depression (for review see<sup>112-114</sup>). A recent pilot study in pregnant

women with major depression shows that 75% of the women who

mental illness often arises. To date, there is a lack of clarity on how

circulating levels of hormones are linked to perinatal mental illness and

how to use them for the treatment of perinatal mental illness (for review see  $^{56,57,111}$ ). There are additional pharmacotherapies used for the

treatment of perinatal mental illness, but further research is needed to

understand how they may alter the structure and function of the

parental brain. Ultimately, understanding the mechanisms of these medications and their ability to treat a given set of symptoms would

greatly advance treatment outcomes for those parents struggling with

Both electroconvulsive therapy and transcranial direct current stimulation (tDCS) are effective in reducing symptoms of perinatal

#### Supplements

perinatal mental illness.

Interventions directly targeting the brain

Several additional therapies and interventions may be beneficial for alleviating parenting stress and symptoms of perinatal mental illness.<sup>115</sup>, <sup>116</sup> With the growing implications of the role of the gut-microbiota-brain axis in maternal mental health,<sup>117</sup> supplements and gut-targeted interventions have started to be investigated. Recent research shows that probiotic treatment during pregnancy may be effective in decreasing postpartum anxiety and depression<sup>118</sup> through effects on the maternal brain<sup>119</sup>. Interestingly, supplementation targeting the monoamine oxidase-A metabolism in the early days postpartum can decrease baby blues.<sup>120</sup> Exactly how these supplements affect the parental brain remains to be determined. Regardless, this is an intriguing area of research, with the possibility of providing additional interventions that can uniquely support and promote parental brain health.

#### Conclusions

The adult human brain undergoes significant modifications in structure and function with the transition to parenthood. Many of the brain areas important for parenting are affected by parenting stress and implicated in perinatal mental illness. Given the high rates of perinatal mental illness, there is an urgency to improve the well-being of parents and positively affect generations to come. To do this, understanding the neurobiological underpinnings of perinatal mental health should be the focus of further research to develop targeted brain-based interventions to promote parental brain health. Although further advancements are needed to develop specific brain-based interventions for parent brain health, for now, we can continue to implement evidence-based interventions and treatments at multiple levels (e.g., individual, institutional, and community) that support parenting. The parental brain is part of the foundation that society is built on. As such, we must prioritize and support its development.

#### Declaration of competing interest

The author has no relevant financial or non-financial interests to disclose.

The question of hormone replacement in the treatment of perinatal

#### J.L. Pawluski

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#### J.L. Pawluski

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