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Vassilios Fanos, Giuseppe Buonocore & Michele Mussap

To cite this article: Vassilios Fanos, Giuseppe Buonocore & Michele Mussap (2014) Neonatomics and childomics: the right route to the future, The Journal of Maternal-Fetal & Neonatal Medicine, 27:sup2, 1-3, DOI: [10.3109/14767058.2014.955956](https://doi.org/10.3109/14767058.2014.955956)

To link to this article: <https://doi.org/10.3109/14767058.2014.955956>



Published online: 06 Oct 2014.



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EDITORIAL

Neonatomics and childomics: the right route to the future

In the last five years, the number of publications on metabolomics in neonatology and pediatrics has greatly increased [1]. This is a subject not only of great scientific interest, but also one that may have strong repercussions on clinical practice in the coming five years [2]. It is an evolution, perhaps a silent revolution, that promises to become a consolidated discipline with which neonatologists and pediatricians will have to come to grips in the immediate future and which will become part of our world: we are thus of the opinion that the time is ripe to propose the neologisms *neonatomics* and *childomics* present in the title of our supplement.

On this subject, we wish to thank the Editor-in-Chief of the Journal of Maternal Fetal Neonatal Medicine, Prof. Gian Carlo di Renzo, who continues to host us this year as well, with a supplement dedicated completely to the Italian metabolomic network and its national and international ramifications, on the occasion of the 10th International Workshop on Neonatology to be held in Cagliari (October, 21st–25th, 2014).

The lesson that David Barker prophetically taught us is that the life of every individual is a continuum from prenatal life to that of the adult, and that early events may cause qualitative and quantitative metabolic changes having a permanent effect on the phenotype and important long-term consequences for the individual [3].

It is from this assumption that comes the subject of the works presented here, which start from obstetrics (the diagnosis of childbirth) and cover the entire field of neonatology, to arrive at the autistic child.

To understand what triggers the time of delivery, what series of events and metabolites press the button of no return, that is, the beginning of delivery, is a challenge that may lead to unimaginable advantages and it is no coincidence that important obstetricians of global renown are pressing on the accelerator of metabolomics [4]. This technique seems of outstanding impact on perinatology [5].

Connected with pregnancy is the contribution of urinary metabolomics at birth of babies with weights that are “not enough” or “too much” [6]. A key role appears to be played by myoinositol and we know from the literature that inositol administered to pregnant women at risk of gestational diabetes greatly reduces its incidence [7]. This part of

nutri-metabolomics has been investigated both with NMR and GC-MS. The knowledge acquired may lead to new advances towards a better understanding of the epidemic of diabetes that has recently characterized babies and adolescents [8,9].

The hard core of the works presented in this supplement is in any case represented by neonatology and the topics, among others, concern two most important themes: nutrition (metabolomic analysis of breast milk) [10] and infections [11], which are the cause of approximately one million neonatal deaths every year.

The composition of the milk of mothers with preterm delivery has been monitored up to the fortieth week of post-conception age. Samples of formula milk have also been analyzed. From the explorative analysis it emerges that breast milk differs from artificial milk. The artificial milk formulated for preterms is instead more similar to natural milk. It is to be noted that in the samples collected in the first week of lactation there is a clear difference between the milk of “early preterm” deliveries (between the 23rd and 25th weeks of gestation) and that of all the others (≥ 29 th weeks of gestation), thus showing that the metabolites analyzed tend to become uniform around the 30th week after conception.

From the results obtained we can also see other differences between breast milk and artificial milk, especially in lactose, present in greater concentrations in breast milk, and galactose 1-phosphate and maltose, which instead are present in greater concentrations in formula. Such results may contribute to determining the ideal metabolic profile of formula for neonates at the different gestational ages [12].

As concerns infections, a review is presented on today's metabolomic knowledge of viral infections [13]; another original paper focuses on the diagnosis and monitoring of fungal sepsis in the single neonate. The latter study fits perfectly in the fields of predictive, prospective and personalized medicine [14].

