Kognitivni razvoj i inteligencija, duševno zdravlje i duševni poremećaji – imaju li antenatalno podrijetlo?

/ Cognitive Development and Intelligence, Mental Health and Mental Disorders – Do They Have an Antenatal Origin?

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Ljudski je mozak nevjerojatan i fascinantan organ u svakom pogledu. Prirodi je trebalo nekoliko milijardi godina da evolucijom konstruira i usavrši tako sofisticiranu arhitekturu s beskonačnim spektrom savršeno koordiniranih funkcija i nevjerojatnom mogućnosti promjene i prilagodbe. Danas nam razvoj tehnologije omogućuje da potraga za razumijevanjem ljudskih kognitivnih sposobnosti i prilagodbe na složeni okoliš obuhvati i ono ključno razdoblje u kojem se odvija razvoj najsloženije strukture u ljudskom tijelu – prenatalno razdoblje. Uvidom u fetalne procese razvoja mozga i živčanog sustava pomalo se potvrđuje teorija kako većina moždanih funkcija koje proučavamo već godinama svoj začetak imaju upravo u prenatalnom razdoblju. Isto tako, međuigra između genoma, epigenoma i okoline oblikuje fenotip ljudskog zdravlja ili bolesti, čak i prije rođenja. Čini se da je došlo pravo vrijeme za promociju nove specijalnosti prenatalne i perinatalne psihijatrije.

/ The human brain is an incredible and fascinating organ in every respect. It took nature several billion years of evolution to construct and perfect such a sophisticated neural architecture with an infinite spectrum of perfectly coordinated functions and amazing capability for change and adaptation. Today, the advancement of technology has enabled us to strive to understand human cognitive capabilities and adaptation to an elaborate environment, which includes that crucial period in which the most complex structure in the human body develops – the prenatal period. Insights into the processes of fetal brain and central nervous system development are gradually confirming the theory that most brain functions we have been studying for years have their origin in the prenatal period. Similarly, the interplay between the genome, epigenome, and environment shapes a phenotype of human health or illness even before birth. It seems that the time has come for a recognized specialty in Prenatal and Perinatal Psychiatry.

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ANATOMIJA OŠTROUMNOSTI

Ništa nije složenije i tajanstvenije od svijeta živčanih stanica koje oblikuju naš mozak. Taj nam organ omogućava spoznaju stvarnosti, kao čarolijom stvara boje, mirise i osjećaje te na zagonetan način proizvodi naše inteligentno ja koje shvaća veze i rješava probleme. Kako se bude, kako funkcioniraju dimenzije naše intelektualne snage?

Zaista naš je mozak misterij: kako tom organu uspijeva prepoznati veze, rješavati problem, pamtiti činjenice i planirati budućnost? I zašto nekim ljudima omogućava da misle brže od drugih? Neuroznanstvenici već dugo pokušavaju dokučiti biologiju inteligencije (1-9).

Od rođenja se 100 milijardi neurona u našoj glavi svake sekunde neprestano mijenja. Svaki dojam, svaka misao, svako sjećanje ostavljaju tragove u mozgu i omogućavaju mu sazrijevanje.

Potpuno razvijen humani mozak sadržava oko 100 milijardi neurona i uglavnom nema stvaranja novih neurona nakon rođenja. Fascinantan je podatak da se neuroni stvaraju u razvijajućem mozgu prosječnom brzinom koja je veća od 250.000 u minuti (10).

ANTENATALNI RAZVOJ MOZGA

Središnji živčani sustav razvija se iz embrionalnog ektoderma. Stanice koje će postati neuroni i glijalne stanice potječu iz neuralne ploče koja

ANATOMY OF INTELLIGENCE

Nothing is more complex or mysterious than the world of neurons shaping our brain. This is the organ that enables us to perceive reality, conjuring, as if by magic, colors, scents, and emotions as well as mysteriously forming our intelligent self, capable of making connections and solving problems. Just how are the dimensions of our intellectual power awoken and how do they function?

Our brain is a true mystery: how is that organ capable of making connections, solving problems, remembering facts and planning the future? Moreover, why are some people capable of thinking faster than others? Neuroscientists have been trying to grasp the biology of intelligence for a long time (1-9).

From the moment we are born and every second thereafter, 100 billion neurons in our head are constantly changing. Every impression, every thought, every memory leaves traces in our brain and enables it to mature.

A completely developed human brain contains around 100 billion neurons, most of which are created before birth. It is fascinating to note that in a developing brain, neurons are created at an average speed greater than 250 000 per minute (10).

ANTENATAL BRAIN DEVELOPMENT

The central nervous system develops from the embryonal ectoderm. Cells which will become neurons and glial cells derive from the neural

se nalazi unutar ektoderma, a sadržava oko 125.000 stanica (11). Neuralna je ploča formirana početkom trećega tjedna trudnoće.

Zahvaljujući primjeni novih metoda i tehnologija u prenatalnim istraživanjima, poput četverodimenzionalnog (4D) ultrazvuka, sve je više spoznaja o funkcionalnom razvoju središnjega živčanog sustava (SŽS) i fetalnim obrascima ponašanja. **Ponašanje fetusa** definira se kao bilo koja aktivnost opažena ili snimljena najčešće ultrazvučnom metodom (nešto rjeđe koristi se i funkcionalna MR), a odraz je razvojnih i maturacijskih procesa SŽS. Razumijevanje odnosa između fetalnih obrazaca ponašanja i tih procesa omogućuje razlikovanje normalnog od poremećenog razvoja mozga, te ranu dijagnozu različitih strukturnih i funkcionalnih poremećaja (12).

Budući da je razvoj ljudskog mozga jedinstven i kontinuirani proces koji traje tijekom trudnoće i dugo nakon rođenja, za očekivati je postojanje kontinuiteta u fetalnim i neonatalnim pokretima, kao i u ponašanju fetusa i novorođenčeta. Našim istraživanjima dokazano je da su svi pokreti nađeni u fetalnom životu bili prisutni i u novorođenčadi. Potvrđeno je postojanje kontinuiteta iz prenatalnog u neonatalno razdoblje čak i finim pokretima, kao što je mimika lica (slika 1) (13,14).

plate located within the ectoderm, containing about 125 000 cells (11). The neural plate forms at the beginning of the third week of gestation.

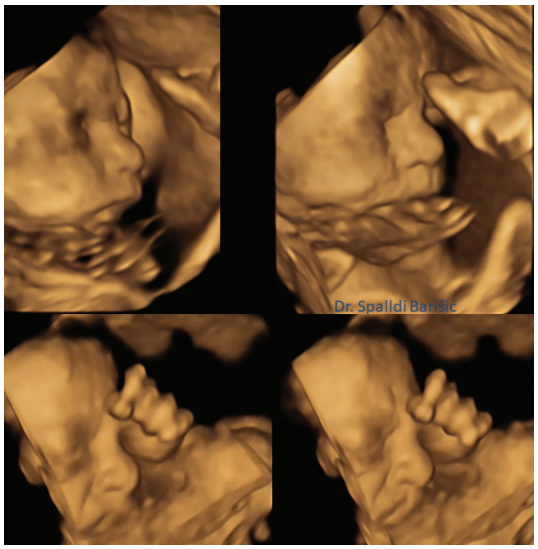
By applying new methods and technology in prenatal research, such as four-dimensional (4D) ultrasound, we have discovered an increasing number of insights into the functional development of the central nervous system (CNS) and the fetal behavior patterns. **Fetal behavior** is defined as any activity detected or recorded by the use of ultrasound, and it is an expression of developmental and maturation processes of the CNS. Understanding the relationship between fetal behavior patterns and these processes enables us to differentiate between normal and abnormal brain development, as well as establish an early diagnosis of different structural and functional disorders (12).

Since human brain development is a unique and continuous process lasting the whole gestation period as well as long after birth, it is reasonable to expect the existence of a continuity in fetal and neonatal movement, along with fetal and infant behavior. The continuity from the prenatal to the neonatal period has been confirmed even in fine motoric movements such as facial expressions (Figure 1) (13,14).

SLIKA 1. Sekvence slika 4D HDlive ultrazvučne snimke površinskog prikaza fetalnog lica u 35. tjednu gestacije. Na prvoj slici vidimo fetus s otvorenim očima, nakon toga grimase lica nalik plakanju djeteta nakon rođenja.

FIGURE 1. Sequences from 4D HDlive surface ultrasound imaging of the fetal face at 35 weeks of gestation. We see a fetus with open eyes, followed by a facial grimacing resembling a baby crying after birth.

