

BENTHAM
SCIENCE

When the Mind Comes to Live Inside the Body: The Ontogeny of the Perceptual Control Clock



Sari Goldstein Ferber^{1,*}, Ronny Geva¹ and Aron Weller¹

¹Department of Psychology and the Leslie and Susan Gonda (Goldschmied) Multidisciplinary Brain Research Center, Bar Ilan University, Ramat Gan, Israel

ARTICLE HISTORY

Received: January 30, 2022
Revised: March 18, 2022
Accepted: April 09, 2022

DOI:
10.2174/1570159X20666220411095508



CrossMark

Abstract: In this editorial, we discuss the neurobiological processes underlying the early emergence of awareness that we term the “when” and “how” the mind comes to live inside the body. We describe an accumulative developmental process starting during embryonic life and continuing to fetal and postnatal development, of coupling of heart rate, body movements, and sleep states on the behavioral level with underlying mechanisms on the structural, functional, cellular, and molecular levels. A developmental perspective is proposed based on Perceptual Control Theory (PCT). This includes a developing sequence of modules starting from early sensing of neural intensities to early manifestation of human mindful capacities. We also address pharmacological treatments administered to preterm infants, which may interfere with this development, and highlight the need to consider this potential “side effect” of current pharmaceuticals when developing novel pharmacogenomic treatments.

Keywords: Fetal development, coupling, thalamus, brainstem, epigenomics, preterm infants.

1. INTRODUCTION

Many terms have been used to address the emergence of human mindful capacities: awareness, self-awareness, attention regulation, executive function, cognition, conscious control and more. An important question regards the timing and the temporal flow of these germinal human capacities or “when the mind comes to live inside the body”.

An executive attention network, termed “the cingulo-opercular network” [1, 2] (comprised of the anterior cingulate and anterior insula (operculum)), provides the infant with the opportunity for voluntary control behaviors in accordance with goals [3]. This network is involved in novelty-seeking, error detection, and resolving conflict between signals [2, 4-6]. The executive network emerges in infancy and activates some of the regions which are activated in adults [3, 7]. Interestingly, recent claims relate the emergence of germinal perceptual capacities at the borderline of viability, 23-25 weeks gestational age (GA), to the first signs of rudimentary awareness/consciousness [8-10]. Others speak of subordinate awareness/consciousness at even earlier stages of gestation (12-14 weeks GA) [10, 11].

We suggest an accumulative developmental process starting during embryonic life and continuing to fetal and postnatal development, by which coupling of heart rate, body movements and sleep states accelerate at 23-28 weeks GA when sensory processing becomes available and the preparation zone for cortical development advances [9, 12, 13]. We further suggest a developmental perspective based on Perceptual Control Theory (PCT). Powers [14, 15] suggested a hierarchy of modules. He suggested that feedback mechanisms are active between modules using a comparison of the actual measure to the desired measure (set-point). Powers suggested the modules as a hierarchy of feedback processes from very basic perception of outside stimuli intensities to full perception aimed at a goal-oriented action. We suggest here a developing sequence of modules running from early sense of neural intensities to early manifestation of human mindful capacities, using comparisons of earlier intrauterine and genetic/epigenetic stimulation progresses towards a desired GA-related neural state with age-appropriate neurobehavioral achievements during gestation. We propose that these neural-based progressions occur *via* changes in the desired measure (set-point) in very sensitive time windows during embryonic, fetal and neonatal life. We aim to show these shifts in the set-points both as a behavioral manifestation and a corresponding neural change towards further maturation. We term this process “the ontogenetic clock of perceptual control development”. We also address pharmacological treatments administered to preterm infants which may interfere with the development of this clock and emphasize the need to consider these potential “side effects” of current pharmaceuticals when developing novel pharmacogenomic treatments.

*Address correspondence to this author at the Department of Psychology and the Leslie and Susan Gonda (Goldschmied) Multidisciplinary Brain Research Center, Bar Ilan University, Ramat Gan, Israel; Tel:-972-544366523; E-mail: sari.goldstein@biu.ac.il

2. EARLY FETAL MINDFUL CAPACITIES

In the neonatal period, human infants show rudiments of awareness which implicitly suggest their-self awareness [16] and body awareness [9]. This implies early maturational processes of sensory-motor and attention development and preparation for the resulting language acquisition [16, 17]. Imaging studies show that older fetuses show long-range connectivity more than younger fetuses, with co-activation of motor, thalamic and contralateral cerebellar regions [18]. Others have shown evidence for early cognitive function from 28 weeks of gestation onwards, including short-term memory [19], language learning [20], and speech perception, *e.g.*, [21], by assessing discriminative abilities in the fetuses. These developments may be related to increase in myelination from mid-gestation onwards [22, 23]. The synaptogenesis from mid-gestation onwards is manifested through creation of neural connections and networks within the developing cerebrum [24, 25]. In addition, fetuses older than 31 weeks of gestation exhibit a module, or connectivity subnetwork that is comprised of the dorsal posterior and medial frontal brain regions [18]. We will go in this editorial from behavior down to further structural/functional developments and their timing and from there down to the cellular/molecular level and its developmental timewise flow as related to the structural/functional and behavior progression.

3. BEHAVIORAL MANIFESTATIONS

Given the data showing early perceptual processes in the fetus, there is a remaining question. How is this process triggered, towards developing into future goal-oriented behaviors? We suggest that around mid-gestation, based on structural and functional changes at the borderline of viability, the coupling of heart rate, body movements and sleep states underlies the emergence of awareness/self-awareness as detected behaviorally. We suggest that this physiology triggers maturation on the behavioral level and then the behavioral early maturation triggers the advancement in perceptual levels such as self-awareness.

During the early stages of gestation, the heart is among the first organs to develop, undergoing proliferation and differentiation through 7 weeks GA with increasing heart rate peaking at 10 weeks GA (170 beats per minute) followed by a gradual decrease (to 120-160 beats per minute) from this peaking age onwards [26, 27].

Fetal motor movements are spontaneously generated and this precedes the manifestation of sensory evoked behaviors, while being modulated by the periphery [28]. The large repertoire of general movements starting with movements of the entire body as early as 8-10 weeks GA is followed by extension of the arm and finger two weeks later (12 weeks GA). Neurologically, it has been suggested that the formation of the subplate coincides with the generation of general movements including mouthing, breathing, hiccoughing and swallowing behaviors [29]. For a full description see [28].

