Predictors of response to behavioral therapy in children with Tourette syndrome – results of the machine learning study
Was moderation explored or only prediction (CBIT+PST or CBIT-only)?

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Background:

- While the **European Society for the Study of Tourette Syndrome** and the **American Academy of Neurology** consider **behavioral therapy** to be the first line treatment of Tourette syndrome (TS), predictors of treatment response remain unclear.

- Initial studies using the combined child-adult sample from **the Comprehensive Behavioral Intervention for Tics (CBIT)** studies found that the presence of **tic medication predicted worse outcome**, while greater tic severity and positive participant expectancy predicted greater tic improvement.

- Meanwhile, other reports suggest that **co-existing psychopathologies** (e.g., anxiety disorder), and stronger premonitory urges predict lower tic reduction.

- Notably, these prior reports studied mixed age samples and have only applied standardized analytical methodology (e.g., linear and logistic regression models), which have some limitations.

- In response, this study utilized machine learning approaches to determine **predictors of treatment response** to behavioral therapy in a large clinical trial of children with TS.

Methods:

- Participants were 126 children (aged 9-17 years) with TS or a chronic tic disorder of at least **moderate severity**, who were enrolled in randomized controlled trial (**NCT00218777**) testing the efficacy of the comprehensive behavioral intervention for tics (CBIT) relative to an active control intervention (psychoeducation and supportive therapy, PST)

- Participants were randomly assigned to receive 8 sessions of either treatment over a period of 10 weeks (61 CBIT, 65 PST).

- We compared a standardized logistic regression model with two multivariable approaches to elucidate possible predictors of treatment response: **recursive partitioning and random forests**.

- A post-treatment Yale Global Tic Severity Scale (YGTSS) reduction of $\leq$ **30%** indicated response.

Results and Conclusions:

- Logistic regression did not consistently identify significant multivariate predictors.

- Meanwhile, **recursive partitioning** and **machine learning** approaches both found ADHD to predict treatment response.

- Adequate model **accuracy** (67%-76%), **sensitivity** (67%-78%), and **specificity** (70%- 85%) were observed.

- Post-hoc analyses indicated that treatment responders had significantly lower rates of ADHD (p=0.04) compared to non-responders.

- Findings suggest that multivariable approaches may be superior to classical regression models for identifying predictors of treatment response in pediatric TS.

- Moreover, these statistical approaches may play a key role in leading to **personalized treatment** recommendations for youth with TS, and lead to the development of targeted treatments for youth who are less responsive to behavioral therapy.