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Cognitive functioning of women in pregnancy and early postpartum

Włodzimierz Płotek¹, Marta Czarnecka-Iwańczuk², Małgorzata Grześkowiak³

¹ Department of Teaching Anaesthesiology and Intensive Therapy, Poznan University of Medical Sciences, Poland

² Department of Clinical Psychology, Poznan University of Medical Sciences, Poland

³ Department of Teaching Anaesthesiology and Intensive Therapy, Poznan University of Medical Sciences, Poland

ABSTRACT

Pregnancy and early postpartum is an extremely stressful time in a woman's life. Emotional and cognitive functioning are mutually interconnected. The psyche also influences the physical health on the functional and physical basis. The physiological hormonal changes adapt woman to the development and labour of a child and reflect in the central nervous system functioning. In the presented manuscript, the basic psychological problems accompanying women in this period, as well as mutual relationships between the hormonal and central nervous systems during pregnancy and early postpartum have been presented.

Keywords: pregnancy, postpartum, cognitive functioning.

Introduction

The functioning of the human consciousness and the interrelations between the mind and the brain have been subject to analysis of numerous scientists representing various branches of science. From Antiquity until the modern times it has been an issue not only philosophical in nature, but also psychological and medical. Despite the centuries of research and the search for more and more precise research tools dealing even with molecular structures and for theories trying to find explanations basing on quantum physics (Hameroff, Penrose), the knowledge of the functioning of human consciousness still remains to a greater extent a secret closely guarded by Nature. In medical practice, the aspect of cognitive and emotional functioning is of extreme importance, yet, quite often not widely acknowledged.

Pregnancy is an exceptional time in a woman's life, as well as in the lives of those closest to her. It is not only a medical situation, but also a psychological and social one. The physiological changes which

take place in an expectant mother are accompanied by a number of psychological ones. Two spheres of expectations arise from of such changes: one – of a medically healthy child, and the other – of the woman becoming a mature and responsible mother, the person most important to her offspring, at least for the time in which she devotes herself to their upbringing and care. Since pregnancy involves so numerous changes within the body and the psyche of the woman in pregnancy, as well as influences her relations with the world, it is a disruption of the biopsychosocial balance requiring readjustment, and, as such, it is a highly stressful time.

Pregnancy (physiological) is defined as "the period and the range of changes taking place in a woman with a foetus developing in her uterus. It is a physiological condition, yet it is very demanding to the woman's body and, as such, it can easily become a pathological state, detrimental to the woman's organism, as well as the child's" [1]. The maternal pregnancy changes involve main body organs and systems and are present within the whole gestation period [2, 3].

Since pregnancy is considered a physiological condition, it does not require a considerable change in one's lifestyle. **The processes taking place in the pregnant woman**, however, require a different approach to such matters as nutrition, physical activity, addictions or hygiene. Thus, it can be stated that although it is a natural condition, it is also an additional burden for the expectant mother [4]. Whereas the whole strain on the body, as well as the changes in it, are a source of physical stressors and may become a source of physiological stress. This immense mobilisation of the body influences, in turn, the psychological well-being of the mother-to-be [5].

Morphological and functional changes influence the alterations in the pregnant woman's psyche. The whole gestation period and labour, in turn, are extremely relevant to her emotional state [6]. From the psychological point of view, even a healthy pregnancy is an extremely challenging time. In order to prepare emotionally and practically for the new child, the woman in pregnancy and her partner have several tasks to complete. These are as follows:

- accepting the reality of the pregnancy;
- facing the consequences of being pregnant;
- coping with physical changes;
- coping with uncertainty and unpredictability;
- coping with changes in role and relationships;
- managing unexpected and untoward events and minor pregnancy complications [7].

The experiences and emotional processes of the expectant mother (and more precisely their character, proportions and intensification) vary in each of the trimesters. **A considerable portion of the maternal changes** can be analysed with respect to the three aspects of the mother's functioning: perception of her own body, perception of herself and changes in social contacts (the physio-psycho-social "I" changes) [8].

Learning about certain elements of the human cognition of "be" may turn out not only to be the matter of discovering new realms of interest, but also translating this into medical practice.

This manuscript presents the character and the role of changes in cognitive functioning in pregnancy and early postpartum.