Temporal organization of sleep states is apparent from 28 weeks GA onwards [30, 31]. Most of the embryonic and fetal life is characterized by indeterminate sleep (*i.e.*, not meeting the criteria for either active/rapid eye movement (REM) sleep or quiet (non-REM) sleep). It has been shown that active sleep cycles are endogenous and do not necessarily reflect a dependency on maternal cycles [32]. REM sleep is regarded as contributing to central nervous system (CNS) development during embryonic and fetal life, while quiet (non-REM) sleep development represents a crucial time window in CNS maturation coinciding with maturation of the thalamocortical network and heightened synaptogenesis [13, 23, 33, 34]. Active sleep is the most archaic mode of sleep, coinciding upon its onset with the earliest brainstem development [33]. Until mid-gestation (26-28 weeks GA), the brainstem modulates and is responsible for active and indeterminate sleep in the embryo and fetus. From mid-gestation and onwards, the thalamus gateway for sensory activation and emerging sensory regions are involved in the consolidation of sleep organization into active and quiet sleep [35].

The functionality of the heart, measured by heart rate, heart rate variability and vagal tone, using ultrasonic tools during embryonic life, has been shown to correspond to neurobehavioral measures such as behavioral sleep-awake states and motor movements, with a coupling of onset of heart rate and movements at 12 weeks GA [36]. Maturation changes in the innervation of sympathetic and parasympathetic autonomic processes [37], including vagal myelination [38], and alterations to central mediation within the medulla oblongata and adjacent loci [39] may underlie the coupling of fetal heart rate, movements, and sleep states from 28 weeks gestation, a major accomplishment in CNS development [40].

4. THE STRUCTURAL/FUNCTIONAL UNDERLYING PROGRESSION

We have recently suggested that the brainstem is responsible for cell migration and differentiation needed for the developing control of the cortex over the brainstem through the corticospinal tract [23]. Its role in controlling active sleep early in gestation is manifested further in the contribution of active sleep to the developing synchrony and maturation within the two branches of the autonomic nervous system (ANS) [23, 33].

As recently suggested, the developing override of the cortex over the brainstem through the largest connection between the two organs, the corticospinal tract, coincides with the penetration of thalamic fibers and the resolution of the transient cortical subplate. These processes meet the developing bidirectional connectivity between the corticospinal tract (CST) and the thalamus [23]. In this sense, the capacity to self-regulate through coupling of heart rate movements and sleep states precedes the capacity for self-awareness as we have recently suggested [23].

The earliest cortical activity is modulated through monoaminergic afferents originating from the brainstem [41]. Recently we have described the complex process of the developing control of the cortex over the brainstem through its largest connection

with the brainstem, the corticospinal tract [23]. We have also suggested that cortical development is dependent on the developing synchronicity between the sympathetic and parasympathetic systems, both originating from the brainstem. We have further reviewed evidence for ANS coupling with the cortex during healthy fetal development [23]. This development is shown to be active in the first organization of cortical activity prior to mid-gestation, mainly supported by transient structures such as the cortical subplate [42, 43]. It is further enhanced from mid-gestation onwards by reorganization of the developing cortical activity, affected by the penetration of thalamic fibers from the sub-plate waiting zone to create the first synapses in the cortical plate [9].

5. TRANSITIONAL PROGRESS IN PERCEPTUAL SET-POINTS INITIATED AT THE CELLULAR LEVEL- A CONTROL THEORY APPROACH

The complex considerations articulated above lead us to a hypothesis of an integrative dynamic model adapted from Control Theory. James Clerk Maxwell first described Control Theory in the 19th century and it has been developed since then. Control Theory suggests the regulation of signals dynamically by controllers. These aim to reach a set-point - an expected level of signal compared to the given level of this signal. After comparison, the corrected signal is provided by the controller. Essential to Control Theory are the feedback mechanisms and the comparisons between the required and the given signal, behavior, outcome or output [44].

According to Powers [45], in the theoretical framework termed PCT adapted from control systems, perceptual cognitions are generated by brain functioning. PCT has recently achieved renewed interest [46-48]. Essential to the understanding of feedback mechanisms between modules described by Powers [45] and their comparisons by controllers between the actual value and the desired value (set-point) is that when physical entities change, as occurs in fetal and infant development, structurally and functionally, the error correction leads to further correction of the current set-point to a higher order value, before any further error correction can be evaluated reliably.

It is noted that PCT has been shown to be applicable to adult perception and has been recently applied to human consciousness [49, 50]. But if viewed sequentially, through the adjustments of the “set-points,” its developmental application may be suggested, from early embryonic life through the onset of rational thinking ability, around the age of 2 years postnatally, when the massive cortical progress and changes in its organization and complexity reach a peak [51].

We have suggested recently that developmental acquisition may be described by the mathematical term “step response” which is a change of a system or organism from zero to one [23]. Acquisition of a new developmental stage (during prenatal and postnatal life), *via* self-regulation, is mediated by one neurobehavioral subsystem dominating the others [52, 53] and by time-limited interactions between age-dependent subsystems [54]. This process can be termed “step-response”, a mathematical concept adapted from Control Theory (and Neural Networks). In a particular state, a system's step response includes the time evolution of its outputs. Its inputs are the source of the step function. Step response in Control Theory, represents the temporal behavior of a general system's output, with its input switching from zero to one rapidly [55].

Fluidity and interconnecting influences between all neurobehavioral subsystems are maintained during the plateau part after achieving a certain developmental goal. The step response occurs all at once within an age-appropriate range for any specific developmental goal concentrated on advancing a particular neurobehavioral subsystem. The plateau, after acquiring a “zero to one” state, a new developmental acquisition, may represent a continuous use of a certain set-point for a limited time until the next age appropriate skill acquisition is driven by the cellular and molecular levels. The change from zero to one may include behavioral, structural and functional fluctuations initiated by the cellular level for a progression of reorganization in the organism's perceptual control.

Looking at a step response of a system, its response depends on the system's levels of damping ratio, which is a term used in engineering to describe how oscillations in a system decay when they are disturbed from their initial position and eventually come to rest. In a given system or organism, one can see that for low damping, there is a lot of overshoot but the settling time is shorter for reaching the plateau (reaching the new set-point of 1). For higher damping, there will be less oscillations\ overshooting, but the settling time of the plateau stage (reaching the new set-point of 1) will be longer [56]. This may explain the disorganized behavior observed prior to a new acquisition of a developmental goal reported earlier [50]. We suggest that genetic and epigenetic individual differences (corresponding to low or high levels of damping typical response of the system) are involved in determining the level of disorganization (low or high levels of oscillations), as well as the characteristics of the given environment, be it intra- or extra-uterine.

