

Effects of Methylphenidate and Atomoxetine on AQT Processing Speed and Efficiency in ADHD Adults

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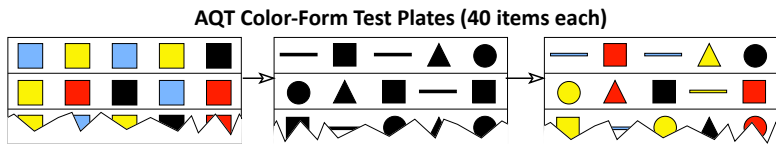
Background

• A Quick Test of Cognitive Speed (AQT) –

a quantitative measure screening test – evaluated and compared treatment effects with Methylphenidate and Atomoxetine in adults with ADHD.

• Objectives:

- Obtain quantitative-processing speed and efficiency measures of executive functions validated to be impaired in ADHD;
- Compare measures before, during and after treatment with Methylphenidate and Atomoxetine.



• AQT was chosen as it:

- Uses rapid, continuous naming tasks and requires from 3-5 minutes for administration and scoring;
- Provides objective, quantitative measure of processing speed and efficiency;
- Is a suitable candidate for screening for a variety of types of cognitive impairments.

• AQT features:

- Two single-dimension tests, **color (C)** and **form (F)** naming with 40 stimuli each;
- One dual-dimension test, **color-form combination (CF)** naming with 40 stimuli;
- C and F measure reaction + retrieval + response times;
- CF measures, in addition, 'switch cost' and increased demands on attention, working memory and set shifting;
- The difference between CF and the sum of C + F naming times (overhead) – **O** = CF - (C + F) – measures processing efficiency.
- rCBF and fMRI of normal adults during CF naming shows bilateral activation of temporal-parietal and sub-cortical brain regions, including the hippocampus.

Methods

Participants

- 13 adults (17 - 44 yr.) referred to an outpatient psychiatric center for evaluation of ADHD symptomatology and possible pharmacological treatment with Atomoxetine.
- 6 met **ICD-10 F90.0** (hyperkinetic disturbances) and 7 **F90.9** (hyperkinetic disturbances, unspecified) criteria. None received prescription medication for ADHD at intake.

Results

Table 2. Descriptive statistics for AQT naming times at intake and after medication with Methylphenidate and Atomoxetine (n = 13).

| AQT | Color Mean (SD) | Form Mean (SD) | Color-Form Mean (SD) | Overhead Mean (SD) |
|----------------------|--------------------|-------------------|-------------------------|-----------------------|
| Intake | 26.15 (5.03) | 30.85 (7.30) | 73.69 (11.26) | 17.38 (9.50) |
| Post-Methylphenidate | 22.00 (3.83) | 25.15 (3.34) | 53.69 (8.27) | 8.23 (7.07) |
| Post-Atomoxetine | 21.15 (3.85) | 23.00 (2.96) | 48.69 (7.91) | 4.31 (3.52) |

- Pre-medication, C and F means were slower-than-normal and CF and O atypical.
- After medication with Methylphenidate C, F, and CF means were normal and O was larger-than-normal. After medication with Atomoxetine C, F, CF and O were normal.
- ANOVA with post-hoc analysis (Tukey HSD) of log-normal C, F, and CF measures are shown in Table 3. Main effects were significant for C, F, and CF.

Figure 1. AQT CF naming times (sec.) for each adult with ADHD at intake, after treatment with Methylphenidate, and after treatment with Atomoxetine.