Cognitive dysfunction during pregnancy

'I swear, I lose brain cells with each pregnancy and I never get them back.'

The above words were written by a woman on an Internet forum. Is there any truth in them? Let us have

a closer look at the results of experimental research on animals providing the basis for further clinical analyses.

Animal research showed an increase in dendritic tree density, a higher concentration of the Brain-Derived Neurotrophic Factor (BDNF), E2 estrogen receptor density (neuroprotection) and NMDA (Long-Term Potentiation processes improving memory), a decrease in the astroglial reactivity, a decrease in apoptosis and an increase in synaptophysin (synaptic vesicle protein, takes part in neurotransmitter release) in the CA1 region of the hippocampus. A decreased activity of the c-Fos gene and a lower density of dendrites was noticed within the amygdala (responsible for experiencing fear, among others). Simultaneously the volume of those cells increases. Hypothalamus is also subject to changes: **there is a change in the immunoreactivity of GFAP** (Glial Fibrillary Acidic Protein – intermediate filament protein, found in glial cells, such as, for instance, astrocytes).

Care over children stimulates neurogenesis and the incorporation of new cells into the existent neural networks. **New neural connections are formed and provide** the basis for development and faster learning. The above changes are accompanied by the changes in the hypothalamic-pituitary axis and opioid receptor sensitivity. The plasticity of sensory cortex increases. The above anatomical changes are reflected in a change in behaviour, with a visible improvement in memory, increased speed, decreased fear and they were persistent throughout the whole life of the animal. What is more, the number of amyloid deposits (responsible for aging of the central nervous system and the development of dementia) is lower in multiparous animals as compared to nonparous ones.

Thus, assuming that cognitive dysfunction in pregnancy in fact occurs, one can notice a paradox between the problem reported by women in pregnancy and the experimental data from animal research (Rodent-human paradox). Obviously, as in any case of an attempt to relate animal research results to humans, one should take into account the enormous differences in physiology of the subjects and methods applied in tests; yet this problem seems to be extremely interesting [9].

Among the many factors which could influence the homeostasis of the central nervous system, the influence of the hormonal changes in pregnant women should be analysed. **The changes in hormone concentrations** are considerable, and literature shows numerous interconnections between the functioning of the central nervous system and the endocrine system in physiology and pathology.

Hormones: neuroprotection and damage

1. Estrogens

Basic science has outlined the role of estrogens as neurotrophic and neuroprotective substances. The preventive role of estrogens for the CNS is stressed, as observational research points to the procognitive effect in women in a good initial neurological condition, undergoing a replacement therapy. Administering estrogens to women with pre-existent neurological damage aggravated the hitherto prevailing bad neurological condition. Details on the above issue are presented by the authors of the WHIMS study (Women's Health Initiative Memory Study) [10]. What is the underlying aspect of estrogen neuroprotection? Complicated relations on the subcellular level include calcium homeostasis, enhanced ATP production in neuronal cells, whereas the common link between those mechanism is the mitochondrion, in which estrogens, through their influence on the expression of several dozen proteins, induce changes in cellular energetics, functioning of oxygen radicals, stress response and cell survival.

2. Androgens

In laboratory and clinical research the neuroprotective role of androgens is quite well-known. On the one hand, it is known that androgens are endogenous negative regulators of beta-amyloid accumulation and that they alter neuronal sensitivity to pathological deposits, on the other, that they play a role in transferring signals inhibiting apoptosis. Brain is an organ strongly reactive to androgens, while mood disorders, cognitive dysfunction and libido disorders constitute a neurological representation of their deficiency. CNS aging processes and the development of neurodegenerative changes are closely related to androgen deficiency. Androgens are neuroprotective thanks to the inhibitory activity of 5 α -androstane-3 α ,17 β -diol metabolite, which activates GABA-A receptors (in the same manner as benzodiazepine anticonvulsants). There are other possible mechanisms responsible for the protection of the CNS. These are: the aromatisation of androgens to estrogens (which role has already been mentioned), the induction of Hsp-70 heat shock proteins production and increased catalase activity (antioxidating function) [12].