We suggest that this reorganization, which includes acquisition of a higher perceptual ability, represents a sinusoidal unsteady transient change (oscillations\overshooting) along a process of a step-response, advancing the change to a higher set-point compared to the highest previously acquired module. This is in accordance with Powers' theory, which resurrected it in cybernetic terms by suggesting that plateaus reflect the learner's shifts in attention to new perceptual variables [57, 58].

Every subsystem within a system, when the environmental conditions change, should adjust itself to the new conditions by changing its set-point. Since neurobehavioral subsystems are interconnected, changing of one subsystem's set-point affects the set-points of the other subsystems (a Multivariable scheme). Multivariable control takes over ‘setting’ a set-point and adjusting the output for groups of related subsystems, including non-linear scenarios. This process typically produces consistent and timely adjustments, less oscillatory responses, and greater optimization. Closed-loop as suggested by Powers, and with multi-

variable control as we suggest here, allows for procedures to approximate actual constraints or benefits of advanced control. Thus, under multivariable control, an automatic, reliable response takes place during changing conditions [59].

We suggest that a multivariable reliable and adaptive control system is the case of healthy fetal and newborn growth. We suggest further, that the weight of earlier set-points is dependent on the degree of reinforcement these set-points gained through experience, by intra- and extra-uterine exposure along the developmental clock's timewise pathway. The case of prematurity suggests that the exposure to sensory stimulation, which is not age-appropriate after preterm birth, strengthens the stability of previously established set-points and increases the weight centrality of hubs in the brainstem-basilar mediated pathways. Thus, atypical programming [62], inappropriate stimulation or experience block the developmental adjustment of set-points which remains rigidly based on basilar pathways rather than on the developing cortices [51].

We further suggest that the molecular components of the cell, such as protein isoforms, are sensitive to the time flow of gestation and elicit the change in the set-points for more complex and mature status of brain development as manifested in change in fetal behavior. Thus, new synapses within the brainstem-CST-thalamus-cortical plate network connectivity trigger, in our view, changes in set-points for elicited further progress in typical healthy fetal behavior. This means turning a desired value into a more development-adaptive and age-appropriate value, aimed at further maturation. The error correction capability of the developing brain is thus doubled, and it includes comparisons between an older set-point and a new one, in addition to regular comparisons between each set-point and the actual value.

To support our claim that the set-points' transition is initiated on the cellular and molecular level, we note that the developing brain is characterized by rapid alterations in neurotransmission and voltage, in a preprogrammed sequence. This is supported by a Na-K pump in neurons, setting cellular firing and recovery times. Non-synaptic calcium plateaus and synaptic depolarization potentials come after the appearance of intrinsic currents [60]. N-Methyl-D-aspartic Acid (NMDA) receptor and Gamma-Aminobutyric Acid (GABA) currents mediate these cellular processes [60]. Weak disorganized connectivity is evident at early developmental stages [61]. However, by mid-gestation, when these currents are coupled with behavior, voltage-gated K⁺ signaling suggests the existence of a preprogrammed "stop-signal" for burst activity. From this point on, older ("senior") neurons connect, establishing networks among themselves, first in older structures such as the brainstem and spinal cord and only later in "younger" structures [24, 62, 63]. Thus, in our view, these changes on the cellular level are the basis for triggering changes in set-points.

The birth event is a massive transition from the intra-uterine to the extra-uterine environment [64]. This requires a shift in all neural and physiological mechanisms. We suggest that during labor, the newborn undergoes a comparison between all last intrauterine updated set-points and that the new set-points rely on feedback from earlier set-points just as a control system needs adjustment of all set-points if physical conditions are significantly changed. The advancement to higher modules, based on earlier levels, is part of the PCT theorem [45].

Among the resulting mindful capacities after birth as imposed by the new set-points and a new perceptual module activity are: the ability to fixate on salient cues in the periphery and visual field and the ability to follow salient visual stimuli including recognition of maternal voice, [65, 66] and maternal face [67]. A special case is the possibility to assess these abilities in infants born before term, at ages equivalent to fetal life. Even in these early born infants, when no brain injury is involved, these faculties are based on increasing involvement of cortical structures following the period of relying on brainstem-basilar mediated pathways [51, 68]. Furthermore, protracted overreliance on brainstem-basilar mediated pathways has been recently suggested to compromise the ability to regulate familiar set-points, a rigidity and a central-cohesion deficit which characterizes autism [69].

A developmental application of PCT shows that phases of reorganization towards an age-appropriate new perceptual capacity occur following phases of disorganized behavior of the infant and child suggesting a non-linear process of development [57, 58]. This may correspond to the costly process of the newborn and infant towards a change in set-points. In this regard, we suggest that this costly, but progressive, process is applicable for normal fetal development and for preterm infants too.

Although the exact terminology of the PCT modules may not precisely fit the developmental pathway along the time that elapses from conception to the acquisition of rational thinking, the control systems principle of an error correction drive to progress from module to module with feedback mechanisms in accumulating order of neural functioning and the comparison between the actual measure to the desired measure (set-point) may pave the way to improved understanding of very early perceptions and their progressive pathway towards the time when the mind resides inside the body.

6. FOR FURTHER RESEARCH

6.1. State of the Art

To the extent that we can advance the diagnosis and elucidation of these developing mechanisms, there are significant potential benefits. These include producing evidence-based treatment approaches and guidelines for pregnant women. The first step to advance the field of very early clocks would be the complex use of tools and maternal stimulations during pregnancy as we outline in the following section.

To assess brain-ANS trajectories it should be considered that optimal ANS maturation is only achieved around 37 weeks GA [70]. Accordingly, indeed, a sympathetic advantage is evident in preterm newborns [71]. During the first trimester, while the vagal myelination increases and the lateral hypothalamus differentiates, the parasympathetic nervous system (PNS) begins

to develop [72, 73]. Vagal regulatory function increases from 32 weeks GA. During this interim a major maturation process occurs. Among the systems emerging are: the baroreflex mechanisms, Heart Rate (HR) increase (indicating increasing sympathetic nervous system (SNS) function), respiratory sinus arrhythmia (HR regulation based on respiratory rate) and fetal movements [74]. The discrimination between quiet and active sleep develops at this time window accordingly [30, 33]. ANS regulation develops until birth (mainly parasympathetic regulation). At that point, the ANS has an important role in fetal-neonatal transition: modifying the respiratory and cardiovascular systems to the novel, extra-uterine conditions [75, 76].

