# Therapeutic response of methylphenidate in ADHD core symptoms depending on dose: Low, medium and high

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## Background

Attention deficit hyperactivity disorder (ADHD) is a highly prevalent disease in childhood, affecting about 7.8% of the school age population.
Studies that evaluate ADHD medication have demonstrated the effectiveness of stimulants in the core symptoms treatment: inattention, hyperactivity and impulsivity. Methylphenidate (MPH) is the most used and best studied substance, and it has been objectified immediate effects of core symptoms, as well as in the cognitive symptoms (like learning and academic performance).
The NICE guideline defines three doses of MPH ranges: low (≤ 0.4 mg / kg / day), medium (> 0.4 < 0.8 mg / kg / day) and high (≥ 0.8 mg / kg / day).
Despite studies is not yet entirely clear whether this response is clearly dose-dependent or if the response is individualized for each patient, and if the dose-response is linear or not. Different studies support that neuropsychological tests of activity and attention and parents and teachers' behavioral questionnaires, are a good measures to assess the therapeutic response to stimulants in children with attention-deficit/hyperactivity disorder.

## Objectives

This poster aims to evaluate:

1. the efficacy of methylphenidate (MPH) in treating ADHD patients treated at our Unit of Child and Adolescent Psychiatry in a Spanish Mental Health Service
2. the effect of three different doses of MPH (low, medium and high) and if the dose-response is linear or not.

## Method

The sample consists of 24 naïve participants, child and adolescents between ages 7 to 15 years (M = 11.03, SD = 2.58). All met ICD -10 criteria for ADHD and were grouped according to the prescribed dose of MPH: low (n = 6, mean = 0.40 mg/kg), medium (n = 9, mean = 0.65 mg/kg) and high (n = 9, mean = 0.93 mg/kg).
For all subjects, repeated assessments were made from baseline (diagnose process) to 1 month (once an effective therapeutic medication dose was found) across different symptom and functioning domains using a Selective and Sustained Attention Test (TASS), a Continuous Performance Test (CPT) and the Conners' Parent Rating Scale (CPRS-48). Obtained variables are specified in Table 1.

**Statistical Analysis:**

1. Mean comparison is made with related samples t test groups before and after treatment, and the variables that have been demonstrated statistically significance between both groups were isolated.
2. It is estimated the effect size (d') of the variables that have been significant (grouped factors: Performance, Attention, Impulsivity / Hyperactivity Disorder, and Emotional).
3. The tendencies of variables inside these 4 factors are studied taking into account the reference values according to Cohen: d' = 0.20 (small effect); d' = 0.50 (moderate effect) and d' = 0.80 (large effect). Results are shown in Figures 1, 2, 3 and 4.

## Results

After one month of treatment with MPH, children and youth with ADHD, We observed significantly improvement in CPT, TASS and CPRS-48, coinciding with the clinical impression (Table 1).
**More specifically:**

a. The performance of work presents an inverse linear relationship between dosage and treatment response, obtaining a higher d' (large effect) with the lowest dose and a smaller increase in performance (small effect) with higher doses. This relationship is more evident in improved academic performance (see Figure 1).
b. Attention shows a linear relationship: improves with increasing doses, so that in high treatment dose yields a greater attention performance (large effect), in middle dose a moderate d', and lower d' with the low dose (see Figure2).
c. Regarding the Impulsivity and Hyperactivity there isn't a linear effect: lower and higher doses obtain better performance (both with large effect size) than the medium dose (with very low effect size, even negative depending on the value of parents in the scale impulsivity/hyperactivity of the CPRS-48) (see Figure 3).
d. Although they have not been significant in the comparison of means, we calculated the effect size of the emotional variables. The mean and the specific variables show that higher doses have more somatization, anxiety and

**Table 1**

| | Variable | Test | | Retest | | | |
|---|---|---|---|---|---|---|---|
| | | *M* | *SD* | *M* | *SD* | *t* | *p* |
| TASS | Revised Fig. | 559,83 | 263,04 | 631,25 | 244,96 | -2,324 | **0,029*** |
| | Hits | 143,21 | 65,92 | 171 | 72,4 | -4,228 | **0.000***** |
| | Omissions | 20,71 | 31,72 | 12,58 | 11,06 | 1,437 | 0,164 |
| | Errors (E) | 2,04 | 6,86 | 0,38 | 0,71 | 1,208 | 0,239 |
| | Err. Fixed (EC) | 1,83 | 2,16 | 1,71 | 1,8 | 0,257 | 0,799 |
| | Quality | 0,87 | 0,11 | 0,93 | 0,06 | -3,126 | **0,005**** |
| | Quality (E + EC) | 0,85 | 0,12 | 0,92 | 0,06 | -3,056 | **0,006**** |
| | Direct score (Hits) | 125,98 | 62,47 | 159,49 | 70,41 | -4,666 | **0,000***** |
| | Direct score (Rev. Fig.) | 483,94 | 214,2 | 586,63 | 234,06 | -4,560 | **0,000***** |
| | Speed | 0,97 | 0,41 | 1,09 | 0,38 | -2,156 | **0,042*** |
| CPT | Hits | 289,63 | 14,56 | 295,79 | 15,26 | -2,209 | **0,037*** |
| | Omissions | 15,25 | 16,14 | 8,79 | 11,52 | 1,873 | 0,074 |
| | Errors | 19,38 | 6,66 | 18,63 | 7,83 | 0,496 | 0,625 |
| | RT Hits | 478,67 | 81,96 | 449,38 | 90,28 | 1,519 | 0,142 |
| | RT Errors | 477,33 | 147,23 | 401 | 119,1 | 2,544 | **0,018*** |
| CPRS-48 | Behavior Prob. | 61,43 | 16,12 | 62,96 | 15,62 | -0,554 | 0,585 |
| | Learning Prob. | 85,52 | 12,82 | 76,04 | 12,45 | 3,413 | **0,002**** |
| | Somatizations | 57,52 | 12,79 | 62,17 | 13,52 | -1,406 | 0,174 |
| | Impulsiv. / Hyperactiv. | 73,52 | 13,12 | 67,3 | 10,33 | 2,187 | **0,040*** |
| | Anxiety | 58,17 | 10,94 | 59,22 | 10,55 | -0,470 | 0,643 |
| | Hyperactivity Index | 79,13 | 10,71 | 71,65 | 14,49 | 3,179 | **0,004**** |

