OPPORTUNITIES AND CHALLENGES OF BIOMEDICAL IMAGING IN FETAL AND NEONATAL BRAIN DISEASE

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ABSTRACT

One in ten children has neurodevelopmental disorders and it is estimated that in about two thirds the problem occurred during fetal or perinatal life. The development of imaging biomarkers to detect and monitor abnormal neurodevelopment is a research and innovation opportunity. There is a strong need of supra-disciplinary researchers with transversal skills encompassing biomedical neuroscience knowledge with engineering/advanced medical imaging processing, and of ambitious projects to generate clinically applicable solutions. In spite of limitations, recent years have seen important advances in the generation of combined multidisciplinary papers which are expected to constitute the seminal work leading to more advanced projects capable of generating true advances in imaging biomarker discovery.

Index Terms— neurodevelopment, brain reorganization, fetal medicine, intrauterine growth restriction.

1. BRAIN INJURY AND REORGANIZATION OF PRENATAL ORIGIN

There is a critical concern about the increasing incidence of neurodevelopmental disorders in children. About one in ten children is affected by some form of neurodevelopmental isorder, which impacts daily functioning, social relationships and quality of life, constituting a major European public health problem. Common disorders include neurodevelopmental delays, learning disabilities, autism and attention deficit and hyperactivity disorder (ADHD). It is widely accepted that in a substantial number of instances neurological dysfunction has a prenatal origin. Major risk factors for abnormal neurodevelopment during fetal life include adverse intrauterine conditions. One of the most clear examples of this is intrauterine Growth Restriction (IUGR), which occurs in 7-10% of pregnancies (>500,000 newborns/y in EU-27). IUGR is a prevalent cause of brain reorganisation, affecting language, behaviour, learning and memory [1].

Perinatal diagnosis and monitoring of abnormal neurodevelopment is a key challenge. Due to the lack of biomarkers subtle brain dysfunction often remains unnoticed during months or years of life, preventing critical early interventions during the first two years so that dysfunctions often become permanent at more advanced stages of development.

Thus, there is a need to develop imaging biomarkers of abnormal neurodevelopment. Among other important challenges, clinical disorders are not associated with obvious brain changes. In most instances the underlying anatomical changes are present in the form of brain reorganization, and this poses important difficulties for conventional brain imaging techniques.

2. OPPORTUNITIES AND CHALLENGES FOR IMAGE BIOMARKER DISCOVERY

The development of imaging biomarkers to detect and monitor abnormal neurodevelopment represents not only a public health, but a research and innovation opportunity. To address the high incidence of neurodevelopmental disorders in children there is a critical need to discover cell/molecular and imaging biomarkers for abnormal neurodevelopment combining emerging technologies and biological models, and transfer them to the private sector for exploitation.

During recent years several lines have been explored to improve quantitative image analysis of brain microstructural changes by ultrasound and MRI [2]. Over recent years our groups has obtained promising results with quantitative ultrasound analysis [3] and with diffusion MRI-based connectomic studies [4].

Main challenges characterizing fetal and neonatal imaging are, among others, a rapidly evolving brain anatomy, lack of detailed atlases for automated parcellation, motion artifacts in fetuses, and an enormous amount of efforts required to undertake clinical studies. Indeed, clinical research is required to correlate imaging findings with neurological outcomes. This must be assessed by means of time consuming tests -entailing a high level of expertise to ensure reliable data- , which in addition can only be performed years later. Finally, there is also a need for experimental animal models, allowing histological 3D validation of imaging biomarkers.

All the above challenges demand ambitious and unconventional research approaches, which traditional research organization fails to address. For instance, despite the existence of a real common supradisciplinary field of knowledge around abnormal neurodevelopment, research

organizations gathering the required knowledge under a single team are rarely found. Thus there is a strong need of supra-disciplinary researchers with an open mind approach and with transversal skills encompassing biomedical neuroscience knowledge with engineering/advanced medical imaging processing. There is also a need to undertake ambitious projects, which combine not only a pathophysiological-clinical-innovatory vision on abnormal neurodevelopment, but also an inter-sectorial component, all of which are required nowadays to generate clinically applicable solutions.

In spite of these limitations, recent years have seen important advances in the generation of combined multidisciplinary papers which are expected to constitute the seminal work leading to more advanced projects capable of generating true advances in imaging biomarker discovery.

3. REFERENCES

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