3. Progesterone

This hormone has numerous functions in the CNS which are not related to procreation and is responsi-

ble for regulating the CNS in many of its aspects. There are progesterone receptors in virtually every cell of the central nervous system. There is an especially high amount of them in the hypothalamus, but they are also present in the hippocampus and the frontal cortex – structures of key importance to human cognitive functioning (diminishing inflammation and the activity of nitric oxide syntase, decrease in the brain barrier permeability, glia activation). Progesterone receptors can be also found in other locations, such as the posterodorsal nucleus of the amygdala (a structure responsible for emotions), brain stem structures, the cerebellum or even the spinal cord (stimulation of Brain-Derived Neurotrophic Factor (BDNF) production, enhanced acetylcholinesterase activity). The basic mechanisms of progesterone activity are as follows: regulating gene expression, modulating neural transmission systems and activating signalling cascades. Certain locations of receptors are related to the anti-apoptotic function (the hypothalamus and the spinal cord). Progesterone and its 5 α -reduced derivatives (dihydroprogesterone and tetrahydroprogesterone) stimulate Schwann cells proliferation and activate them to produce myelin. Other functions: stimulation of aerobic metabolism, decreasing the production of oxygen free radicals and lipoperoxidation. It stimulates mitosis of neural progenitor cells and their proliferation. These positive effects of progesterone are currently reflected in the trials consisting in the application of this hormone in experimental models of CNS trauma and inflammation. As it turns out, however, the relationship between estrogens and progesterone may be antagonistic in nature and reduce the neuroprotective influence of estrogens. On the clinical level, a progesterone metabolite – allopregnanolone – has anticonvulsant and tranquilising properties (stimulation of GABA-A receptors). Clinical research on Premenstrual Dysphoric Disorder (PMDD) showed that negative mood changes in the luteal phase are at least partly related to the high level of progesterone. Single doses of progesterone administered orally to young women impair face perception [13].

4. Corticosteroids

The influence of a high level of corticosteroids on lower memory word retrieval results, but not on working memory or recognition in pregnant women was presented by Laura Glynn. It should be remembered that for the optimum functioning of the CNS the optimum level of corticoids is indispensable. Both, their too low and too high level disrupt mental processes [14]. The hippocampus (memory) and the frontal lobes (work-

ing memory) are CNS structures susceptible to the fluctuation of steroid levels, and cognitive dysfunctions have been widely described among patients with Cushing's and Addison's diseases [15]. Steroid therapy may cause dysfunctions of the declarative or verbal memory and may occur even after 4–5 days of dexamethasone or prednisone therapy. The dysfunction occurrence is dose-dependent, and the dysfunctions resolve once the therapy is terminated. Patients undergoing steroid therapy present psychiatric symptoms early in its course. The symptoms which include manic episodes (short term therapy), depression (longer therapy) or mixed states. 1/6 of patients treated with steroids experience acute psychotic disorders in the form of delirium. It should be stressed that women are minimally, yet statistically significantly, more prone to psychiatric side effects of the steroid therapy [16].

5. Oxytocin

In mammals oxytocin is responsible for complex emotional and social behaviours: it increases group attachment, social recognition and lowers aggression. What is more, it also lowers anxiety and has effect on the level of fear. In the human being oxytocin administration enhances trust, which suggests that the target of its effect is the amygdala. In Kirsch's study involving the use of the functional magnetic resonance imaging with BOLD technology, the administration of 27 IU of oxytocin nasally to men resulted in the lack of reaction of the amygdala to the presented image of an angry or fearful face as compared to placebo (especially on the left) [17].

Changes in the CNS occurring during pregnancy

1. Quantitative changes.

Oatridge et al. conducted MRI brain volume measurements in 9 healthy women and 5 women with pregnancy induced hypertension (PIH). As a result it was stated that both groups of women were characterised by the decrease in brain volume, which was the highest at the peripartum period, and regained its normal volume within 52 weeks after labour. A statistically significant difference was also recorded referring to a greater decrease in brain volume in women with the PIH. Simultaneously, no discrepancies regarding the volumes of brain ventricles were noted. The probable aetiology of the aforementioned changes may be hormonal, vascular and metabolic changes. The authors suggest the role of high levels of corticosteroids, which