Note: Significance levels * p < 0.05; ** p < 0.01; *** p < 0.01

**Figure 1: Effect sizes treatment (d') in Work Performance**

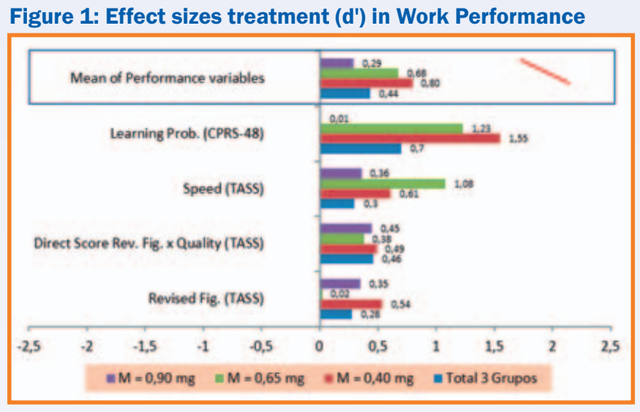



**Figure 2: Effect sizes treatment (d') in Attention**

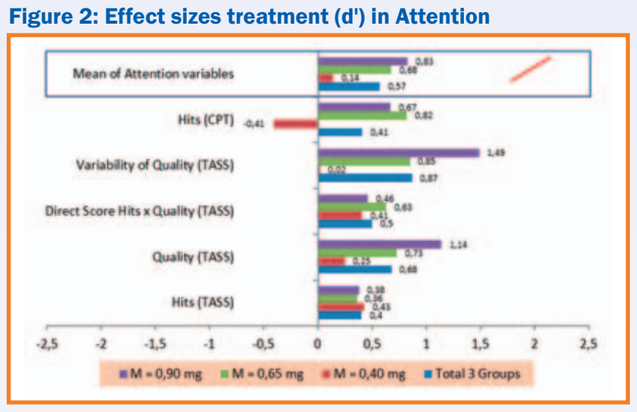



**Figure 3: Effect sizes treatment (d') in Hyperactivity/Impulsivity**

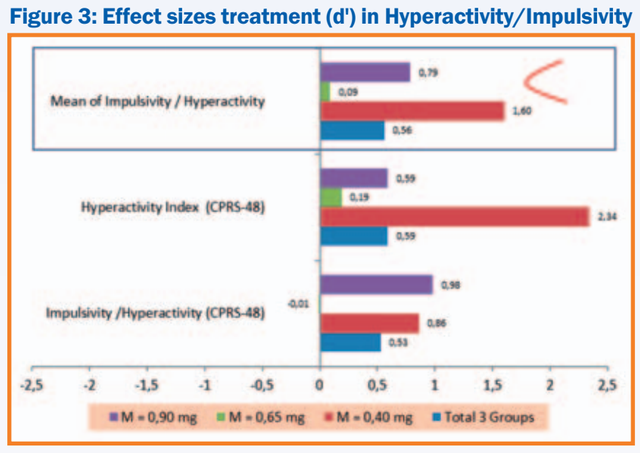
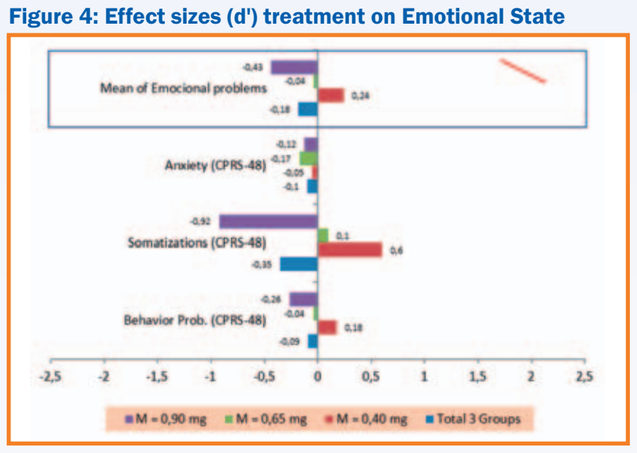



**Figure 4: Effect sizes (d') treatment on Emotional State**




## Conclusions

1. Neuropsychological measures and behavioral assessment are useful for monitoring stimulant medication for ADHD, and corroborate the clinical impression.
2. According to the results obtained in our study, linear or not linear response would not be identical in all symptoms, and it depends to the areas of assessment and the constructs assessed.
3. Data obtained should be reinterpreted based on neurobiological mechanisms knowledge underlying the different constructs assessed (such as the role of catecholamine in the prefrontal cortex in the regulation of cognitive functions or emotional and motivational processing), in order to assess the possibility of a more selective drug dosage depending on the symptoms and try to promote the therapeutic efficacy MPH.

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