Osim pokreta i tjelesne aktivnosti, važnu ulogu u životu fetusa ima i **poticajni matriks taktilnih, zvučnih, okusnih i drugih osjeta**. Njegov neurosenzorički razvoj započinje vrlo rano. Taktilni osjeti, poput dodira i boli, među prvima se počinju razvijati oko 7. tjedna trudnoće. Odavno se već među stručnjacima različitih područja znanosti vode polemike o tome osjeća li fetus bol (11). Da bi se bolni podražaj mogao svjesno doživjeti, moraju postojati neuralne veze između perifernih živčanih završetaka, koji ga zamjećuju i moždane kore (slika 2) (15). Talamokortikalni put formira se između 22. i 26. tjedna, te je nakon tog razdoblja fetus najvjerojatnije sposoban svjesno zamijetiti bolni podražaj. Somatosenzorički evocirani potencijali, koji ukazuju na procesiranje osjeta boli u somatosenzoričkom korteksu, mogu se zabilježiti od 29. tjedna trudnoće. Nadalje, lučenje kortizola i katekolamina, kao odgovora na bolni podražaj, primjerice ubod



SLIKA 2. Sekvence slika 4D ultrazvučne snimke površinskog prikaza fetalnog lica u 29. tjednu gestacije. Na slici uočavamo fetus s dva puta omotanom pupkovinom oko vrata. Pokušava ju maknuti rukom, ali ne uspijeva. Uočite bolan izraz lica na dvije donje slike.
FIGURE 2. Sequences of 4D ultrasound images, surface view; fetal face at 29 weeks of gestation. In the picture we see a fetus with a double-wrapped umbilical cord around its neck. The baby tries to remove it with his hand, but fails. Note a painful-like facial expression in the following two pictures (below).

In addition to movement and physical activity, the **stimulating matrix of tactile, auditory, gustatory, and other senses** plays a crucial role in the life of the fetus. **Its neurosensory** development begins very early. Tactile sensations, such as touch and pain, are among the first to develop, around the 7th week of gestation. Specialists from different areas have long debated whether the fetus feels pain (11). In order for a painful stimulus to be consciously perceived, neural connections have to exist between the peripheral nerve endings perceiving it and the cerebral cortex (**Figure 2**) (15). Thalamocortical pathways are developed between 22 and 26 weeks, after which the fetus is most likely capable of consciously perceiving a painful stimulus. Somatosensory evoked potential, pointing to the processing of pain sensation in the somatosensory cortex, can be recorded from the 29th week of gestation. Furthermore, the production of cortisol and catecholamine in response to painful stimuli, such as a needle prick during blood transfusions, can be observed as early as the 18th week of gestation. Despite great interest in conscious experience and remembering of pain, it is precisely the unconscious reactions, primarily the production of harmful hormones and their long-term harmful effects, which are more dangerous to the development of the human fetus than any potential scary memories (12,16).

It is important to note that hormonal, metabolic, and autonomous responses of the fetus to painful stimuli are successfully repressed by the use of analgesics, and from a clinical perspective it is very significant that both the reaction to stress and its consequences can be prevented by the appropriate pain treatment (17).

The fetus lives in a stimulating environment where **hearing development** is concerned. According to electrophysiological examinations of evoked potentials in prematurely delivered healthy infants, cochlear function develops between 22 and 25 weeks of gestation, and its

iglom pri transfuziji krvi opaža se u fetusa već u 18. tjednu trudnoće. Unatoč velikom zanimanju za svjesno doživljavanje i pamćenje boli, upravo nesvjesne reakcije, pogotovo lučenje stresnih hormona i njihov dalekosežni štetni učinak, vjerojatno su za razvoj ljudskog ploda opasniji od eventualnih zastrašujućih uspomena (12,16). Važno je naglasiti da se hormonski, metabolički i autonomni odgovori fetusa na bolne podražaje potiskuju analgeticima, a iz kliničke perspektive su od velikog značenja nalazi da se reakcija na stres i njegove posljedice mogu spriječiti odgovarajućim tretmanom boli (17).

Fetus živi i u poticajnom okolišu **vezanom uz razvoj sluha**. Funkcija pužnice uspostavlja se, prema rezultatima elektrofizioloških ispitivanja prijevremeno rođene djece, između 22. i 25. tjedna trudnoće, dok njezino sazrijevanje traje prvih 6 mjeseci nakon rođenja (18-20). Majčini otkucaji srca i pokreti probavnog sustava stvaraju u maternici buku od 60-90 decibela, što odgovara buci najprometnije ulice (21). Tijekom zadnjih tjedana trudnoće, od 36. gestacijskog tjedna nadalje, fetus reagira na majčin glas i druge poznate glasove, refleksnim pokretima tijela, okretanjem glave, te povećanom frekvencijom srca. Dakle, fetus raspoznaje, razlikuje zvukove, a još je fascinantnija spoznaja da pokazuje sklonost prema majčinom ili nekom drugom bliskom glasu. Ovo zapažanje se objašnjava tonotopskom organizacijom kohlearnih jezgara i sazrijevanjem moždanog debla tijekom zadnjih tjedana trudnoće (22). Moždano deblo ima sposobnost pamćenja sličnom kognitivnoj aktivnosti. Nadalje, primijećeno je da razvoj slušnog sustava može biti poremećen pod utjecajem štetnih čimbenika (konzumiranje cigareta) te u nekim patološkim stanjima tijekom trudnoće (intrauterini zastoj rasta, hipertenzija majke) (23-25). Utvrđena je i povezanost između razvoja slušnog sustava te kasnijeg učenja govora i usvajanja jezika (12).

maturation continues during the first 6 months after delivery (18-20). Maternal heartbeats and motility of the gastrointestinal tract during digestion appear to generate 60-90 decibels of sound in utero, corresponding to the noise level of heavy street traffic (21). During the last weeks of pregnancy (from the 36th week onward), the fetus responds to external noises, even to the sound of the mother's voice, with reflexive body movements, head-turning, and heart-rate acceleration. The fetus therefore recognizes different noises and displays selective preference for the mother's voice or other familiar voices. These findings can be explained by the tonotopic organization of the cochlear nuclei and by the maturation of the brain stem during the last weeks of pregnancy (22). The brain stem has a learning capability similar to cognitive activity. Furthermore, it has been observed that the development of the auditory system can be disrupted by the influence of harmful factors (cigarette use) as well as by some pathological conditions (intrauterine growth restriction, hypertension in the mother) (23-25). A connection between the development of the auditory system and later language acquisition and learning has also been established (12).

Experiments have indicated that the intrauterine environment is not completely deprived of light. Furthermore, according to experimental results and comparative physiology, the development of **visual and auditory organs** would not be possible without any light or auditory stimulation (26,27). As in other fetal organs, the development of the structure and the function is simultaneous. In the primary visual cortical area, synaptogenesis persists between 24 weeks of gestation and 8 months after delivery (26), while myelination of the optical tract begins at 32 weeks of gestation (27). It has been established that flash stimuli over the maternal abdomen after the 28th week can cause evoked brain activity in the fetal primary visual cortex, recorded by magnetoencephalography (28).

Istraživanja pokazuju da u maternici ne vlada potpuna tama. Na temelju eksperimentalnog rada i usporedne fiziologije zaključeno je da se **vidni i slušni sustav** ne bi ni mogli pravilno razvijati u uvjetima potpunog mraka i tišine (26,27). Kao i u drugim fetalnim organima, i ovdje se razvoj strukture i funkcije odvija usporedno (slika 3). Sinaptogeneza u primarnom vidnom korteksu razvije se od 24. tjedna trudnoće do 8 mjeseci nakon rođenja (26), mijelinizacija optičkog trakta započinje oko 32. tjedna trudnoće (27). Utvrđeno je da svjetlosni podražaj iznad majčina abdomena izaziva od 28. tjedna fetalnu moždanu aktivnost u primarnom vidnom korteksu, zabilježenu magnetoencefalografijom (28). Sazrijevanje vidnog korteksa započinje između 36. i 40. tjedna trudnoće, te se nastavlja nakon rođenja (29).

Kemijski osjeti, poput osjeta okusa, također se razvijaju tijekom intrauterinog života. Fetus doživljava prve okuse hrane u maternici gutajući amnijsku tekućinu. Okusni se pupoljci pojavljuju već u 7. tjednu trudnoće. Izlučivanje glavnih regulatora uzimanja hrane, neuropeptida Y (NPY) i leptina započinje između 16. i 18. tjedna. NPY je hipotalamična tvar koja snažno potiče apetit, a leptin je faktor sitosti. Eksperimentalni podatci upućuju na zaključak da leptin značajno potiče gutanje fetusa. Neki istraživači vjeruju da je izostanak inhibicijskog

Maturation of the visual cortex occurs between the 36th and 40th weeks of gestation and continues after birth (29).

Chemical senses, such as the sense of taste, are also developed during the intrauterine period. The fetus experiences the first food tastes in the uterus by swallowing the amniotic fluid. Taste buds develop as early as the 7th week of gestation. The production of primary food intake regulators, neuropeptide Y (NPY) and leptin, starts between 16 and 18 weeks. NPY is a hypothalamic substance that powerfully increases appetite, while leptin is the satiety inducer. Experimental data has led to the conclusion that leptin significantly prompts the fetus to swallow. Some scientists believe that the lack of leptin's inhibitory effect is responsible for increased food intake and increased body weight of infants, despite a high percentage of fat in the total body mass. It has also been discovered that fetal swallowing depends on the sensation of thirst as well as the taste of the amniotic fluid. Swallowing is greatly reduced with the presence of sour or bitter taste and increased with the presence of sweet taste. It is important to note that the prenatal period influences the regulation of appetite and body mass in childhood and adulthood (30,31). Unfavorable intrauterine circumstances, interfering with the development of hypothalamic nuclei and the satiety and food intake centers in the brain, can

SLIKA 3. Sekvence slika 4D ultrazvučnog prikaza fetalnog lica u 33. tjednu gestacije. Fetus je budan i promatra naokolo. Uočite različiti smjer pogleda i istraživanja okoline i strukture na kojem je lice prislonjeno (posteljica).