are known to cause neuronal atrophy during exogenous administration. The biochemical changes in the cerebrospinal fluid resulting in a decrease in density in the peripartum period may constitute the cause for the change in the metabolic state and the size of the CNS cells. The increase in triglycerides, LDL and HDL cholesterol may be answerable for the changes in the volume of cell membranes. The authors suggest that the changes in cell membranes may occur as a result of the foetus drawing the necessary fatty acids, contributing with that to the occurrence of the aforementioned cell membrane changes. A greater brain volume decrease in women with the PIH may be related to the typical to this condition intravascular hypovolemia aggravated by second-line diuretic therapy, endothelial dysfunction resulting from oxidative stress, anomalous vessel reactivity with vasoconstriction and higher vessel permeability [18].

2. Cognitive changes

One of the most important cognitive functions is memory. Many authors have dealt with the problem of the potential occurrence of memory dysfunctions. Many of them agreed that the problem exists in reality (Condon et al. 1991, Sharp et al. 1993, Keenan et al. 1998, Buckwalter et al. 1999, Shetty, Pathak 2002, de Groot, Horstra et al. 2003, Lurie et al. 2005, de Groot, Vuurman 2006, Rendell, Henry 2008, Glynn 2010). On the other hand, there are a number of researchers questioning such a possibility (Casey et al. 1999, Christansen 1999, McDowall, Moriarty 2000, Crawley 2003, Christensen 2010). The issue is difficult to settle.

Where can such dysfunctions originate? It seems that if they occur they are stimulated by metabolic conditions related to hormonal changes or the changes in CNS neurotransmitters. Cultural stereotypes and lifestyle-related factors are also relevant. Let us have a closer look at the hormonal changes. As early as in 1998 Buckwalter et al. examined 19 women in the final 2 months prior labour and after labour. **They were evaluating** the relations between various hormones (cortisol, DHEA, estradiol, progesterone, testosterone) and cognitive tests results (21 tests assessing various functions). It turned out that in their statistical analysis no uniform pattern of the dependence between the levels of the said hormones and changes in cognitive functions was found [19]. Studies analysing various levels of plasma neurotransmitters and memory tests in healthy women in pregnancy were carried out by Shetty and Pathak in 2002. The researchers evaluated the levels of epinephrine, norepinephrine, serotonin and dopamine

and stated a significant decrease in the levels of epinephrine, serotonin and dopamine in each of the trimesters as compared to healthy not pregnant women. Additionally, a statistically significant increase in the level of norepinephrine in pregnant women was noted. Psychometric studies confirmed a significant ($p < 0.001$) memory loss. In their final conclusions the authors suggest interrelations among the measured parameters [20].

It may be a relevant question to pose whether cognitive dysfunctions are more common in the case of multiparous or primiparous pregnant women. Parsons et al. analysing pregnancy histories and comparing them to the results of psychometric measurements of verbal functions believe that the highest risk of dysfunction occurrence is borne by the woman in her first pregnancy [21]. Brindle et al., in turn, stress the finding that memory dysfunctions are more common in multiparous women [22]. Moriarty and McDowall challenged the results of these studies, as they found no discrepancies in the declarative and non-declarative memory tests carried out on women [23]. The pregnancy trimester may constitute a different issue. Brindle et al. suggested the relevance of the second trimester of pregnancy as the time most susceptible to the occurrence of dysfunctions [22]. Keenan et al. do not concur, as according to their findings it is the third trimester that bears the greatest risk of dysfunction occurrence [24]. De Groot et al. seem to have assumed a mediative role in this dispute. Cognitive dysfunctions are characteristic to the whole duration of pregnancy [25]. Bearing in mind the lack of a joint stance and so many, often exclusive, conclusions, it is important to note the scientific work carried out by Helen Christiansen et al. In The Personality and Total Health (PATH) Through Life Project the subjects were 2404 women aged 20–24. Within 8 years of observing the cohort group 188 women were pregnant and became mothers. The authors evaluated cognitive functions in 4 domains: cognitive speed, working memory, as well as short-term and long-term memory. The final conclusion of such a large study as it was, was the rejection of the hypothesis that pregnancy and maternity are related to the impairment of mental functions [26].

3. Interpretation problems.

It seems that when analysing data and studies on as complicated a field as cognitive psychology in pregnancy one should take into account a manner of additional factors. These may include:

- sleep disorders,
- depression,

- anxiety and fear,
- aspect of social perception,
- research conditions.