Following development of the Functional Fetal Autonomic Brain Age Score (fABAS), Schmidt *et al.* [77], claim that universal indices, derived from phylogeny and evolution, can even better characterize fetal development from 20 weeks GA onwards. These authors used a modeling procedure on indices of heart rate variability (HRV). They reported that their models estimated the maturation age of the fetuses. Developmental disturbances such as those due to intrauterine growth restriction (IUGR) are reflected in altered fABAS [78, 79] as well as in these more recent developmental indices. These and other deviations from the trajectory of normal maturation (reported by [77]) suggest deviations from optimal integrated structure-function development. There are scarce reports on the assessment tools of developmental trajectories such as the above-mentioned approach.

6.2. Very Early Novel Assessment and Intervention Approaches

As a further contribution to the field, we would like to suggest the use of magnetic resonance imaging (MRI) and functional MRI (fMRI) for fetal brain imaging, in addition to measuring the complexity of HRV. We also propose that the crucial neuro-behavioral indices are manifested by the fetus on the developmental pathways of the heart rate-movement-states coupling. Measuring brain structure and function concomitantly (at the same time units) with sonographic measurements to capture and then calculate the complexity of HRV, would enable gathering more knowledge on the time trajectories of the clock development based on the brain-heart associations, together with the neurobehavioral coupling of movements-states-heart rate. This type of coupling is suggested as a developmental measure of the clock. The scientific literature shows that this type of coupling is gradually accomplished by the fetus with a peak of development at the time window of mid-gestation. Recent scientific investigations measured each part of this crucial progress of coupling independently, movements, heart-rate or states, if at all [28, 30, 31, 33, 80, 81]. Measuring the trajectories of fetal coupling is a novel idea. Additionally, older studies on maternal stimulation during pregnancy, *e.g.*, [82-84] may serve to elicit the coupling of neurobehavioral reactions. These suggestions may pave the way towards very early interventions if they would first be based on validated measures of coupling. Use of assessment tools, investigating fetal reactions to maternal stimulation during pregnancy, is another novel idea aimed at “correcting” the developmental delays of the neurobehavioral clock as potential interventions in cases identified as IUGR, risks for early delivery, or different developmental anomalies. This approach goes beyond the conventional clinical measures of fetuses which are still mainly growth and heart rate. In general, the above may assist in early detection of developmental dysfunctions and in development of (control) system-theory-based therapeutic strategies.

7. CONSIDERATIONS FOR FUTURE PHARMACOGENOMICS

It is well accepted that the balance between central noradrenergic and serotonergic activity and acetylcholine is relevant for active sleep generation and the onset of sleep organization [85, 86]. Several drugs widely used during pregnancy and the neonatal period may interfere with establishing behavioral states and CNS maturation, and thus they may delay the clock of ontogenetic self-awareness. For example, theophylline, commonly used to treat apnea in preterm infants, affects adenosine receptors, catecholamine levels, and cyclic adenosine monophosphate (cyclic AMP), changes sleep-wake patterns, and may also disorganize the emergence of attention regulation difficulties [87] and distinct behavioral states after a few weeks of use [88].

Therefore, we suggest that the next generation of pharmacological and pharmacogenomic treatments of preterm infants may need to target receptor composition beyond the numerical availability of receptors [48, 89]. Drug developers should consider the potential risk to induce insults to the endogenous ontogenetic timewise development of mindful human capacities. The genetic and epigenetic impact on the developmental transition of set-points towards progressing very early mindful capacities should be also considered. In this sense, it is suggested that the emergence of the mind starts in cellular patterns [48] and depends on protein isoforms, including their supporting role in adaptation to the given environment with gradual growth [48]. In terms of PCT, the onset and temporal flow of any shift in set-points along fetal and newborn life to create the granular human perceptions is initiated on the molecular and cellular level and represents the time when the mind comes to live inside the body.

LIST OF ABBREVIATIONS

ANS	=	Autonomic nervous system
CNS	=	Central nervous system
CST	=	Corticospinal tract
Cyclic AMP	=	Cyclic adenosine monophosphate
fABAS	=	Fetal Autonomic Brain Age Score
GA	=	Gestational age

GABA	=	Gamma-Aminobutyric Acid
HR	=	Heart rate
HRV	=	Heart rate variability
IUGR	=	Intrauterine growth restriction
MRI	=	Magnetic resonance imaging
NMDA	=	N-Methyl-D-aspartic Acid
PCT	=	Perceptual Control Theory
PNS	=	Parasympathetic nervous system
REM	=	Rapid eye movement
SNS	=	Sympathetic nervous system