FIGURE 3. Sequences of 4D ultrasound images of the fetal face at 33 weeks of gestation. The fetus is awake and looking around. Note the different direction of watching and investigating the environment and the structure on which the face rests (placenta).

učinka leptina odgovoran za poticanje unosa hrane i povećanje tjelesne mase u novorođenčadi, unatoč visokom udjelu masti u ukupnoj tjelesnoj masi. Također je utvrđeno da fetalno gutanje ovisi o osjetu žeđi, ali i o okusu plodove vode. Ono se značajno smanjuje pri gorkom ili kiselom, a povećava pri slatkom okusu. Važan je podatak da prenatalna zbivanja utječu na regulaciju apetita i tjelesne mase u djetinjstvu i odrasloj dobi (30,31). Nepovoljan intrauterini okoliš, interferirajući s razvojem hipotalamičkih jezgara i centara za sitost i hranjenje, može rezultirati poremećenim ponašanjem vezanim uz uzimanje hrane, hiperfagijom i pretilošću u djetinjstvu i/ili odrasloj dobi.

U prehrani mozga tijekom embrionalnog i fetalnog razdoblja života važnu ulogu ima koroidni pleksus, difuzno, veoma prokrvljeno tkivo koje zajedno s arahnoidnom membranom čini barijeru između krvi i cerebrospinalne tekućine. Ova struktura nalazi se unutar moždanih komora, a sudjeluje u održavanju kemijske stabilnosti cerebrospinalne tekućine te u ranom razvoju mozga. Njegova funkcija može se usporediti s funkcijom bubrega u životu nakon rođenja. Tijekom fetalnog života kroz koroidni se pleksus prenose u cerebrospinalnu tekućinu ne samo esencijalni ioni, vitamini, folati, nego i makromolekule, glukoza i niz drugih važnih tvari. Fetalni koroidni splet mnogo je veći od onog u odrasloj dobi i ispunjava mnogo više prostora u moždanim komorama. Naši rezultati pokazuju da se protok krvi u koroidnom pleksusu može prikazati već u desetom tjednu trudnoće (32). Ispitivanje vaskularizacije ove strukture potvrđuje postojanje specifičnih hemodinamičkih značajki koje slijede njegove morfološke promjene.

Učenje i pamćenje, kao i mnoge druge aktivnosti, imaju svoje temelje u prenatalnom životu. Psihobiološka su istraživanja potaknula razvoj hipoteze da intrauterini okoliš, izložen akustičnim i drugim podražajima, potiče razvoj učenja (slike 3 i 4) (33). Intrauterino po-

result in a food intake disorder, hyperphagia, and obesity in childhood and/or adult age.

During the embryonal and fetal period, a key element in brain nutrition is the choroid plexus, a diffuse, strongly perfused tissue, which, along with the arachnoid membrane, forms the barrier between blood and the cerebrospinal fluid. This structure is located within the cranial cavity and maintains the chemical stability of the cerebrospinal fluid as well as participating in early brain development. Its function can be compared to the function of the kidneys in life after birth. During the fetal period, the choroid plexus transports not just essential ions, folates, and vitamins into the cerebrospinal fluid but also macromolecules, glucose, and a series of other important elements. The fetal choroid network is much larger than the one in adults and it takes much more space in the cranial cavity. Results from a study we have performed previously show that the blood flow through the choroid plexus can be observed as early as the 10^{th} week of gestation (32). Investigation of the vascularization of this structure confirms the existence of specific hemodynamic features which follow its morphological changes.

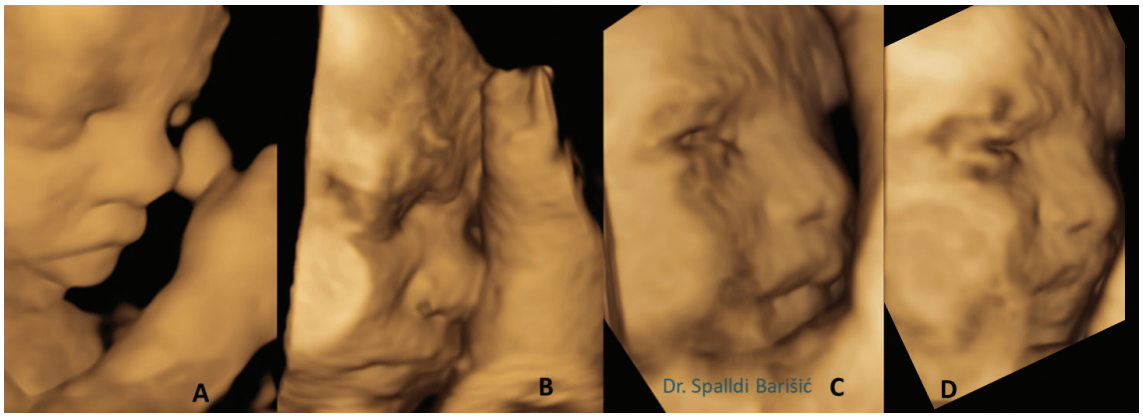
Learning and memory, as well as many other activities, have their origin in prenatal life. Psychobiological research has inspired the development of a hypothesis that the intrauterine environment, which includes exposure to acoustic and other stimuli, prompts the development of learning (Figure 3 and Figure 4) (33). The intrauterine origin of simple forms of memory and learning has been investigated using habituation methods, classical conditioning, and exposure learning. It has been confirmed that the fetus is capable of remembering tastes it was exposed to during the intrauterine period. Namely, the first experiences of different flavors and scents depend on the mother's diet. It has been proven that the propensity for certain foods is also acquired during intrauterine

drijetlo jednostavnih oblika pamćenja i učenja proučavano je primjenom metoda habituacije, klasičnog kondicioniranja te učenja izlaganjem određenom podražaju. Utvrđeno je da fetus ima sposobnost pamćenja okusa kojima je bio izložen za vrijeme intrauterinog razdoblja. Naime, prva iskustva različitih okusa te mirisa ovise o majčinoj prehrani. Dokazano je i da se sklonost određenoj hrani stječe za vrijeme intrauterinog razvoja (34). Veća je vjerojatnost da će nam se svidjeti okus one hrane koju je naša majka konzumirala za vrijeme trudnoće. **Fetus pamti i različite mirise, a posebno zvučne informacije**. Rudimentarni kapacitet za zadržavanje informacija postoji već od 30. tjedna trudnoće, a najnovija istraživanja pokazuju da osim kratkotrajnog pamćenja, fetus posjeduje i dugotrajno pamćenje (35).

Nakon rođenja uglavnom se ne stvaraju novi neuroni i ne postoji migracija neurona, ali su procesi sinaptogeneze i neuralne diferencijacije vrlo intenzivni. U donošena ploda sve primarne motoričke, somatosenzoričke, vidne i slušne kortikalne regije mogu biti prikazane karakterističnim slojevima specifičnih stanica. Visok stupanj zrelosti pokazuje moždano deblo, a u malom mozgu postoje svi oblici histogenetskih procesa. Dakle, **novorođenče dolazi na**

development (34). There is a greater probability that we will like the taste of food our mother consumed during pregnancy. **The fetus also remembers different smells, and especially acoustic information.** The rudimentary capacity for retaining information exists as early as the 30th week of gestation, and most recent research shows that the fetus also possesses long-term memory in addition to short-term memory (35).

After birth, there are mostly no neurons being created and there is no migration of neurons, but the processes of synaptogenesis and neural differentiation greatly intensify. In full-term infants, all primary motoric, somatosensory, visual, and auditory cortical areas can be displayed in characteristic layers of specific cells. The brain stem displays a high level of maturity and the cerebellum has all the forms of histogenesis. Therefore, **the infant is born with completely formed areas of subcortical structures and the simplest primary zones of the cortex** (36). The development of associative areas of the cortex, which play an important role in realizing the most complex forms of psychic activity, happens after birth. Recent research conducted with the use of NMR has shown that infants have well-devel-



SLIKA 4. Sekvence slika (A-D) 4D ultrazvučne snimke površinskog prikaza fetalnog lica u 36. tjednu gestacije. Na slici A uočava se fetus sa zatvorenim očima i miran, spokojan izraz lica, opuštenu muskulaturu lica. Na slici B vidi se mrštenje, oči su pritom zatvorene; potom na slici C otvara oči. Na slici D vidimo otvorene oči i tužan izraz lica.