A truly innovative preliminary datum, compared with the current literature [15,16], that emerges from one of the studies presented concerns pulmonary bronchodysplasia, which appears to be a congenital disease (genetics and intrauterine epigenetics) and the most the neonatologist can do is limit its severity, but not its presence or absence. All appears to occur on the basis of a genetic predisposition inside the womb,

when negative events lead to cell hypodysplasia and a reduction of the ramification of essential structures inside the parenchymas (the lung in our case, but also the ureteral bud, the cerebral connectome and so on).

Again, we present a study on Italian autistic children, expanding a previous study [17]: the network of urinary metabolites, some of which in major quantities compared to controls, suggests a strategic role played by the microbiome and particular bacterial species involved in determining the disease. In particular, in subjects with a genetically predetermined pathology, only the application of a given diet with a determined microbiome can form metabolites capable of conditioning the organism and especially the central nervous system (the brain–gut connection). This leaves open prospects and expectations of acting through diet to treat, but most of all to prevent, certain symptoms and thus significantly improve the quality of life of these children.

Finally, the triple-i (interactive, intersectorial, interdisciplinary) approach to validate proteomic investigations on body fluids and tissues in perinatal medicine is presented.

In particular, two fields are covered: the correlations between the salivary proteome in human neonate with immunostochimistry of developing salivary glands [18] and the correlations of urinary proteome/metabolome with kidney histology and immunohistochemistry in experimental models of neonatal asphyxia [19].

The interpretation of the large amount of integrated “omics” data needs a reinventing of the scientific approach to the study of biological systems, including tissues and body fluids, with the application of the so called “direct intelligence of data”, moving towards the new era of the networked science [20].

What emerges globally from these studies and from what we find in the literature is the prospective, predictive and personalized dimension of perinatal and pediatric metabolomics [21]. The issue of asphyxia is exemplary. The capacity to respond to and survive an extremely strong and acute stimulus, such as asphyxia seems an intrinsic property of the subject, in practice relatively independent of the application or non-application of treatment protocols: some newborns are fragile to face strong obstacles and die, while others are resilient and could survive, with or without insufficiency of one or more organs.

No one is surprised by the major basal capacity of the winner of the 100-meter dash at the Olympic Games or the winner of an uphill time trial compared to a “normal” person. Their basal metabolisms are quite different. Instead, the knowledge of the existence of a marked interindividual basal variability in the case of stress, of the fact that this variability increases greatly following an important stimulus (asphyxia, infection, fasting and so on) and its extreme importance in clinical practice is still insufficient in the medical world, nor should we be surprised by its total absence in the society and the courtrooms. It is evident that these data must be accompanied by careful bioethical reflections, but most of all they raise questions of a clinical nature since it is probable that some of these neonates, instead of having all of them follow the same protocol (potentially too drastic for some and inadequate and/or not well focused for others),

could be saved through application of personalized treatments, whether customized or not.

Abraham Jacobi wrote, once again prophetically: “Pediatrics does not deal with miniature men and women...”. On the contrary, perhaps we can say: “The adult deals with grown-up neonates and children”. We can go even farther back in time and say, paradoxically: “The fetus and the neonate are the fathers of grown-ups”. According to Aristotle, “those who see things from the beginning have a better knowledge of them”.

The Italian neonatologists [22] and the Italian metabolomic network [23], together with other groups, is contributing actively to progress towards an early understanding of life and the dissemination of metabolomic studies in perinatology and pediatrics. At present, there are surely more questions than answers.

On the subject of questions, in an editorial published exactly one year ago the authors asked in the title [24]: *Could proteomics and metabolomics solve some mysteries of the newborn?* In our opinion, the answer is totally affirmative: it is the right route to the future.

Vassilios Fanos

Neonatal Intensive Care Unit

Puericulture Institute and Neonatal Section

Department of Surgery, AOU and University of Cagliari

Monserato (CA), Italy

E-mail: vafanos@tiscali.it; vafanos@tin.it

Giuseppe Buonocore

Department of Molecular and Developmental Medicine

University of Siena, Siena, Italy

Michele Mussap

Department of Laboratory Medicine

IRCCS University-Hospital San Martino-IST

National Institute for Cancer Research

Genoa, Italy

Declaration of interest

The authors declare that they have no conflict of interest.

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