Sub a) Sleep disorders.

The REM cycle is shortened as a result of high concentrations of estrogens, whereas progesterone causes the non-REM phase to lengthen. Frequent urination, coexistent gastroesophageal reflux and breathing difficulties contribute to the poorer quality of sleep. The clinical symptoms are insomnia, parasomnia, restless leg syndrome, snoring, sleep apnea syndrome, excessive daytime somnolence [27].

Sub b) Depression.

Even up to 10% of pregnant women comply with the major depression criteria, whereas in 18% of cases it is possible to notice symptoms characteristic for depression. In the first 6 weeks after the labour 10–15% of women suffer from depression, and if they experienced depression episodes prior to labour the percentage is higher – even up to 25–50% of cases. The occurrence of depression during pregnancy and in postpartum results in: a higher percentage of peripartum complications, aversion to breastfeeding, infants' sleep disorders, a poorer relationship between the mother and the child, inappropriate affective control, and even poorer results in children's psychological tests [28]. Sleep disorders and depression are linked and the correlation between them was proven by Okun et al., who showed, basing on a study involving 56 women with a prior history of depression, that bad sleep quality in the first 17 weeks after labour increases the risk of depression relapse [29].

Sub c) Anxiety.

It is a common phenomenon. Multiparous women are exposed to a higher level of anxiety as compared to the primiparous, in whose case the level of anxiety grows gradually [30]. Analysing the degree of anxiety intensity and depressive symptoms in pregnancy one can notice a specific pattern of their occurrence. Anxiety has the pattern resembling the letter 'U', whereas the aggravation of depression has a tendency for gradual decline [31]. The influence of mother's anxiety is not neutral to the child – Beijers et al. conducted a study among 174 mothers and their children which showed that stress and anxiety in the prenatal period may have an influence on the increased incidence of infections in infants (increase by 9.3% in the number of respiratory tract infections, by 10.7 in systemic infections and

by 8.9% in skin infections) and the need to administer antibiotics (7.6%), even after taking into account many external factors. There were no indication of the influence of prenatal anxiety on the development of digestive system dysfunctions [32].

Sub d) Aspect of social perception.

It should be also taken into consideration that a large part of society expects, or even imposes, the coexistence of mental dysfunctions in pregnant women. In a simulation research on workplace conflicts the behaviour of subordinate men or women towards the female team manager was studied. Each of the participants in the study took part in two 10-minute interactive sessions with two managers, one of who pretended to be pregnant. The meetings were recorded and the emotional responses of the participants were recorded basing on an appropriate questionnaire. The research showed that the participants had more negative emotional responses and a lower level of satisfaction following the interaction with the 'pregnant' manager. The subjects expected the pregnant manager to be more passive, nicer and prone to suggestions and were astonished at her authoritarian behaviour [33]. Such results constitute an example of the dominance of our expectations over objective judgement.

Sub e) Research conditions.

What is evaluated in laboratories does not have to correspond to the real life situation. The short duration of research in laboratories may be misleading. Rendell and Henry ran a comparative study on 20 women in pregnancy and 20 not pregnant women to evaluate their prospective memory. And, while in laboratory no dysfunctions were noted, the home part of the study, involving longer memory tasks showed the existence of memory dysfunctions. The above results provide a new research perspective and partly explains the discrepancies among various studies [34].

Summary

Although professional experience and observations quite clearly suggest the occurrence of CNS dysfunctions in pregnancy and early postpartum, studies have not yet been able to provide a clear-cut basis to diagnose them. Perhaps the new suggestions of a different research methodology shall constitute a basis for more decisive tests.

The functioning of the human brain maintains largely a 'terra incognita'. Despite the incredible

progress in cognitive science, many problems are, and most certainly will remain, unsolved for a long time. The presented results of various studies show how many contradictions and newer and newer questions are yet to be tackled.

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Conflict of interest statement

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Correspondence address:

Marta Czarnecka-Iwańczuk
Poznan University of Medical Sciences
Department of Clinical Psychology
70 Bukowska Street, 60-812 Poznan, Poland
phone: +48 61 8547274
email: tunell@wp.pl