FIGURE 4. Sequences of (A-D) 4D ultrasound images, surface view of the fetal face at 36 weeks of gestation. In Figure A we notice a calm fetus with closed eyes, serene facial expression, and relaxed facial muscles. In Figure B we see a frown with the eyes closed, and then in Figure C the fetus opens his eyes. In Figure D we see open eyes and a sad-looking facial expression.

svijet s potpuno formiranim područjima supkortikalnih struktura i najjednostavnijim, primarnim zonama kore (36). Razvoj asocijacijskih područja moždane kore, koja imaju važnu ulogu u ostvarivanju najsloženijih oblika psihičke djelatnosti, događa se nakon rođenja. Novija istraživanja provedena NMR-om pokazala su da novorođenče ima dobro razvijene supkortikalne strukture, veliku aktivnost primarnih kortikalnih područja (somatosenzoričkog, motoričkog, slušnog i vidnog korteksa), ali i malu aktivnost u asocijacijskim područjima (37).

Znanost i dalje nema odgovor na zagonetno pitanje: koji su uvjeti morali biti ispunjeni u razvoju mozga da bi nastao **čovječji duh**?

Zaista, tijekom svog razvoja fetus obavlja sve više funkcija, postaje sve samostalnije biće. Osim srčane akcije, plod u majčinoj utrobi izvodi pokrete poput disanja, reagira na bolne podražaje i majčine emocije, ima razvijena osjetila okusa. On odgovara na zvukove, svjetlo, dodir, slabije ili jače izraženim pokretima. Za njegov rast, razvoj organa i organskih sustava ključna je tjelesna aktivnost te izvođenje pojedinih pokreta. Fetus također ima utjecaj na tijek i trajanje trudnoće. U tih 9 mjeseci ispreplićу se veliki, burni događaji, trenutci važni kao ni u jednoj godini, ni u jednom razdoblju nakon rođenja. Srce, pluća, bubrezi, središnji živčani sustav, endokrini sustav već tada funkcioniraju zadivljujuće. Za postizanje savršena sklada svih funkcija potrebno je vrijeme. Dijete dolazi na svijet spremno započeti i održavati samostalan život. Stoga ne čudi preciznost kojom su regulirani i usklađeni razvoj i sazrijevanje organa i organskih sustava.

Već tijekom intrauterina života postoje kompenzacijski mehanizmi koji štite život fetusa za vrijeme patoloških stanja. Određivanjem granice u kojoj prestaju fiziološki, a započinju patofiziološki mehanizmi otvaraju se nove mogućnosti sprječavanja fetalnih oštećenja različitih organskih sustava, osobito mozga. Primjena

oped subcortical structures and high levels of activity in the primary cortical areas (somatosensory, motoric, auditory, and visual cortex), but that there are also low levels of activity in the associative areas (37).

Science is left with one mysterious unsolved question: which prerequisites have to be fulfilled in the development of the brain for the **human spirit** to be created?

The fetus preforms an increasing number of functions during its development, effectively becoming an increasingly independent being. In addition to its heartbeat, the offspring in the mother's womb preforms actions like breathing, reacting to painful stimuli and the emotions of its mother, and using its developed sense of taste. It responds to sounds, light, and touch by stronger or weaker movement. Physical activity and certain motions are crucial for its growth and the development of certain organs and organ systems. The fetus also has an influence on the course and length of the pregnancy. Those 9 months are a series of intertwined events of huge significance, moments more important than any year or period of life after birth. The heart, lungs, kidneys, central nervous system, and endocrine system already function impressively well in that period. It takes time to achieve a perfect balance of all those functions. The infant is born ready to begin and maintain an independent existence. With that in mind, the precise regulation of the development and maturation of organs and organ systems is not such a surprise.

During the intrauterine period, compensation mechanisms are already in place to protect the life of the fetus in case pathological conditions arise. By determining the line where normal physiological mechanisms stop and pathophysiological ones start, we open new possibilities of preventing fetal damage to different organ systems, and especially the brain. The application of new ultrasound methods, such as the four-dimensional ultrasound, has greatly improved our

novih ultrazvučnih dijagnostičkih metoda, poput četverodimenzionalnog ultrazvuka, znatno je poboljšala naše razumijevanje prenatalnih neurofizioloških procesa te pružila dodatne informacije o stanju i funkciji fetalnog središnjeg živčanog sustava. *Kurjak Antenatal Neurodevelopmental Test* (KANET) test omogućio je po prvi puta procjenu neurološkog statusa fetusa te razlikovanje normalnih, graničnih te abnormalnih fetalnih obrazaca ponašanja. Otvorene su nove mogućnosti dijagnostike, prevencije i intervencije u slučaju moždanih te drugih oštećenja i poremećaja.

Vrijedna je i zanimljiva spoznaja da su temelji za većinu našeg života u odrasloj dobi postavljeni upravo tijekom intrauterinog razdoblja. Uredan fiziološki razvoj fetusa, te fiziološki intrauterini okoliš neophodni su preduvjeti dobrog zdravlja u djetinjstvu i u odrasloj dobi.

O ovome je nedavno i u opsežnom preglednom radu pisala Aida Salihagić-Kadić. Prenosimo značajni dio njenog rukopisa uz dozvolu autorice, izdavača i urednika (38).

JE LI NAŠ MOZAK RAČUNALO?

U opsežnoj raspravi o funkciji fetalnog mozga Robert Epstein nedavno je detaljno i precizno opisao mnoge dvojbe oko funkcije mozga u antenatalnom razdoblju (39). U uvodu on ističe da naš mozak nije računalo, ali nije ni prazan. No, on ne sadržava većinu stvari koje ljudi vjeruju da sadrži – čak ni jednostavne stvari kao što su „sjećanja“.

Naši pogrešni dojmovi o mozgu imaju duboke povijesne korijene započete izumom računala 1940-tih godina. Danas nam već preko pedeset godina psiholozi, lingvisti, neuroznanstvenici i ostali stručnjaci za ljudsko ponašanje tvrde kako ljudski mozak djeluje **poput naprednog računala**.

Osjetila, refleksi i mehanizmi učenja – s time svi počinjemo, a kad malo razmislimo to je za-

understanding of prenatal neurophysiological processes and given us additional information on the state and function of the fetal central nervous system. The KANET test has made it possible, for the first time ever, to evaluate the neurological state of the fetus and to differentiate normal, borderline, and abnormal fetal behavior patterns. This has created new diagnostic, preventative, and intervention options in cases of brain damage and other disorders.

Knowing that the foundation of most our lives as adults is set precisely during the intrauterine period is very valuable and interesting. Regular physiological development of the fetus and an appropriate physiological intrauterine environment are necessary prerequisites for good health in childhood and adulthood.

Recently, this has been the topic of a comprehensive paper by Aida Salihagić-Kadić. With the permission of the author, editor and publisher, we present a significant portion of her manuscript herein (38).

IS OUR BRAIN A COMPUTER?

In a comprehensive discussion on the fetal brain function, Robert Epstein recently provided a detailed description of numerous uncertainties about brain function in the antenatal period (39). In the introduction, he pointed that our brain is not a computer but that it is also not completely empty. However, it does not contain most of the things people think it does – not even simple things such as “memories”.

In this interesting essay, Epstein wrote that “our shoddy thinking about the brain has deep historical roots, but the invention of computers in the 1940s got us especially confused. For more than half a century now, psychologists, linguists, neuroscientists and other experts on human behavior have been asserting that the human brain works **like a computer**.” He also mentioned that “Senses, reflexes and learning

pravo mnogo. Kad bismo se rađali bez ijedne od ovih sposobnosti, šanse za preživljavanje bi nam bile mnogo lošije.

Ali popis onoga bez čega se rađamo je mnogo duži: informacije, podatci, pravila, *software*, znanje, leksikoni, reprezentacije, algoritmi, programi, modeli, uspomene, prizori, procesori, potprogrami, uređaji za kodiranje i dekodiranje, simboli ili međuspremnici – svi elementi dizajna digitalnih računala koji im omogućuju donekle inteligentno ponašanje. Ne samo da se mi rađamo bez njih, već ih ni ne razvijemo – ikada (39).

Ključan događaj koji je pokrenuo ono što se danas široko naziva „kognitivna znanost" je objavljivanje knjige „Jezik i komunikacija" psihologa Georgea Millera 1951. godine. Miller je iznio ideju da se misaoni svijet može rigorozno proučavati koristeći koncepte iz informatičke teorije, računarstva i lingvistike.

mechanisms – this is what we start with, and it is quite a lot, when you think about it. If we lacked any of these capabilities at birth, we would probably have trouble surviving" (39).

Epstein concluded that there are some things that we are *not* born with, like "*information, data, rules, software, knowledge, lexicons, representations, algorithms, programs, models, memories, images, processors, subroutines, encoders, decoders, symbols, or buffers*, which are design elements that allow digital computers to behave somewhat intelligently. Not only are we not *born* with such things, we also don't *develop* them – ever" (39).

The landmark event that launched what is now broadly called "cognitive science" was the publication of *Language and Communication* (1951) by the psychologist George Miller. Miller proposed that the mental world could be studied rigorously using concepts from information theory, computation, and linguistics.