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

- [1] Rueda, M.R.; Pozuelos, J.P.; Cómbita, L.M. Cognitive neuroscience of attention. *AIMS Neurosci.*, **2015**, 2(4), 183-202.
- [2] Neta, M.; Nelson, S.M.; Petersen, S.E. Dorsal anterior cingulate, medial superior frontal cortex, and anterior insula show performance reporting-related late task control signals. *Cereb. Cortex*, **2017**, 27(3), 2154-2165. PMID: 26972752
- [3] Posner, M.I.; Rothbart, M.K.; Voelker, P. Developing brain networks of attention. *Curr. Opin. Pediatr.*, **2016**, 28(6), 720-724. <http://dx.doi.org/10.1097/MOP.0000000000000413> PMID: 27552068
- [4] Posner, M.I.; Rothbart, M.K.; Sheese, B.E.; Voelker, P. Developing attention: Behavioral and brain mechanisms. *Adv. Neurosci. (Hindawi)*, **2014**, 2014, 405094. <http://dx.doi.org/10.1155/2014/405094> PMID: 25110757
- [5] Schmidt, E.L.; Burge, W.; Visscher, K.M.; Ross, L.A. Cortical thickness in frontoparietal and cingulo-opercular networks predicts executive function performance in older adults. *Neuropsychol.*, **2016**, 30(3), 322-331. <http://dx.doi.org/10.1037/neu0000242> PMID: 26460586
- [6] Geva, R.; Gardner, J.M.; Karmel, B.Z. Feeding-based arousal effects on visual recognition memory in early infancy. *Dev. Psychol.*, **1999**, 35(3), 640-650. <http://dx.doi.org/10.1037/0012-1649.35.3.640> PMID: 10380856
- [7] Conejero, Á.; Guerra, S.; Abundis-Gutiérrez, A.; Rueda, M.R. Frontal theta activation associated with error detection in toddlers: Influence of familial socioeconomic status. *Dev. Sci.*, **2018**, 21(1), e12494. <http://dx.doi.org/10.1111/desc.12494> PMID: 27981736
- [8] Judaš, M.; Sedmak, G.; Kostović, I. The significance of the subplate for evolution and developmental plasticity of the human brain. *Front. Hum. Neurosci.*, **2013**, 7(JUL), 423. PMID: 23935575
- [9] Kostović, I.; Judaš, M. The development of the subplate and thalamocortical connections in the human foetal brain. *Acta Paediatr.*, **2010**, 99(8), 1119-1127. <http://dx.doi.org/10.1111/j.1651-2227.2010.01811.x> PMID: 20367617
- [10] Lagercrantz, H. *Infant brain development: Formation of the mind and the emergence of consciousness*; Springer International Publishing, **2016**. <http://dx.doi.org/10.1007/978-3-319-44845-9>
- [11] Kurjak, A.; Stanojević, M.; Salihagić-Kadić, A.; Spalldi Barišić, L.; Jakovljević, M. Is four-dimensional (4D) ultrasound entering a new field of Fetal Psychiatry? *Psychiatr. Danub.*, **2019**, 31(2), 133-140. <http://dx.doi.org/10.24869/psyd.2019.133> PMID: 31291216
- [12] Kostovic, I.; Vasung, L. Insights from *in vitro* fetal magnetic resonance imaging of cerebral development. *Semin. Perinatol.*, **2009**, 33(4), 220-233. <http://dx.doi.org/10.1053/j.semperi.2009.04.003> PMID: 19631083
- [13] Vasung, L.; Raguz, M.; Kostovic, I.; Takahashi, E. Spatiotemporal relationship of brain pathways during human fetal development using high-angular resolution diffusion MR imaging and histology. *Front. Neurosci.*, **2017**, 11(JUL), 348. <http://dx.doi.org/10.3389/fnins.2017.00348> PMID: 28744187
- [14] Powers, W.T. *Making Sense of Behavior: The Meaning of Control*; Benchmark: New Canaan, CT, **1998**.
- [15] Mansell, W.; Marken, R.S. The origins and future of control theory in psychology. *Rev. Gen. Psychol.*, **2015**, 19(4), 425-430. <http://dx.doi.org/10.1037/gpr0000057>
- [16] Rochat, P. The ontogeny of human self-consciousness. *Curr. Dir. Psychol. Sci.*, **2018**, 27(5), 345-350. <http://dx.doi.org/10.1177/0963721418760236>
- [17] Orr, E.; Geva, R. Symbolic play and language development. *Infant Behav. Dev.*, **2015**, 38, 147-161. <http://dx.doi.org/10.1016/j.infbeh.2015.01.002> PMID: 25658200
- [18] Thomason, M.E.; Grove, L.E.; Lozon, T.A., Jr; Vila, A.M.; Ye, Y.; Nye, M.J.; Manning, J.H.; Pappas, A.; Hernandez-Andrade, E.; Yeo, L.; Mody, S.; Berman, S.; Hassan, S.S.; Romero, R. Age-related increases in long-range connectivity in fetal functional neural connectivity networks in utero. *Dev. Cogn. Neurosci.*, **2015**, 11, 96-104. <http://dx.doi.org/10.1016/j.dcn.2014.09.001> PMID: 25284273

