

# A New Old Tale: Dopamine Transporter implications in an animal model of Attention-Deficit Hyperactivity Disorder

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**Manuscript Authors:** Fernández Guillermo, Krapacher Favio, Ferreras Soledad, Quassollo Gonzalo, Mari Macarena Mariel, Pisano María Victoria, Montemerlo Antonella, Rubianes María Dolores, Bregonzio Claudia, Arias Carlos & Paglini María Gabriela

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### Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

Title      **A New Old Tale: Dopamine Transporter implications in an animal model of Attention-Deficit Hyperactivity Disorder**

### **S1 [001]      ABSTRACT**

**S1 [002]**      Attention deficit/Hyperactivity disorder (ADHD) is one of the most diagnosed psychiatric disorders nowadays.

Attention deficit/Hyperactivity disorder ...  
... (ADHD) ...  
... is one ...  
... of the most diagnosed psychiatric disorders nowadays.

**S1 [003]**      The core symptoms of the condition include hyperactivity, impulsiveness and inattention.

The core symptoms ...  
... of the condition include hyperactivity, ...  
... impulsiveness ...  
... and inattention.

**S1 [004]**      The main pharmacological treatment consists of psychostimulant drugs affecting Dopamine Transporter (DAT) function.

The main pharmacological treatment consists ...  
... of psychostimulant drugs affecting Dopamine Transporter ...  
... (DAT) ...  
... function.

**S1 [005]**      We have previously shown that genetically modified mice lacking p35 protein (p35KO), which have reduced Cdk5 activity, present key hallmarks resembling those described in animal models useful for studying ADHD.

We have previously shown ...  
... that genetically modified mice lacking p35 protein ...  
... (p35KO), ...  
... which have reduced Cdk5 activity, ...  
... present key hallmarks resembling those described ...  
... in animal models useful ...  
... for studying ADHD.

**S1 [006]**      The p35KO mouse displays spontaneous hyperactivity and shows a calming effect of methylphenidate or amphetamine treatment.

The p35KO mouse displays spontaneous hyperactivity ...  
... and shows a calming effect ...  
... of methylphenidate ...  
... or amphetamine treatment.

**S1 [007]** Interestingly, dopaminergic neurotransmission is altered in these mice as they have an increased Dopamine (DA) content together with a low DA turnover.

Interestingly, ...  
... dopaminergic neurotransmission is altered ...  
... in these mice ...  
... as they have an increased Dopamine ...  
... (DA) ...  
... content together ...  
... with a low DA turnover.

**S1 [008]** This led us to hypothesize that the lack of Cdk5 activity affects DAT expression and/or function in this animal model.

This led us ...  
... to hypothesize ...  
... that the lack ...  
... of Cdk5 activity affects DAT expression ...  
... and/or function ...  
... in this animal model.

**S1 [009]** In this study, we performed biochemical assays, cell-based approaches, quantitative fluorescence analysis and functional studies that allowed us to demonstrate that p35KO mice exhibit decreased DA uptake and reduced cell surface DAT expression levels in the striatum.

In this study, ...  
... we performed biochemical assays, ...  
... cell-based approaches, ...  
... quantitative fluorescence analysis ...  
... and functional studies ...  
... that allowed us ...  
... to demonstrate ...  
... that p35KO mice exhibit decreased DA uptake ...  
... and reduced cell surface DAT expression levels ...  
... in the striatum.

**S1 [010]** These findings are supported by in vitro observations in which the inhibition of Cdk5 activity in N2a cells induced a significant increase in constitutive DAT endocytosis with a concomitant increase in DAT localization to recycling endosomes.

These findings are supported ...  
... by in vitro observations ...  
... in which the inhibition ...  
... of Cdk5 activity ...  
... in N2a cells induced a significant increase ...  
... in constitutive DAT endocytosis ...  
... with a concomitant increase ...  
... in DAT localization ...  
... to recycling endosomes.

**S1 [011]** Taken together, these data provide strong evidence regarding the role of Cdk5 activity in DAT trafficking and function, thus contributing to the knowledge of DA neurotransmission physiology and also providing therapeutic options for the treatment of DA pathologies such as ADHD.

Taken together, ...  
... these data provide strong evidence regarding the role ...  
... of Cdk5 activity ...  
... in DAT trafficking ...  
... and function, ...  
... thus contributing ...  
... to the knowledge ...  
... of DA neurotransmission physiology ...  
... and also providing therapeutic options ...  
... for the treatment ...  
... of DA pathologies ...  
... such as ADHD.

**S1 [012]** HIGHLIGHTS  
HIGHLIGHTS

**S1 [013]** Mice lacking p35 (p35KO) exhibit diminished surface DAT expression in the striatum

Mice lacking p35 ...  
... (p35KO) ...  
... exhibit diminished surface DAT expression ...  
... in the striatum

**S1 [014]** Amperometric experiments show decreased DA uptake in the striatum of p35KO mice

Amperometric experiments show decreased DA uptake ...  
... in the striatum ...  
... of p35KO mice

**S1 [015]** Cdk5 inhibition increases DAT endocytosis in N2a cells

Cdk5 inhibition increases DAT endocytosis ...  
... in N2a cells

**S1 [016]** Lack of Cdk5 activity increases DAT localization in Rab11 positive endosomes

Lack ...  
... of Cdk5 activity increases DAT localization ...  
... in Rab11 positive endosomes

**S2 [017]** INTRODUCTION

**S2 [018]** Attention Deficit Hyperactivity Disorder (ADHD) is a complex, chronic and highly heritable neurodevelopmental disorder with typical onset in childhood and known persistence into adulthood (Sharma and Couture, 2014).

Attention Deficit Hyperactivity Disorder ...  
... (ADHD) ...  
... is a complex, ...  
... chronic ...  
... and highly heritable neurodevelopmental disorder ...  
... with typical onset ...  
... in childhood ...  
... and known persistence ...  
... into adulthood ...  
... (Sharma ...  
... and Couture, 2014).

**S2 [019]** Like other neuropsychiatric disorders, ADHD presents a spectrum of behavioral alterations with motor hyperactivity features, impulsivity, and/or inattention; offering the diagnostic criteria used for diagnosis (American Psychiatric Association, 2013).

Like other neuropsychiatric disorders, ...  
... ADHD presents a spectrum ...  
... of behavioral alterations ...  
... with motor hyperactivity features, ...  
... impulsivity, ...  
... and/or inattention; ...  
... offering the diagnostic criteria used ...  
... for diagnosis ...  
... (American Psychiatric Association, 2013).

**S2 [020]** So far, the most effective pharmacotherapy for the disorder comprises long-term treatments with stimulant drugs, such as amphetamine (AMPH) and methylphenidate.

So far, ...  
... the most effective pharmacotherapy ...  
... for the disorder comprises long-term treatments ...  
... with stimulant drugs, ...  
... such as amphetamine ...  
... (AMPH) ...  
... and methylphenidate.

**S2 [021]** These drugs enhance Dopamine (DA) neurotransmission by altering Dopamine Transporter (DAT) normal function (Faraone et al., 2005; German et al., 2015; Hong and Amara, 2013).

These drugs enhance Dopamine ...  
... (DA) ...  
... neurotransmission ...  
... by altering Dopamine Transporter ...  
... (DAT) ...  
... normal function ...  
... (Faraone et al., 2005; ...  
... German et al., 2015; ...  
... Hong ...  
... and Amara, 2013).

## **End of Sample Audit**

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