EMOCIONALNI RAZVOJ FETUSA

Jedan od ključnih vanjskih pokazatelja emocija su izrazi lica. U drugom i trećem tromjesečju trudnoće, korištenjem 4D ultrazvuka, potvrđeno je postojanje punog raspona izraza lica kod fetusa, uključujući mrgođenje, smješkanje i plakanje, baš kao i kod odraslih pojedinaca. Kako se fetus razvija, njegovi izrazi lica postaju sve složeniji, uz pojavljivanje cjelovite mimike lica koje se smije ili lica koje plače u trećem tromjesečju. Ova saznanja bi mogla doprinijeti komunikaciji između majke i fetusa, povezivanju poslije poroda, kao i regulaciji roditeljske brige za dijete. Izrazi lica povezani s boli ili uznemirenosti također postaju složeniji i kompletniji sa sazrijevanjem fetusa, što se može smatrati prilagodbenim procesom od kojeg fetus ima koristi poslije rođenja.

Moguće je da pokreti lica pokazuju fiziološke refleksne uzorke endogenog porijekla. Zaista, reakciju smješkanja, plakanja ili vrištanja mo-

EMOTIONAL DEVELOPMENT OF THE FETUS

One of the important external signs of emotion is facial expressions. The existence of a full range of facial expressions, including grimacing, smiling, and crying, similar to emotional expressions in adults, has been observed by 4D sonography in the 2nd and 3rd trimesters of pregnancy. As the fetus matures, the complexity of facial expressions increases, with the appearance of the "cry-face gestalt" or "laughter-face gestalt" in the third trimester. This may be beneficial for fetal and maternal communication and bonding in postnatal life, as well as for the regulation of parental care. Facial expressions of pain or distress also become more complete as gestational age increases, and this may be considered an adaptive process which is useful to the fetus postnatally.

It is possible that facial movements demonstrate endogenously generated physiolog-

guće je izazvati stimulacijom moždanog debla čak i u slučajevima kada je veliki mozak u potpunosti uništen. Ipak, sudeći prema opažanjima uz pomoć 4D ultrazvuka, izrazi lica i ponašanje koje nalikuje izražavanju emocija možda ipak predstavljaju svojevrsnu fetalnu osjećajnost i svjesnost. Štoviše, noviji podatci ukazuju da ovi fetalni pokreti ne služe samo izražavanju različitog usmjerenja, već iskazivanju emotivnog stanja i pokazivanju namjere (slika 5) (11). Emocije se rađaju tijekom fetalnog razvoja. Kao što smo već spomenuli, fetus je također sposoban izražavati uživanje ili neodobravanje kad su u pitanju okusi ili mirisi.

Primjerice danas 73-godišnja Marilyn vos Savant kao djevojka je imala najviši ikad izmjereni kvocijent inteligencije: 228 bodova. Znanstvenici međutim sumnjaju da su vrijednosti iznad 150 uopće smislene. Drugi prigovaraju da testovi prije mjere prilagodbu suvremenom svijetu nego inteligenciju. Ipak, kvocijent inteligencije spada među najvažnija pomoćna sredstva psihologije: može predvidjeti akademsko-poslovna dostignuća do 25 posto.

Limbički sustav prednjeg dijela mozga odgovoran je za izražavanje i doživljaj emocija. Druga ključna struktura u mozgu, amigdala, upravlja emotivnom memorijom, pažnjom, uzbuđenjem, iskustvom ljubavi, straha, užitka i veselja. Ona sadrži neurone zadužene za prepoznavanje izraza lica kojima se raspoznaje emotivno značenje pojedinih izraza lica. Procjena lica kao dio uspostavljanja društvenih veza područje je spoznaje specifično za amigdalu. Razvoj amigdale počinje u ranoj fazi embrionalnog razvoja i doseže uznapredovali stupanj zrelosti tijekom prve godine života djeteta (6).

Osjećaji su se dugo smatrali izvorom pogrešaka razuma. Danas su znanstvenici složni: samo onaj tko razumije vlastite emocije, donosi pametne odluke - pa i one vezane za način ponašanja prema okolini. Popularni koncept „emotivne inteligencije" većina istraživača mozga

ic reflex patterns. In fact, smiling as well as screaming and crying can be induced by brainstem stimulation even with complete forebrain transection or destruction. However, according to observations obtained by 4D ultrasound, the facial expressions and emotion-like behaviors may represent some kind of fetal emotion and awareness. Moreover, recent data indicate that fetal movements serve not only to express different orientations, but also emotional states and manifestations of intentions (Figure 5) (11). Emotions are being born during fetal life. As we have already mentioned, the fetus is also able to express pleasure or disapproval regarding tastes and smells.

When Marilyn vos Savant, now 73 years old, was a young girl, she had the highest IQ ever recorded: 228 points. However, scientists believe that values above 150 are pointless. Others object that the tests measure our adaptation to the contemporary world more than our intelligence. Nevertheless, IQ remains one of the most important auxiliary tools of psychology: it can predict academic-business achievements with an accuracy of 25 percent.

The limbic forebrain is responsible for the expression and experience of emotions. One of the very important structures, the amygdala, mediates emotional memory, attention, arousal, and the experience of love, fear, pleasure, and joy. It contains facial recognition neurons which discern the emotional significance of different facial expressions. The evaluation of faces in social processing is an area of cognition specific to the amygdala. The development of the amygdala begins in early embryonic life and reaches an advanced stage of maturity during the first postnatal year (6).

Feelings were long considered to be the source of rational mistakes. Today, scientists are in agreement: only someone who understands their own emotions can make smart decisions – even those about their behavior towards their surroundings. The popular concept of

smatra beskorisnim: previše rasteže pojam inteligencije. Usto ga je teško izmjeriti, pa se ne može kvalitetno znanstveno istraživati.

UČENJE I PAMĆENJE TIJEKOM FETALNOG ŽIVOTA

Razne visoko specijalizirane biokemijske tvari (hormoni, neurotransmiteri i druge polipeptidne strukture) potrebne su u izravnoj vezi sa stimulansom za transformaciju i pohranu senzornih i mentalnih informacija. Ključne za oblikovanje primarnog centralnog živčanog sustava na razini hipotalamusa-hipofize-adrenalne žlijezde, neke od ovih funkcija moguće je opaziti na samom početku razvoja ljudskog bića. Stoga fetus postepeno razvija visoku osjetljivost i sposobnost za potencijalne vještine percepcije i učenja (42).

Unutarmaternično iskustvo je ujedno i proces učenja za dijete. Ovo učenje je ključni preduvjet za preživljavanje budući da omogućuje organizmu prilagođavanje na nove okolnosti. Bez prilagodbe nema preživljavanja, a prilagodba nije moguća bez prijašnjih iskustava na kojima se može zasnivati. Takav proces nužno traži pamćenje, bilo da je riječ o svjesno zadržanom pamćenju ili podsvjesno utisnutim dojmovima. Procesuiranje informacija koje dolaze do djeteta od samog početka njegovog razvoja biti će primljeno putem različitih biokemijskih puteva i potom preoblikovano i spremljeno kao tragovi sjećanja (ovo može vremenom biti korisno za teorijsko razumijevanje određenih psihoterapijskih postupaka, kao što su hipnoza, analiza snova, prenatalno pamćenje itd). Embrij već pokazuje naznake odgovaranja na i zadržavanja utisnutih senzornih iskustava u biokemijskom jeziku koji ostaju kao potencijalni izvor učenja. Ovi prenatalni memorijski utisci mogu, s vremenom, biti prizvani kao izvori informacija (bilo negativnog, pozitivnog ili ambivalentnog karaktera) tijekom kasnijeg života (39).

"emotional intelligence" is considered useless by most researchers: it stretches the concept of intelligence too far. Additionally, it is almost impossible to measure and thus cannot be scientifically studied.

LEARNING AND MEMORY IN FETAL LIFE

Numerous highly specialized biochemical functions (hormones, neurotransmitters, and other polypeptide structures) are necessary, along with a direct link to a stimulus, in order to transform and store sensory and mental information. Being crucial for the formation of the primary central nervous system on the level of hypothalamus-pituitary-adrenal gland, some of these functions are observable at the very beginning of human development. Thus, the fetus gradually develops high sensitivity and the capability of potential perception and learning skills (42).

The intrauterine experience is also a process of learning for the child. This learning is a key presumption of survival because it enables the organism to adapt to new circumstances. Without adaptation there is no survival, and adaptation is impossible without prior experiences as a base. This process inevitably requires memory, whether it is consciously retained memory or subconscious impressions. Information reaching the fetus from the very beginning of its development will be received via different biochemical pathways and then reshaped and stored as memory fragments (this can in time be useful for the theoretical understanding of certain psychotherapeutic procedures, such as hypnosis, dream analysis, prenatal memory, etc.) The embryo already displays indications of responding to and retaining imprinted sensory experiences in a biochemical language which remain as potential learning sources. These prenatal memory imprints can, in time, be recalled as information sources (negative, positive or ambivalent in character) during later life (39).

Učenje i pamćenje fetusa je opsežno proučavano, korištenjem metoda habituacije, klasičnog kondicioniranja i učenja izlaganjem.

