Method for determining the Attention Deficit Hyperactivity Disorder (ADHD).

KEYWORDS

- ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)
- DOPAMINE TRANSPORTER
- DNA METHYLATION
- AUTO-ANTIBODIES (AABS) TO NEURO-RECEPTORS
- EPIGENETICS IN NEURO-PSYCHIATRY

AREA

- CHEMISTRY & BIOTECHNOLOGY

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Patent Type
Patent for invention.

Co-Ownership
Sapienza University of Rome 20%, Higher Institute of Health (ISS) 50%, University of Teramo 30%.

Inventors
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Industrial & Commercial Reference
Diagnostic kits based on the presence of auto-antibody directed to DAT and the quantification of DAT promoter methylation levels.

Time to Market
The protocol overall results in a very short completion time, allowing a rapid detection of ADHD markers in a clinical setting.

Availability
Cession, Licensing, Research, Development, Experimentation, Collaboration, Start-up and Spin-off.

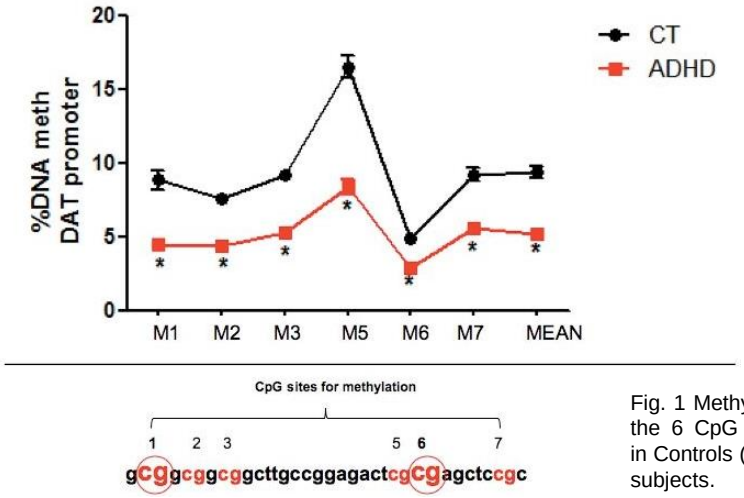

Fig. 1 Methylation levels of the 6 CpG sites analyzed in Controls (CT) and ADHD subjects.

Abstract
The present invention provides strategies for diagnosing and for monitoring of treatment efficacy, in case of ADHD in human patients.
The present invention is an index, composed on a first side by levels of methylation within the promoter for the gene coding for Dopamine Transporter (DAT), to be used alone or in combination with levels (in serum) of auto-antibodies directed towards DAT (hDAT aAbs). The inventors have also discovered that the present invention can predict and/or monitor the efficacy of therapeutic strategies, being them a cognitive-behavioral therapy or the alike, as well as the use of "Ritalin-like" psycho-stimulants: these therapeutic strategies, when combined with the prognostic methods of the present invention, can be practiced more effectively.

Publications

- Adriani W, Romano E, Pucci M, Pascale E, Cerniglia L, Cimino S, Tambelli R, Curatolo P, Granstrem O, Maccarrone M, Laviola G, D'Addario C. Potential for diagnosis versus therapy monitoring of Attention Deficit Hyperactivity Disorder: a new epigenetic biomarker interacting with both genotype and autoimmunity. Eur Child Adolesc Psychiatry 2017 (DOI 10.1007/s00787-017-1040-9).

Method for determining the Attention Deficit Hyperactivity Disorder (ADHD).

Technical Description

The protocol of the present invention involves the DNA isolation from buccal swabs and the quantification of the methylation levels of specific CpG sites in the DAT gene promoter.

This value alone or in combination with auto-antibodies (aABS) to specific peptide fragments of hDAT, which are naturally found in serum, is a significant and reliable indicator to be used as ADHD markers both in the diagnostic and evaluation of therapy.

Technologies & Advantages

Nowadays, the clinical diagnosis of ADHD is solely based on structured interviews or on questionnaires.

Nevertheless, the validity of these criteria for ADHD diagnostics is yet a debated question.

This invention is a new and inventive tool, very useful for diagnosis since our clinical experimentation demonstrated that the determination of DNA methylation amount in specific CpG sites within the promoter region of SLC6A3 gene coding for the human dopamine transporter (hDAT), alone or in combination with auto-antibodies (aAbs) to specific peptide fragments of hDAT, naturally occurring in the serum, is a significant and reliable marker of ADHD.

The protocol overall results in a very short completion time, allowing a rapid detection of ADHD markers in a clinical setting.

It allows the provision of results to patients, and accordingly allows the prescription of a treatment to patients, in less time than that required for completion of questionnaires.

Applications

Companies manufacturers of diagnostic kits for biomedical and biotechnology area:

- diagnostic aid in ADHD;
- detection of ADHD markers in a clinical setting.

	DAT 10/10	DAT 9/x
Mean	0.212	0.359
CpG 1	**0.469**	0.285
CpG 2	−0.082	**0.524**
CpG 3	0.022	0.289
CpG 5	0.177	0.248
CpG 6	0.394	**0.455**
CpG 7	0.065	0.117

Table 1 Correlation (Pearson's) between high titer of antibodies to aAbs and methylation levels at site 1 and 6 in subjects with genotype DAT 10/10 and DAT 9/x.

	CGAS	Conners' mother, initial (score at enrolment)			
		defiant opponent	inattentive	hyper-active	ADHD index
MEAN	-0,227	-0,180	0,130	-0,177	0,138
posM1	-0,487	0,018	0,254	0,112	0,267
posM2	0,033	-0,202	0,200	-0,180	0,187
posM3	0,033	-0,151	-0,082	-0,272	0,023
posM5	-0,192	-0,268	0,165	-0,278	0,063
posM6	-0,018	-0,255	0,128	-0,198	0,034
posM7	-0,069	-0,005	-0,105	-0,019	0,077

Table 2 Elevated methylation levels at the M1 site correlate with disease severity (CGAS).

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