- [19] Partanen, E.; Kujala, T.; Tervaniemi, M.; Huottilainen, M. Prenatal music exposure induces long-term neural effects. *PLoS One*, **2013**, 8(10), e78946. <http://dx.doi.org/10.1371/journal.pone.0078946> PMID: 24205353
- [20] Huottilainen, M. A new dimension on foetal language learning. *Acta Paediatr.*, **2013**, 102(2), 102-103. <http://dx.doi.org/10.1111/apa.12122> PMID: 23278627
- [21] Anderson, A.L.; Thomason, M.E. Functional plasticity before the cradle: A review of neural functional imaging in the human fetus. *Neurosci. Biobehav. Rev.*, **2013**, 37(9 Pt B), 2220-2232. <http://dx.doi.org/10.1016/j.neubiorev.2013.03.013> PMID: 23542738
- [22] Tsuneishi, S.; Casar, P. Effects of preterm extrauterine visual experience on the development of the human visual system: A flash VEP study. *Dev. Med. Child Neurol.*, **2000**, 42(10), 663-668. <http://dx.doi.org/10.1017/S0012162200001225> PMID: 11085293
- [23] Goldstein Ferber, S.; Weller, A.; Ben-Shachar, M.; Klinger, G.; Geva, R. Development of the Ontogenetic Self-Regulation Clock. *Int. J. Mol. Sci.*, **2022**, 23(2), 993. <http://dx.doi.org/10.3390/ijms23020993> PMID: 35055184
- [24] Jaimes, C.; Machado-Rivas, F.; Afacan, O.; Khan, S.; Marami, B.; Ortinau, C.M.; Rollins, C.K.; Velasco-Annis, C.; Warfield, S.K.; Gholipour, A. *In vivo* characterization of emerging white matter microstructure in the fetal brain in the third trimester. *Hum. Brain Mapp.*, **2020**, 41(12), 3177-3185. <http://dx.doi.org/10.1002/hbm.25006> PMID: 32374063
- [25] Hooker, J.D.; Khan, M.A.; Farkas, A.B.; Lirette, S.T.; Joyner, D.A.; Gordy, D.P.; Storrs, J.M.; Roda, M.S.; Bofill, J.A.; Smith, A.D.; James, J.R. Third-trimester in utero fetal brain diffusion tensor imaging fiber tractography: A prospective longitudinal characterization of normal white matter tract development. *Pediatr. Radiol.*, **2020**, 50(7), 973-983. <http://dx.doi.org/10.1007/s00247-020-04639-8> PMID: 32399686
- [26] Brade, T.; Pane, L.S.; Moretti, A.; Chien, K.R.; Laugwitz, K.L. Embryonic heart progenitors and cardiogenesis. *Cold Spring Harb. Perspect. Med.*, **2013**, 3(10), a013847. <http://dx.doi.org/10.1101/cshperspect.a013847> PMID: 24086063
- [27] Burton, G.J.; Jauniaux, E. Development of the human placenta and fetal heart: Synergic or independent? *Front. Physiol.*, **2018**, 9(APR), 373. <http://dx.doi.org/10.3389/fphys.2018.00373> PMID: 29706899
- [28] Einspieler, C.; Prayer, D.; Marschik, P.B. Fetal movements: The origin of human behaviour. *Dev. Med. Child Neurol.*, **2021**, 63(10), 1142-1148. <http://dx.doi.org/10.1111/dmcn.14918> PMID: 33973235
- [29] Lühchinger, A.B.; Hadders-Algra, M.; van Kan, C.M.; de Vries, J.I.P. Fetal onset of general movements. *Pediatr. Res.*, **2008**, 63(2), 191-195. <http://dx.doi.org/10.1203/PDR.0b013e31815ed03e> PMID: 18091359
- [30] Graven, S.N.; Browne, J.V. Sleep and brain development: The critical role of sleep in fetal and early neonatal brain development. *Newborn Infant Nurs. Rev.*, **2008**, 8(4), 173-179. <http://dx.doi.org/10.1053/j.nainr.2008.10.008>
- [31] Brändle, J.; Preissl, H.; Draganova, R.; Ortiz, E.; Kagan, K.O.; Abele, H.; Brucker, S.Y.; Kiefer-Schmidt, I. Heart rate variability parameters and fetal movement complement fetal behavioral states detection via magnetography to monitor neurovegetative development. *Front. Hum. Neurosci.*, **2015**, 9, 147. <http://dx.doi.org/10.3389/fnhum.2015.00147> PMID: 25904855
- [32] Anders, T.F.; Roffwarg, H.P. The relationship between maternal and neonatal sleep. *Neuropadiatrie*, **1973**, 4(2), 151-161. <http://dx.doi.org/10.1055/s-0028-1091736> PMID: 4352213
- [33] Peirano, P.; Algarin, C.; Uauy, R. Sleep-wake states and their regulatory mechanisms throughout early human development. *J. Pediatr.*, **2003**, 143(4)(Suppl.), S70-S79. [http://dx.doi.org/10.1067/S0022-3476\(03\)00404-9](http://dx.doi.org/10.1067/S0022-3476(03)00404-9) PMID: 14597916
- [34] Kostović, I.; Sedmak, G.; Judaš, M. Neural histology and neurogenesis of the human fetal and infant brain. *Neuroimage*, **2019**, 188, 743-773. <http://dx.doi.org/10.1016/j.neuroimage.2018.12.043> PMID: 30594683
- [35] Flower, M.J. Neuromaturation of the human fetus. *J. Med. Philos.*, **1985**, 10(3), 237-251. <http://dx.doi.org/10.1093/jmp/10.3.237> PMID: 4045332
- [36] Zizzo, A.R.; Kirkegaard, I.; Hansen, J.; Uldbjerg, N.; Mølgaard, H. Fetal heart rate variability is affected by fetal movements: A systematic review. *Front. Physiol.*, **2020**, 11, 578898. <http://dx.doi.org/10.3389/fphys.2020.578898> PMID: 33101059
- [37] Dalton, K.J.; Dawes, G.S.; Patrick, J.E. The autonomic nervous system and fetal heart rate variability. *Am. J. Obstet. Gynecol.*, **1983**, 146(4), 456-462. [http://dx.doi.org/10.1016/0002-9378\(83\)90828-1](http://dx.doi.org/10.1016/0002-9378(83)90828-1) PMID: 6859165
- [38] Sachis, P.N.; Armstrong, D.L.; Becker, L.E.; Bryan, A.C. Myelination of the human vagus nerve from 24 weeks postconceptional age to adolescence. *J. Neuropathol. Exp. Neurol.*, **1982**, 41(4), 466-472. <http://dx.doi.org/10.1097/00005072-198207000-00009> PMID: 7086467
- [39] Longin, E.; Gerstner, T.; Schaible, T.; Lenz, T.; König, S. Maturation of the autonomic nervous system: Differences in heart rate variability in premature vs. term infants. *J. Perinat. Med.*, **2006**, 34(4), 303-308. <http://dx.doi.org/10.1515/JPM.2006.058> PMID: 16856820
- [40] Visser, G.H.A.; Poelmann-Weesjes, G.; Cohen, T.M.N.; Bekedam, D.J. Fetal behavior at 30 to 32 weeks of gestation. *Pediatr. Res.*, **1987**, 22(6), 655-658. <http://dx.doi.org/10.1203/00006450-198712000-00009> PMID: 3431947
- [41] Olson, L.; Boréus, L.O.; Seiger, A. Histochemical demonstration and mapping of 5-hydroxytryptamine- and catecholamine-containing neuron systems in the human fetal brain. *Z. Anat. Entwicklungsgesch.*, **1973**, 139(3), 259-282. <http://dx.doi.org/10.1007/BF00519968> PMID: 4707937
- [42] Kostović, I. The enigmatic fetal subplate compartment forms an early tangential cortical nexus and provides the framework for construction of cortical connectivity. *Prog. Neurobiol.*, **2020**, 194, 101883. <http://dx.doi.org/10.1016/j.pneurobio.2020.101883> PMID: 32659318
- [43] Kostović, I.; Radoš, M.; Kostović-Srzić, M.; Krsnik, Ž. Fundamentals of the development of connectivity in the human fetal brain in late gestation: From 24 weeks gestational age to term. *J. Neuropathol. Exp. Neurol.*, **2021**, 80(5), 393-414. <http://dx.doi.org/10.1093/jnen/nlab024> PMID: 33823016
- [44] Bennett, S. *A history of control engineering, 1930-1955*; Peter Peregrinus, **1993**. <http://dx.doi.org/10.1049/PBCE047E>
- [45] Powers, W. *Living control systems III: The fact of control*; Williams & Company: Savannah, GA, **2008**.
- [46] Mansell, W. The perceptual control model of psychopathology. *Curr. Opin. Psychol.*, **2021**, 41, 15-20. <http://dx.doi.org/10.1016/j.copsyc.2021.01.008> PMID: 33662864