Habituacija, tj. smanjenje reakcije opetovanom prezentacijom istog stimulansa, uspješno je demonstrirana od 22. tjedna razvoja nadalje. Neki istraživači su zabilježili razvojni trend habituacije na vibracijsko-akustični stimulans, gdje je potrebno češće izlaganje stimulansu mlađih fetusa nego starijih. Treba napomenuti kako neka majčina stanja poput depresije ili stresa mogu negativno utjecati na habituaciju fetusa ukazujući na kašnjenje u razvoju. Mogu biti povezana i sa smanjenom funkcijom cerebralnog korteksa kod fetusa. Prefrontalno područje mozga i hipokampus sudjeluju u rapidnom automatskom opažanju i habituaciji na neočekivane okolišne poticaje, te su ključni elementi orijentacijskog refleksa kod ljudi.

Klasično kondicioniranje je metoda koja uključuje spoj dvaju različitih stimulansa: uvjetovani stimulans (koji samostalno ne izaziva nikakvu reakciju) i neuvjetovani stimulans (koji samostalno izaziva reakciju fetusa). Nakon opetovanog izlaganja spoju ovih dvaju stimulansa, uvjetovani stimulans počinje izazivati reakciju fetusa nazvanu „uvjetovana reakcija". Koristeći čisti ton kao uvjetovani stimulans, a vibracijsko-akustični stimulans kao neuvjetovani, Hepper je otkrio uvjetovanu reakciju kod fetusa od 32 tjedna do 39 tjedana. Međutim, istu je reakciju moguće izazvati kod fetusa s anencefalijom. Štoviše, pokazano je da se primjenom klasičnog uvjetovanja, fetus čimpanze može naučiti informaciju i zadržati ju barem dva mjeseca nakon rođenja

Treća metoda je učenje izlaganjem u kojoj se fetus ponovno izlaže stimulansu kojem je već izlagan niz puta te se njegova reakcija uspoređuje ili s reakcijom na 'nepoznat' stimulans ili na reakciju fetusa koji prvi put biva izložen tom istom stimulansu. U 37. tjednu zabilježene su različite reakcije fetusa na poznate i nepoznate zvukove, dok fetusi u 30. tjednu

Fetal learning and memory have been investigated extensively, employing habituation methods, classical conditioning, and exposure learning.

Habituation, i.e., response decrement following repeated presentation of the same stimulus, was demonstrated from 22 weeks of gestation onwards. Some investigators have registered developmental trends in habituation to vibroacoustic stimuli, with younger fetuses requiring more presentations of the stimulus than older fetuses. It should be pointed out that maternal conditions, such as depression and stress, affect fetal habituation in a negative way, indicating developmental delays. They may be linked to impaired function of the fetal cerebral cortex. Prefrontal and hippocampal regions are involved in rapid automatic detection and habituation to unexpected environmental events and are key elements of the orienting response in humans.

Classical conditioning is the method which involves the pairing of two stimuli: a conditioned stimulus (which elicits no response when presented alone) and an unconditioned stimulus (which elicits a fetal response when presented alone). Following repeated paired exposure to these two stimuli, the conditioned stimulus also elicits a response termed a "conditioned response". Using a pure tone as the conditioned stimulus and a vibroacoustic stimulus as the unconditioned one, Hepper found a conditioned response in fetuses ranging from 32 to 39 weeks of gestation. However, the same response could be demonstrated in fetuses with anencephaly. Furthermore, it has been shown that, with classical conditioning, a chimpanzee fetus can learn and retain obtained information for at least two months after birth.

The third method is exposure learning, where the fetus is re-exposed to a stimulus after a number of exposures, and this response is then compared either to the response to the "unfamiliar" stimulus or to the response of an unexposed fetus to the same stimulus. Different

jednako reagiraju i na poznate i na nepoznate zvukove. Ova je metoda također dovela do otkrića da fetus preferira zvuk glasa svoje majke od nepoznatih glasova. Kad je uspoređena reakcija na majčin glas nakon poroda i majčin glas kako je zvučao u maternici (koji zvuči drugačije zbog prigušivanja u maternici), novorođenčad su pokazala kako preferiraju zvuk majčinog glasa kako je zvučao prije rođenja. Ovime je potvrđeno da fetusi mogu čuti i naučiti prepoznavati zvuk glasa svoje majke prije rođenja. Novi podatci pokazuju, u fetusa od 34 tjedna, selektivno fetalno kortikalno procesuiranje majčinog glasa u usporedbi s nepoznatim glasovima. Štoviše, novorođenčad čije su se majke neprestano odmarale pred određenim televizijskim programom tijekom trudnoće, kad bi nakon poroda čula glazbenu temu programa postala bi oprezna, smanjio bi im se puls i prestala bi se micati. Rezultati ovog zanimljivog istraživanja pokazuju da je fetus sposoban naučiti i zapamtiti poznati auditorni stimulans te zadržati te informacije poslije poroda. Dokazano je kako rudimentarni kapacitet za zadržavanje informacija postoji već u 30. tjednu trudnoće i da se prenatalno stečene auditorne informacije mogu zadržati čak šest tjedana (6).

Prvorođena djeca u prosjeku pokazuju kvocijent inteligencije viši za 2,3 boda od mlađe braće i sestara: to je pokazalo istraživanje za koje su znanstvenici obradili testove inteligencije gotovo 250.000 mladih Norvežana. Znanstvenici su fenomen objasnili time da starija djeca pomažu mlađoj braći i sestrama u svladavanju brojnih vještina.

Istraživanje je obuhvatilo i druge aspekte fetalnog pamćenja. Prenatalno olfaktorno učenje je dokazano kod svih vrsta kralježaka, uključujući sisavce. Fetus može naučiti razlikovati okuse i steći preferenciju za neke okuse. Kao što smo već spomenuli, fetus može razlikovati pojedine zvukove govora u maternici. Prenatalno iskustvo govora može biti početak usvajanja

responses of fetuses at 37 weeks of gestation to familiar and unfamiliar sounds have been detected, whereas fetuses at 30 weeks of gestation did not react differently to familiar and unfamiliar sounds. This method also led to the finding that an infant prefers its mother's voice over an unfamiliar voice. When the mother's voice as it sounded after birth was compared with the mother's voice as it sounded in utero (different due to the sound attenuation in the uterus), newborn infants showed a preference for their mother's voice as it sounded before birth. These findings confirmed that fetuses are able to hear and learn their mother's voice before birth. Recent data reported on selective fetal cortical processing for the mother's vs. an unfamiliar voice at 34 weeks of gestation. Furthermore, babies whose mothers consistently rested in front of a popular television program during pregnancy became alert, showed slowing of their heart rate and stopped moving a few days after birth when the theme tune of the program was played. The results of this interesting study indicate that the fetus is able to learn and remember familiar auditory stimuli and retain this information over the birth period. It has been shown that the rudimentary capacity for retention of information may be expressed as early as 30 weeks of gestation and that prenatally acquired auditory memory can last as long as six weeks (6).

On average, firstborn children have an IQ several points higher than their younger siblings, as shown by the research involving IQ tests of almost 250 000 Norwegian youths. Scientists explain the phenomenon by the fact that older children help their younger siblings in overcoming numerous situations.

Other aspects of fetal memory have also been investigated. Prenatal olfactory learning has been reported in all vertebrate species, including mammals. The fetus can learn tastes and acquires a preference for these tastes through such learning. As we have already mentioned, the fetus is able to discriminate between differ-

jezika. Naposlijetku, moguće je da prenatalno učenje i pamćenje ima važnu ulogu u razvoju prepoznavanja majke, razvijanja bliskosti, hranjenja i društvenog prepoznavanja. Dugoročno auditorno pamćenje možda ima važnu ulogu u razvojnoj psihobiologiji pažnje i percepcije, uključujući i ranu percepciju govora.

Sanjarenje može uposliti mozak jednako snažno kao i svjesno rješavanje problema. Iza čela i iznad sljepoočnica znanstvenici su identificirali „mrežu praznog hoda", osobito aktivnu kod besciljnog razmišljanja. Pretpostavljaju da mozak tamo povezuje informacije sa sjećanjima i osjećajima, raspoređuje, slaže i umrežuje dojmove - otvarajući put novim mislima i idejama.

Slike četverogodišnje Marle Olmstead izgledaju poput radova iskusnih umjetnika. Kreativnost i inteligencija često dolaze u paru, no ne uvjetuju se: natprosječno inteligentni ljudi većinom razmišljaju „konvergentno", probleme rješavaju analitički, prema provjerenim obrascima. Kreativnost međutim zahtijeva „divergentno" razmišljanje pri čemu mozak radi asocijativno te uključuje emocije i neobične ideje.

DUŠEVNO ZDRAVLJE I DUŠEVNI POREMEĆAJI : IMAJU LI ANTENATALNE TEMELJE?

