CEREBRAL MATURATION AND FUNCTIONAL IMAGING

Catherine Chiron*1,2 and Isabelle Jambaqué1

1Service de Neuropédiatrie and INSERM U29
Hôpital Saint Vincent de Paul
82 Avenue Denfert Rochereau
75674 Paris Cedex 14, France and
2Service Hospitalier Fréderic Joliot
Département de Recherche Médicale
Centre à l’Énergie Atomique, Orsay
France

INTRODUCTION

Normal cerebral maturation and therefore development of sensory and cognitive functions are sustained by neurobiological changes that are better known in animals than in humans. Postnatal developmental changes can now be approached in humans by means of non-invasive methods using external detection of brain signals. These cerebral functional imaging techniques include PET (positron emission tomography), SPECT (single photon emission computed tomography) and fMRI (functional magnetic resonance imaging). PET and fMRI recently experienced rapid development for stimulation studies because they can detect and localize the activation produced in the brain by selective cognitive tasks. Unfortunately, technical constraints make such studies almost impossible to realize in children. PET and SPECT can also measure at rest, respectively the local metabolism for glucose and regional cerebral blood flow, both parameters being proportionally close to the neuronal activity in the same region. These “at rest studies” are available in young children and are now being used in pathological conditions such as childhood epilepsy or developmental disorders. Most of the data available about postnatal functional brain maturation have been obtained by PET and SPECT “at rest studies”. They have the advantage of providing measures at the regional level. It is therefore interesting to correlate the regional changes in metabolism or in cerebral blood flow during maturation with the development of sensory and cognitive functions in humans.

*To whom correspondence should be addressed

Neuropsychology of Childhood Epilepsy, edited by Jambaqué et al.

75
However, these “at rest” techniques also have some limitations: longitudinal studies are restricted because radioactive tracers are used, normal populations cannot be studied for ethical considerations, and one must bear in mind that the correspondence between cognitive functions and functional cerebral activity at rest remains indirect.

PET and SPECT “at rest” are also extensively used in the field of epilepsy. When epilepsy appears in very young children, it raises the question of the potential relationship between epilepsy and development since epileptogenic phenomena and developmental processes involve the same neuronal pathways within the brain. Some answers can be brought up by functional imaging, measuring cerebral blood flow and brain metabolism in infants.

1. TECHNIQUES

PET and SPECT “at rest” provide the two main types of functional imaging techniques applicable in very young children. PET uses positron emitters obtained from a cyclotron, namely $^{18}$F-Fluodeoxyglucose ($^{18}$FDG) and PET cameras have less than 8mm plane resolution that allow the study of cerebral metabolism. Multiple arterial samples are needed to measure absolute values of metabolism; this procedure, together with the high cost of cameras and cyclotron, causes PET not to be routinely used but dedicated only to research in children. SPECT tracers and SPECT cameras are not as expensive, and they are more accessible in nuclear medicine activity. SPECT studies the regional cerebral blood flow. Tracers are gamma emitters, $^{99}$m-Technetium in static SPECT—the most often used in epilepsy studies—and 133-xenon in dynamic SPECT method—which is indicated for maturation studies—. Static SPECT-cameras provide high resolution images (8 mm), but absolute quantification of cerebral blood flow is not available. Using dynamic SPECT and 133-xenon, resolution of the images is not as good (12mm) but absolute measures of cerebral blood flow are obtained, a necessary condition to study maturational changes.

There are particular difficulties in performing PET and SPECT in children. Sedation is needed under 6 years of age. When a barbiturate is administered before the injection of the tracer like in SPECT with 133-xenon, it produces a decrease in global CBF by about 15%, but the regional CBF distribution is not modified. Another issue is related to the very stringent ethical limits to the administration of radioactive tracers in children. In adults, control populations for PET and SPECT studies are rather easily obtained from normal volunteers. Such a practice is ethically and legally prohibited in children so that normal control population *stricto sensu* is unobtainable in this age range. The only means to assess control values is to collect a population of children *a posteriori* considered normal, that means a series of patients exhibiting transient neurological or apparently neurological events but who later proved to develop normally.

Stimulation studies, still exceptional in children, are performed either with PET using $^{15}$H$_2$O as a positron emitter or with fMRI. Both lie on the comparison of images obtained during one or several stimulation tasks and a “control” task. PET assesses the increase of regional cerebral blood flow during the stimulation whereas fMRI measures the changes in the magnetic signal of hemoglobin in vessels during the stimulation, changes related with cerebral blood flow variations. Elementary and passive sensory stimulations as well as complex cognitive operations can be tested since a task mentally imagined induces the same changes as a task “truly” performed. Sophisticated statistical analyses are needed in order to detect, select, and localize the significant changes produced by the stimulation.