- [47] Carver, C.S.; Scheier, M.F. Control theory: A useful conceptual framework for personality-social, clinical, and health psychology. *Psychol. Bull.*, **1982**, 92(1), 111-135.
<http://dx.doi.org/10.1037/0033-2909.92.1.111> PMID: 7134324
- [48] Goldstein Ferber, S.; Als, H.; McAnulty, G.; Klinger, G.; Weller, A. Multi-level hypothalamic neuromodulation of self-regulation and cognition in preterm infants: Towards a control systems model. *Compr Psychoneuroendocrinology.*, **2022**, 9, 100109.
<http://dx.doi.org/10.1016/j.cpnec.2021.100109>
- [49] Mansell, W. An integrative control theory perspective on consciousness. *Psychol. Rev.* **2022**. <https://doi.org/10.1037/rev0000384>
- [50] Plooi, F. The phylogeny, ontogeny, causation and function of regression periods explained by reorganizations of the hierarchy of perceptual control systems. *The Interdisciplinary Handbook of Perceptual Control Theory: Living Control Systems IV*; Mansell, W., Ed.; Academic Press, **2020**, pp. 199-225.
<http://dx.doi.org/10.1016/B978-0-12-818948-1.00008-3>
- [51] Burstein, O.; Zevin, Z.; Geva, R. Preterm birth and the development of visual attention during the first 2 years of life: A systematic review and meta-analysis. *JAMA Netw. Open.*, **2021**, 4(3), e213687.
<http://dx.doi.org/10.1001/jamanetworkopen.2021.3687> PMID: 33783515
- [52] Als, H. A synactive model of neonatal behavioral organization: Framework for the assessment of neurobehavioral development in the premature infant and for support of infants and parents in the neonatal intensive care environment. *Phys. Occup. Ther. Pediatr.*, **1986**, 6(3-4), 3-53.
http://dx.doi.org/10.1080/J006v06n03_02
- [53] Als, H. Toward a synactive theory of development: Promise for the assessment and support of infant individuality. *Infant Ment. Health J.*, **1982**, 3(4), 229-243.
[http://dx.doi.org/10.1002/1097-0355\(198224\)3:4<229::AID-IMHJ2280030405>3.0.CO;2-H](http://dx.doi.org/10.1002/1097-0355(198224)3:4<229::AID-IMHJ2280030405>3.0.CO;2-H)
- [54] Ferber, SG; Makhoul, IR The effect of skin-to-skin contact (Kangaroo Care) shortly after birth on the neurobehavioral responses of the term newborn: A randomized, controlled trial. *Pediatrics*, **2004**, 113(4 1), 858-865.
<http://dx.doi.org/10.1001/jama.292.11.858>
- [55] Antsaklis, P.; Gao, Z. Control system design. *The Electronics Engineers' Handbook*, 5th ed; McGraw-Hill: New York, **2005**, pp. 19.1-19.30.
- [56] Dorf, R.C.; Bishop, R.H.; Columbus, B.; New, I.; San, Y.; Upper, F. *Modern Control Systems*; Pearson, **2011**.
- [57] Robertson, R.J.J.; Glines, L.A.A. The Phantom Plateau returns. *Percept. Mot. Skills*, **1985**, 61(1), 55-64.
<http://dx.doi.org/10.2466/pms.1985.61.1.55> PMID: 4047889
- [58] Powers, W.T. Comment on the "Phantom Plateau". *Percept. Mot. Skills*, **1985**, 61(1), 329-330.
<http://dx.doi.org/10.2466/pms.1985.61.1.329>
- [59] Kern, A. Understanding multivariable control: The missing metric: An improved understanding of the role of multivariable control in industrial process operations will lead to more cost-effective solutions and engage a wider circle of people in the process automati. *Control Eng.*, **2020**, 67(4), 26-28.
- [60] Dehorter, N.; Vinay, L.; Hammond, C.; Ben-Ari, Y. Timing of developmental sequences in different brain structures: Physiological and pathological implications. *Eur. J. Neurosci.*, **2012**, 35(12), 1846-1856.
<http://dx.doi.org/10.1111/j.1460-9568.2012.08152.x> PMID: 22708595
- [61] Hartley, C.; Farmer, S.; Berthouze, L. Temporal ordering of input modulates connectivity formation in a developmental neuronal network model of the cortex. *PLoS One*, **2020**, 15(1), e0226772.
<http://dx.doi.org/10.1371/journal.pone.0226772> PMID: 31923200
- [62] Fisch-Gómez, E.; Vasung, L.; Meskaldji, D.E.; Lazeyras, F.; Borradori-Tolsa, C.; Hagmann, P.; Barisnikov, K.; Thiran, J.P.; Hüppi, P.S. Structural brain connectivity in school-age preterm infants provides evidence for impaired networks relevant for higher order cognitive skills and social cognition. *Cereb. Cortex*, **2015**, 25(9), 2793-2805.
<http://dx.doi.org/10.1093/cercor/bhu073> PMID: 24794920
- [63] Tau, G.Z.; Peterson, B.S. Normal development of brain circuits. *Neuropsychopharmacol.*, **2009**, 35(1), 147-168.
- [64] Hillman, N.H.; Kallapur, S.G.; Jobe, A.H. Physiology of transition from intrauterine to extrauterine life. *Clin. Perinatol.*, **2012**, 39(4), 769-783.
<http://dx.doi.org/10.1016/j.clp.2012.09.009> PMID: 23164177
- [65] Moon, C.M.; Fifer, W.P. Evidence of transnatal auditory learning. *J. Perinatol.*, **2000**, 20(8 Pt 2), S37-S44.
<http://dx.doi.org/10.1038/sj.jp.7200448> PMID: 11190699
- [66] Carvalho, M.E.S.; de Miranda Justo, J.M.R.; Gratier, M.; da Silva, H.M.F.R. The impact of maternal voice on the fetus: A systematic review. *Curr. Women's Heal. Rev.*, **2018**, 15(3), 196-206.
- [67] Coulon, M.; Guellai, B.; Streri, A. Recognition of unfamiliar talking faces at birth. *Int. J. Behav. Dev.*, **2011**, 35(3), 282-287.
<http://dx.doi.org/10.1177/0165025410396765>
- [68] Geva, R.; Feldman, R. A neurobiological model for the effects of early brainstem functioning on the development of behavior and emotion regulation in infants: Implications for prenatal and perinatal risk. *J. Child Psychol. Psychiatry*, **2008**, 49(10), 1031-1041.
<http://dx.doi.org/10.1111/j.1469-7610.2008.01918.x> PMID: 18771507
- [69] Burstein, O.; Geva, R. The brainstem-informed autism framework: Early life neurobehavioral markers. *Front. Integr. Neurosci.*, **2021**, 15, 759614.
- [70] Hugues, P.; Vincent, P.; Sophie, F.; Antoine, G.; Patricia, F.; Patrick, P.; Alain, B.; Frédéric, R.; Jean-Claude, B. Autonomic maturation from birth to 2 years: normative values. *Heliyon*, **2019**, 5(3), e01300. DOI: 10.1016/j.heliyon.2019.e01300
- [71] Yiallourou, S.R.; Sands, S.A.; Walker, A.M.; Horne, R.S.C. Maturation of heart rate and blood pressure variability during sleep in term-born infants. *Sleep*, **2012**, 35(2), 177-186. DOI: 10.5665/sleep.1616
- [72] Koutcherov, Y.; Mai, J.K.; Paxinos, G. Hypothalamus of the human fetus. *J. Chem. Neuroanat.*, **2003**, 26(4), 253-270. DOI: 10.1016/j.jchemneu.2003.07.002
- [73] Cheng, G.; Zhou, X.; Qu, J.; Ashwell, K.W.S.; Paxinos, G. Central vagal sensory and motor connections: human embryonic and fetal development. *Auton. Neurosci.*, **2004**, 114(1-2), 83-96. DOI: 10.1016/j.autneu.2004.06.008
- [74] DiPietro, J.A.; Hodgson, D.M.; Costigan, K.A.; Hilton, S.C.; Johnson, T.R.B. Fetal neurobehavioral development. *Child. Dev.*, **1996**, 67(5), 2553-2567. PMID: 9022256
- [75] Mulkey, S.B.; du Plessis, A.J. Autonomic nervous system development and its impact on neuropsychiatric outcome. *Pediatr. Res.*, **2019**, 85(2), 120-126. DOI: 10.1038/s41390-018-0155-0
- [76] Marco, C.; Francesco, C.; Alessandro, C.; Nicola, B.; Dario, B.; Francesco, C.; Carla, G. Corti, Andrea, M. Heart rate variability in the perinatal period: A critical and conceptual review. *Front. Neurosci.*, **2020**, 14. DOI: 10.3389/fnins.2020.561186
- [77] Schmidt, A.; Schukat-Talamazzini, E.G.; Zöllkau, J.; Pytlík, A.; Leibl, S.; Kumm, K.; et al. Universal characteristics of evolution and development are inherent in fetal autonomic brain maturation. *Auton. Neurosci.*, **2018**, 212, 32-41. DOI: 10.1016/j.autneu.2018.02.004
- [78] Dirk, H.; Florian, T.; Susan, J.; Samuel, N.; Otto, W.W.; Ekkehard, S.; Uwe, S. Fetal functional brain age assessed from universal developmental indices obtained from neuro-vegetative activity patterns. *PLoS One*, **2013**, 8(9). DOI: 10.1371/journal.pone.0074431
- [79] Dirk, H.; Uwe, S.; Eva-Maria, K.; Alexander, S.; Otto, W.W.; Ekkehard, S.; Wolfgang, H.; Dietrich, H.W.G.; Peter, van L. Validation of functional fetal autonomic brain age score fABAS in 5 min short recordings. *Physiol. Meas.*, **2015**, 36(11), 2369-2378. DOI: 10.1088/0967-3334/36/11/2369