Međuigra između genoma, epigenoma i okoline oblikuje fenotip ljudskog zdravlja ili bolesti, čak i prije rođenja. Prenatalno ili fetalno programiranje rizika za mentalne poremećaje u odrasloj dobi vrlo je važna i intrigantna tema istraživanja (43). Dobro je poznata činjenica da novorođenčad dolazi na svijet s nekom vrstom protoselfa, osjećaja znanja da tijelo postoji (44,45) i različitim tipovima temperamenta; neki su mirni i „laki" s dobrim samo-umirujućim sposobnostima, a drugi vrlo senzitivni i reaktivni na okolinu sa slabim samo-umirujućim sposobnostima i koje je teško umiriti.

ent speech sounds in the womb. The prenatal experience of speech may begin the process of language acquisition. Finally, it has been suggested that prenatal learning and memory play an important role in the development of maternal recognition, attachment, feeding behavior and social recognition, etc. Long-term auditory memory may be important for the developmental psychobiology of attention and perception, including early speech perception.

Daydreaming can activate the brain just as strongly as conscious problem-solving. Behind our forehead and above our temples, scientists have identified a "resting state network" which is especially active in aimless thought. They assume that this is how the brain connects information to memory and feelings and allocates, orders, and networks impressions – forging a path to new thoughts and ideas.

The paintings of the four-year old Marla Olmstead appear like the work of seasoned artists. Creativity and intelligence often come in pairs, but they are not mutually conditioned: exceedingly intelligent people mostly think convergently and solve problems analytically, using tested patterns. Creativity, however, demands divergent thinking, where the brain functions in an associative manner and includes emotions and unusual ideas.

MENTAL HEALTH AND MENTAL DISORDERS – DO THEY HAVE AN ANTENATAL ORIGIN?

The interplay between the genome, epigenome, and environment shapes a phenotype of human health or illness even before birth. Prenatal or fetal programming of risk for adult mental disorders has become an important and intriguing research topic (43). It is well-known that babies enter the world with some kind of protoself, some kind of the feeling of the knowing that the body exists (44,45), and different tempera-

Uterus može osiguravati idealne ili štetne uvjete za razvoj fetalnog mozga (46). Iz perspektive reproduktivne i preventivne psihijatrije istraživanja fetalnih temelja temperamenta, mentalnog zdravlja i mentalnih poremećaja je veliki i težak izazov. Prema tzv. hipotezi o tri udarca („*three-hit hypothesis*“) o vulnerabilnosti za i rezilijenciji na bolesti genetska predispozicija predstavlja prvi udarac („*hit 1*“), prenatalna okolina drugi udarac („*hit 2*“) koji oštećuje gensku ekspresiju i dovodi do fenotipa različite prijemčivosti za različite bolesti zbog različitog reagiranja na životne stresove i nevolje („*hit 3*“). Prenatalno programiranje koje dovodi do povećane rezilijencije i antifragilnosti u sučeljavanju s životnim stresovima, nedaćama i traumama je iznimno važno iz perspektive promocije duševnog zdravlja. Razumijevanje rizičnih čimbenika u ranim fazama razvoja kao što su prenatalni stres, socijalna podrška, anksioznost, depresija i drugi duševni poremećaji majke, temperament novorođenčeta/djeteta, rane traume, itd. je iznimno važno za prevenciju i zbrinjavanje kasnijih, odnosno budućih duševnih poremećaja (47). Međutim, prenatalnu primarnu prevenciju duševnih poremećaja tek treba uvesti u kliničku praksu (48). Čini se da je došlo pravo vrijeme za promociju nove specijalnosti prenatalne i perinatalne psihijatrije (49).

ZAKLJUČAK

Fetus živi u simulirajućem okruženju pokreta kao i taktilno, kemijsko i auditorno osjetilnih informacija. Štoviše, fetus svakodnevno doživljava stotine jedinstvenih i ponavljajućih stimulansa. Ti stimulansi oblikuju strukturu i funkciju fetalnog mozga. Rezultati nedavnih istraživanja pokazali su kako o iskustvu ovisi plastičnost primarnog auditornog korteksa prije nego mozak dosegne potpunu zrelost. Izrazito prerano rođena nedonoščad izložena zvukovima svoje majke su imala značajno veći

ments; some babies are easy-to-handle and calm with good self-calming ability, while others are more sensitive and reactive to environment, with poor self-calming ability and difficult to soothe. The maternal in-utero milieu can provide the ideal or deleterious conditions for fetal brain development (46). From the perspective of reproductive, pre-emptive, and preventive psychiatry, research on the fetal origins of temperament and mental health as well as mental disorders is a formidable challenge (46). According to the “three-hit hypothesis of disease vulnerability and resilience”, genetic predisposition represents “hit 1”, the prenatal environment is “hit 2”, altering gene expression and leading to phenotypes with differing susceptibility to later life experiences and exposures (“hit 3”). Prenatal programming that may lead to increased resilience and antifragility in the face of later life adversities is very important from the perspective of mental health promotion. Understanding of early life risk factors such as prenatal stress, social support, maternal anxiety, depression and other mental disorders, baby and childhood temperament, early life trauma, etc. is crucial for the prevention and management of future psychiatric disorders (47). But prenatal primary prevention of mental illness has yet to be established for clinical use (48). It seems that the time has come for a recognized specialty in Prenatal and Perinatal Psychiatry (49).

CONCLUSION

The fetus lives in a stimulating matrix of motion as well as a wealth of tactile, chemical, and auditory sensory information. Moreover, the fetus is exposed to hundreds of specific and patterned stimuli each day. The structure and function of the brain are shaped by these stimuli. The results of recent investigation have shown experience-dependent plasticity in the primary auditory cortex before the brain has reached full-term maturation. Extremely pre-

auditorni korteks od kontrolne skupine koja je dobivala standardnu njegu. Također je bitno naglasiti da fetus može opažati, reagirati na, i relativno dugoročno zapamtiti stimulans doživljen u prenatalnom razdoblju. Osjetna percepcija višeg reda započinje tijekom fetalnog života. Funkcionalne talamokortikalne veze su esencijalne za fetalnu svijest o škodljivom stimulansu. Iako je dokaz o svjesnoj percepciji boli tijekom maternicnog života neizravan, nepobitno je dokazana podsvjesna inkorporacija fetalne boli u neurološki razvoj i plastičnost.

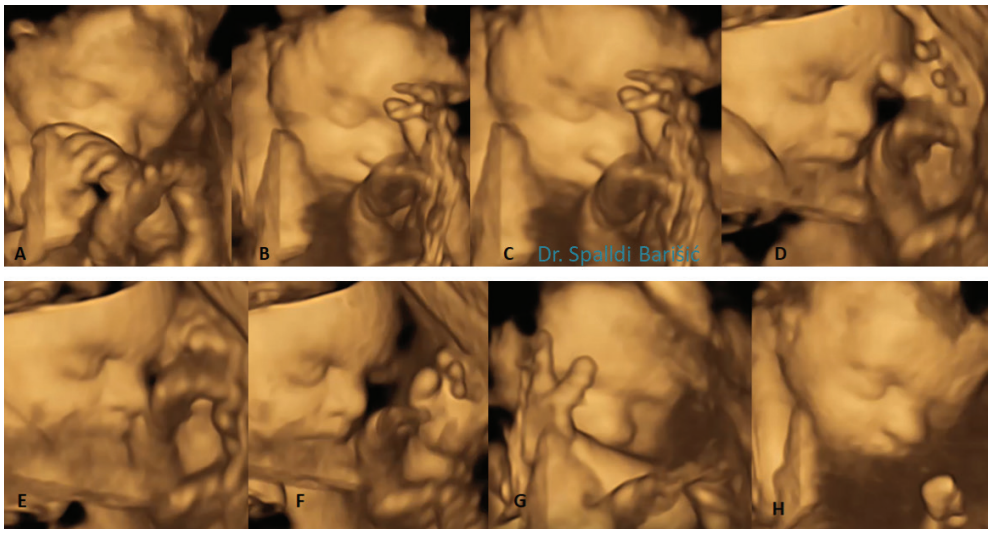
Početak razvoja sposobnosti planiranja djelovanja i fetalnog učenja motoričkih vještina su fascinantni. Ono što je najvažnije, fetalni pokreti mozgu pružaju senzorne podražaje koji potiču njegov razvoj. Napredak bihevioralne složenosti počinje spontanim fetalnim pokretima i dosiže vrhunac s pretpostavljenom preferencijom za zvuk majčinog glasa, odražavajući tijek sazrijevanja koji se odvijaju u moždanom deblu te potom u strukturama prednjeg mozga (diencefalonu i cerebrumu). Nadalje, fetalno motoričko ponašanje nedvojbeno odražava integraciju raznovrsnih kognitivnih, senzornih i motoričkih sustava. Nedavno je dokazano da se primarni poremećaji senzorno-motoričke i afektivne integracije kao i slaba kontrola nad motoričkim namjerama nalaze u pozadini poremećaja iz autističnog spektra. Novi val istraživanja je također ukazao kako se oblici ponašanja nalik emocijama te korijeni emotivnog ponašanja pojavljuju tijekom fetalnog života.

