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Press release

An anti-diabetic drug corrects dyspraxia

Researchers from Inserm and physicians from the Department of Paediatric Endocrinology, Gynaecology and Diabetology at Necker Hospital for Sick Children (AP-HP, Inserm U1016, Paris Descartes University, Imagine Institute) have developed an improved treatment for a rare form of early childhood diabetes associated with cognitive disorders. Their work, conducted in collaboration with the Neurophysiology Department of Pitié-Salpêtrière Hospital, AP-HP, shows that a drug used for decades to treat type 2 diabetes in older subjects acts on the brain of these children. It reduces their hyperactivity and improves their ability to perform precise movements such as writing. The work has recently been the subject of a publication in the journal *Diabetes Care**.

Neonatal diabetes is a disease that develops in the first months of life. There are many causes, but several years ago, researchers discovered that a mutation in the potassium channels that maintain membrane polarisation is often responsible. In the pancreas, this genetic defect affects secretion of insulin, which becomes trapped in the insulin-producing cells. However, the consequences do not end there, since these defective receptors are also present in the muscle and brain cells. They cause hypotonia and dyspraxia in the children.

Although treatment with insulin injections controls the children's blood sugar levels, it does not correct the other symptoms.

In 2006, this same team of researchers and physicians had shown that use of glibenclamide, a drug used for decades to treat type 2 diabetes in older patients, eliminated the need for insulin injections in its own patients. This drug allows insulin secretion in accordance with the quantity of sugar present in the child's bloodstream. It therefore enables better control of blood sugar levels without causing hypoglycaemic episodes.

In the study which has just been published*, the team shows that this drug also reduces the hyperactivity observed in the children, problems with fine movement (writing, spatial orientation), and impairment of muscle tone and complex brain functions (task planning) in the children. This enables a clear improvement in their socialisation and family and school life.

The study was carried out in 19 children with this rare form of neonatal diabetes, in whom insulin injections were replaced with oral glibenclamide. Electrophysiological muscle tests, brain imaging and tests for fine and precise psychomotor skills were carried out before and 12 months after introducing the drug. Results made it possible to show that the neuropsychomotor improvement observed was not related to an action of the drug on muscle, but to an effect of the drug on the brain.

"This study is the first to show that an oral diabetes can also act directly on the brain of these children," explains Dr Jacques Beltrand, coordinator of the study. "It also shows that the effect is better in young children. This drug should therefore be given to these patients as early as possible."

This work repositions a drug which previously had no indication for paediatric use, and was not available in a suitable dosage form for infants. The team of researchers from Inserm and Necker Hospital for Sick Children, AP-HP, is now involved in the development of a syrup suitable for children, which will allow easy administration and the most accurate dose possible (NEOGLI Study, NCT02375828).

About AP-HP: AP-HP is an internationally renowned university hospital system with a European dimension. Its 39 hospitals receive 7 million patients a year: in clinics, emergency departments, and through planned admissions or home hospitalisation. It provides a public health service for all, on a 24-hour basis, which is a matter of both duty and pride for AP-HP. AP-HP is the biggest employer in Ile de France: It employs 95,000 staff – physicians, researchers, allied medical staff, administrative staff and other workers. <http://www.aphp.fr>

*Reference: *Sulfonylurea therapy benefits neurological and psychomotor functions in patients with neonatal diabetes owing to potassium channel mutations.* Diabetes Care - DOI: 10.2337/dc15-0837 - Date of publication: published online 5/10/2015

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