- [80] Colleen, P.; Christa, E.; Toril, F.; Lars, A.; Michael, D.S.; Alexander, D.; Jeremy, D.M. Correlates of normal and abnormal general movements in infancy and long-term neurodevelopment of preterm infants: Insights from functional connectivity studies at term equivalence. *J. Clin. Med.*, **2020**, *9*, 834. DOI: 10.3390/jcm9030834
- [81] Shuffrey, L.C.; Myers, M.M.; Odendaal, H.J.; Elliott, A.J.; du Plessis, C.; Groenewald, C. Larry, B.; Jyoti, A.; David, J.N.; Joseph, R.; William, P.F. Fetal heart rate, heart rate variability, and heart rate/movement coupling in the Safe Passage Study. *J. Perinatol.*, **2019**, *39*(5), 608-618. DOI: 10.1038/s41372-019-0342-9
- [82] Monk, C.; Myers, M.M.; Sloan, R.P.; Ellman, L.M.; Fifer, W.P. Effects of women's stress-elicited physiological activity and chronic anxiety on fetal heart rate. *J. Dev. Behav. Pediatr.*, **2003**, *24*(1), 32-38. DOI: 10.1097/00004703-200302000-00008
- [83] Monk, C.; Fifer, W.P.; Sloan, R.P.; Myers, M.M.; Bagiella, E.; Ellman, L.; Hurtado, A. Physiologic responses to cognitive challenge during pregnancy: effects of task and repeat testing. *Int. J. Psychophysiol.*, **2001**, *40*(2), 149-159. DOI: 10.1016/s0167-8760(00)00158-6
- [84] Zimmer, E.Z.; Fifer, W.P.; Kim, Y.I.; Rey, H.R.; Chao, C.R.; Myers, M.M. Response of the premature fetus to stimulation by speech sounds. *Early Hum. Dev.*, **1993**, *33*(3), 207-215. DOI: 10.1016/0378-3782(93)90147-m
- [85] Adrien, J.; Bourgoin, S.; Hamon, M. Midbrain raphe lesion in the newborn rat I. Neurophysiological aspects of sleep. *Brain Res.*, **1977**, *127*(1), 99-110.
[http://dx.doi.org/10.1016/0006-8993\(77\)90382-1](http://dx.doi.org/10.1016/0006-8993(77)90382-1) PMID: 861756
- [86] Jouvet, M. The role of monoamines and acetylcholine-containing neurons in the regulation of the sleep-waking cycle. *Ergeb. Physiol.*, **1972**, *64*, 166-307.
PMID: 4403272
- [87] Geva, R.; Yaron, H.; Kuint, J. Neonatal sleep predicts attention orienting and Distractibility. *J. Atten. Disord.*, **2016**, *20*(2), 138-150.
<http://dx.doi.org/10.1177/1087054713491493> PMID: 23893532
- [88] Hunt, C.E. The cardiorespiratory control hypothesis for sudden infant death syndrome. *Clin. Perinatol.*, **1992**, *19*(4), 757-771.
[http://dx.doi.org/10.1016/S0095-5108\(18\)30429-9](http://dx.doi.org/10.1016/S0095-5108(18)30429-9) PMID: 1464189
- [89] Ferber, S.G.; Roth, T.L.; Weller, A. Epigenetic fragility of the endocannabinoid system under stress: Risk for mood disorders and pharmacogenomic implications. *Epigenomics*, **2020**, *12*(8), 657-660.
<http://dx.doi.org/10.2217/epi-2020-0037> PMID: 32396405