Fetus je sposoban za interakciju s okolišem i posljedično, za procesuiranje informacija u službi pamćenja i učenja (slika 5). Fetalno učenje i pamćenje treba smatrati rudimentarnim, iako danas znamo kako to pamćenje traje duže nego što se prije mislilo. Dugoročno pamćenje zahtijeva funkcionalni integritet limbičkog sustava i diencefalona (hipokampusa, amigdale, prednje i mediodorsalne jezgre talamusa te jezgre mamilarnog tijela), a te strukture su kod novorođenčadi već potpuno razvijene i funk-

mature infants exposed to maternal sounds had a significantly larger auditory cortex compared with control infants receiving standard care. It is also important to emphasize that the fetus can detect, respond to, and remember stimuli experienced during the prenatal period for a relatively long time. Higher order sensory perception begins in fetal life. Functional thalamocortical connections are also required for fetal awareness of noxious stimuli. Evidence for conscious pain perception during intrauterine life is indirect, but evidence for the subconscious incorporation of fetal pain into neurological development and plasticity is incontrovertible.

Early action planning development and fetal motor learning are fascinating. Importantly, fetal movements provide the brain with sensory input that spurs its development. Progression in behavioral complexity begins with spontaneous fetal movements and culminates with the presumed preference for the sound of the mother's voice, reflecting maturational events that take place in the brain stem, followed by the forebrain structures (the diencephalon and cerebrum). Furthermore, fetal motor behavior undoubtedly reflects development of diverse cognitive, sensory, and motor systems. It has recently been shown that primary sensory-motor and affective integration errors and poorly regulated motor intentions underlie autistic spectrum disorders. A new wave of investigations has also indicated that emotion-like behaviors and roots of emotions appear during fetal life.

The fetus is able to interact with the environment, and, as a result, processes information in the service of memory and learning (Figure 5). Fetal learning and memory should be considered rudimentary, although it is now known that memory lasts longer than previously thought. Long-term memory requires functional integrity of the limbic system and diencephalon (the hippocampus, amygdala, anterior and mediodorsal thalamic nuclei, and mammillary nuclei), and these structures are



SLIKA 5. Sekvence slika (A-H) 4D ultrazvučne snimke površinskog prikaza fetalnog lica u 35. tjednu gestacije. Na slici A uočava se fetus sa zatvorenim očima i rukom ispred lica. Iza ruke nalazi se pupkovina. Na slici B fetus podiže (lijevu) ruku. Na slici C fetus otvara oči i gleda u pupkovinu. Na slikama D-G pokušava ciljano uhvatiti pupkovinu koja mu smeta i odgurnuti je. Na slici H to napokon i uspijeva.

FIGURE 5. Sequences (A-H) of 4D ultrasound images of the surface view, fetal face at 35 weeks of gestation. In Figure A we see a fetus with closed eyes and a hand in front of the face. The umbilical cord is behind the arm. In Figure B the fetus raises the (left) arm. In Figure C the fetus opens his eyes and looks at the umbilical cord. In figures D-G, the fetus tries to grab the umbilical cord that is bothering him and pushes it away. In Figure H, the fetus finally succeeds.

cionalne. Stanične, sinaptičke i molekularne promjene nužne za pamćenje i učenje ovise o plastičnosti mozga, za koju se zna da je na vrhuncu u kasnom prenatalnom razdoblju i tijekom natalnog razdoblja.

Glazbeno vrlo nadarena djeca često pokazuju i talent za matematiku: Danili Bojko, polaznik šestog razreda iz Rusije, već je skladao 60 glazbenih djela, među njima i jednu operu, a piše i računalne programe. Istraživanja pokazuju da se kod djece koja rano nauče svirati neki instrument pojačava gustoća živčanih stanica u žuljevitom tijelu (corpus callosum) - strukturi koja povezuje lijevu i desnu polovicu našega misaonog organa.

Važno je ukazati na činjenicu da su u novorođenčadi u potpunosti razvijene samo supkortikalne strukture te primarna kortikalna područja. Stoga možemo zaključiti kako upravo te formacije imaju ključnu ulogu u kognitivnim funkcijama fetusa na kraju trudnoće. Asocijativni korteksi u novorođenčadi pokazuju nisku razinu aktivnosti na snimkama funkcional-

well developed and functioning in newborns. The cellular, synaptic, and molecular changes required for memory and learning depend on brain plasticity, which is known to be highest during the late prenatal and neonatal periods.

Musically very talented children often display a talent for mathematics: Danili Bojko, a sixth-grader from Russia, has so far composed 60 musical pieces, among which one is an opera, and he is also involved in writing computer programs. Research shows that children who learn to play an instrument at an early age display greater density of neurons in their corpus callosum – the structure connecting the left and right hemispheres of our brain.

It is important to point out that only subcortical formations and primary cortical areas are well-developed in a newborn. Therefore, we can conclude that these formations play an important role in cognitive functions of the fetus at the end of pregnancy. Association cortices display low activity in a newborn as recorded by functional magnetic resonance imaging.

nom magnetnom rezonancom. Postnatalno oblikovanje sinapsi u područjima asocijativnih korteksa, koje se ubrzava u razdoblju između osmog mjeseca i druge godine života, prethodi početku viših kognitivnih funkcija kao što su govor i jezik.

Pitanje fetalnih kognitivnih funkcija nije samo predmetom interesa znanstvenika već i ključno pitanje kliničke prakse, pogotovo u svjetlu napretka metoda medicinske dijagnostike i tehnologije koja nam omogućuje invazivne prenatalne medicinske zahvate. Klinički relevantni podatci o kognitivnim funkcijama fetusa mogu biti važni za ograničavanje boli fetusa, terapiju nedonoščadi kao i za poboljšane neurorazvojne ishode fetusa u trudnoćama visokog rizika. Štoviše, razvoj mozga u prenatalnom razdoblju vrlo je osjetljiv proces i neki od kognitivnih oštećenja i nedostataka u djetinjstvu ali i odrasloj dobi (poteškoće u učenju i pamćenju, nedostatak pažnje, odgođen jezični razvoj, intelektualni invaliditet, itd.) možda izviru iz prenatalnog života. Tek počinjemo istraživati fetalne kognitivne funkcije i vjerujemo kako će nam nove tehnologije, kao što su različiti 3D i 4D oblici ultrazvuka te snimanje funkcionalnom magnetnom rezonancom značajno pomoći u razumijevanju kognitivnih sposobnosti i funkcija fetusa, ali i dopustiti rano otkrivanje nepravilnog razvoja mozga i na taj način nam pružiti mogućnost rane terapijske intervencije.

Postoji li granica ljudske inteligencije? Evolucija je naš mozak učinila tako sposobnim da neki njime mogu shvatiti najsloženije sadržaje, kao što fizičar Abhay Ashtekar razumije kvantnu gravitaciju petlji. No naš je um najvjerojatnije dosegao svoju biološku granicu, argumentiraju psiholozi. U najboljem su slučaju moguća sitna poboljšanja - no vjerojatno ih prate gubitci u drugim područjima.

Razvoj fetalnog mozga, inteligencije i mentalnih poremećaja odražava međuigru između genoma, epigenoma i okoline (stanja unutar

Postnatal formation of synapses in association cortical areas, which intensifies between the 8th month and the 2nd year of life, precedes the onset of higher cognitive functions, such as speech and language.

The issue of fetal cognitive functions has been not only an object of interest for scientists but also an important issue in clinical practice, in light of advances in medical diagnostic methods and technology that allow invasive prenatal medical interventions. Clinically relevant data on cognitive functions of the fetus could be important for the management of fetal pain and treatment of preterm infants as well as for improved neurodevelopmental outcomes in fetuses from high-risk pregnancies. Furthermore, brain development in the prenatal period is a fragile process, and some of the cognitive impairments and deficits in childhood and adulthood (impaired learning and memory, deficits in attention, delayed language development, intellectual disability, etc.) may have their origins in prenatal life. We are just beginning to investigate cognitive functions of the fetus and we believe that new methods and techniques, such as different 3D/4D ultrasound modes and functional magnetic resonance imaging, will significantly help in understanding the cognitive abilities and functions of the fetus and allow early detection of abnormal brain development, thus providing the opportunity for early therapeutic intervention.

Are there limits to human intelligence? Evolution developed our brain to be so capable that some people can grasp even the most complex of issues, allowing for instance the physicist Abhay Ashtekar to understand loop quantum gravity. However, psychologists argue that our mind has probably reached its biological limits. At best, small improvements are still possible, but they would probably be accompanied by losses in other fields of function.

Fetal brain development, intelligence, resilience, and mental disorders are predicated on the interplay between the genome, epigenome,

maternice) pri čemu važnu ulogu ima mentalno zdravlje trudnice, njezin stav prema trudnoći, reakcije na stres, prehrana, mikrobiom, infekcije, itd, Čini se da je došlo pravo vrijeme da se prepozna važnost nove discipline prenatalne i perinatalne psihijatrije.

and environment in the womb, influenced by the mother's mental health, attitude to pregnancy, response to stress, nutrition, microbiome, infection, etc. It seems that the time has come for a recognized specialty in Prenatal and Perinatal Psychiatry.

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