Mathematical modelling discriminates medication persisters from non-persisters in adult ADHD

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Objectives
Long-term continuation of stimulant treatment is low in adult ADHD, and seems not to be readily explained by self-reported lack of medication efficacy. Predicting who is likely not to persist with pharmacotherapy can reduce the risks and costs associated with unnecessary medication.

As a novel approach to this problem, mathematical modelling was used to derive latent cognitive parameters from Continuous Performance Test (CPT) data. Patients continuing with medication after a year – persisters – were retrospectively compared with those having withdrawn during the same period – non-persisters – on these parameters at baseline and shortly after medication start-up.

Methods
242 adults (17 – 58 years) newly diagnosed with ADHD (all subtypes) were followed for approximately 1 year. All performed a Conners’ CPT-II before and 8 weeks after medication start-up. Using a Bayesian estimation of Drift Diffusion Model (DDM) parameters, the group of persisters were compared to the group of non-persisters with respect to response caution (boundary separation, \(a\)) and cognitive processing speed (drift rate, \(v\)) at baseline and at 8 weeks.

Flow diagram of participant progress:

Week 0
- N = 242
- CPT nr. 1
- Off drugs

Week 8
- N = 242
- CPT nr. 2
- On drugs
- Off drugs (persisters) = 67 %
- Off drugs (non-persisters) = 28 %

Retrospective grouping and DDM modelling of CPT data

The Continuous Performance Test:

**Drift Diffusion Modelling**

DDM allows disentangling of the cognitive processes underlying two-alternative decision tasks. The accumulation of net evidence for an alternative is depicted as a random walk with drift towards decision boundaries. DDM modelling fits free parameters such as drift rate (\(v\)) and boundary separation (\(a\)) to predict reaction time (RT) distributions and accuracy data.

**Results**

At baseline, persisters showed markedly lower response caution than non-persisters, indicating higher impulsivity, with 95 % confidence intervals not overlapping. Persisters also had slower processing speed. In addition, the groups differed in initial medication response, with persisters showing a greater improvement both in terms of response caution and processing speed.

**Conclusions**

Our results show that medication persisters and non-persisters differed already at baseline on cognitive mechanisms underlying CPT performance. Persisters were more impulsive and had somewhat slower processing speed. Treatment also benefited this group more. An objective method to determine patient response and predict benefit from stimulant use is urgently needed for clinical monitoring. The current method of analysis may be fruitful in achieving this goal. Conventional measures of symptom response to medication has been found to predict persistence, but not at such an early point. Future studies should assess the ability of mathematical modelling of psychological tasks to also predict medication persistence on an individual level.

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**References**