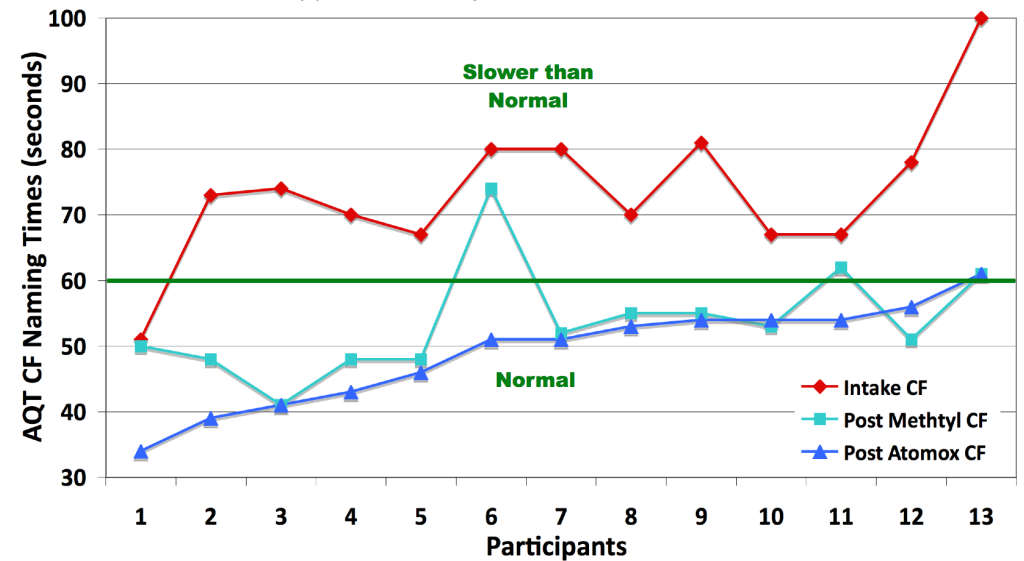


Table 3. ANOVA with post hoc analyses (Tukey HSD) for the significance of differences between intake and after treatment with Methylphenidate and Atomoxetine (n = 13).

| AQT | df | SS | MS | F | p | Tukey HSD Test Statistics |
|-----|---------|--------------------|------------------|-------|--------|----------------------------------|
| C | 2 36 | 186.21 657.38 | 93.10 18.26 | 5.10 | 0.0112 | Intake vs Methylph 3.50 accepted |
| | | | | | | Intake vs Atomox 4.22 accepted |
| | | | | | | Methyl vs Atomox 0.71 rejected |
| F | 2 36 | 4434.00 878.31 | 217.00 24.40 | 8.89 | 0.0007 | Intake vs Methylph 4.15 accepted |
| | | | | | | Intake vs Atomox 5.78 accepted |
| | | | | | | Methyl vs Atomox 1.14 rejected |
| CF | 2 36 | 4550.00 3192.31 | 2275.00 85.90 | 26.49 | 0.0000 | Intake vs Methylph 7.78 accepted |
| | | | | | | Intake vs Atomox 9.73 accepted |
| | | | | | | Methyl vs Atomox 1.95 rejected |

Treatment

- Treatment protocols followed Danish psychiatric practice starting with referral for diagnostic evaluation of possible ADHD based on psychiatric interviews, **ICD-10** and **ASRS-V1.1** criteria.
- After establishing responsiveness to Methylphenidate, medication was changed to Atomoxetine and dosage was increased until stabilization of ADHD symptoms was determined with patient's acceptance, shared evaluation and discussion with the psychiatrist.

Table 1. Representative treatment protocol for a young-adult, male (ICD-10 F90.9).

| Medication | Color | Form | CF | Overhead | ASRS-1.1 |
|-----------------------|---------|---------|---------|----------|----------|
| None | 29 sec. | 44 sec. | 70sec. | -3sec. | 38 |
| Methylphenidate 30 mg | 22 sec. | 23 sec. | 55 sec. | 10 sec. | - |
| Methylphenidate 50 mg | 20 sec. | 20 sec. | 48 sec. | 8 sec. | - |
| Atomoxetine 50 mg | 18 sec. | 23 sec. | 44 sec. | 3 sec. | - |
| Atomoxetine 60 mg | 18 sec. | 20 sec. | 48 sec. | 10 sec. | - |
| Atomoxetine 60 mg | 17 sec. | 20 sec. | 43 sec. | 6 sec. | - |
| Atomoxetine 60 mg | 20 sec. | 21 sec. | 41 sec. | 0 sec. | 16 |

Measurements

- Patients completed **ASRS-V1.1** at intake without medication and ratings ranged from 22 to 70 points ($M = 47.4$), indicating likely ADHD (i.e. >20 points).
 - Psychiatric interviews and **AQT** were administered concurrently during treatment, first with Methylphenidate and subsequently with Atomoxetine.
 - **AQT C**, **F**, and **CF** assessed processing speed (a) at intake, without medication, (b) to monitor responsiveness to Methylphenidate, and (c) after stabilization of ADHD symptoms with Atomoxetine.
 - Overhead (**O**) measured processing efficiency [norm-referenced with 270 normals adults].
- Statistical Analysis**
- Log-normal transformations of **C**, **F** and **CF** raw scores (sec.) were used.
 - One-way ANOVA with post hoc analyses compared processing speed between (a) intake and after medication with Methylphenidate; (b) at intake and after medication with Atomoxetine; and (c) after medication with Methylphenidate **and** Atomoxetine.
 - T-tests, assuming unequal variances, compared overhead (**O**) measures.

References

1. Wiig, E.H., Nielsen, N.P., Minthon, L., & Warkentin, S. *A Quick Test of Cognitive Speed (AQT)*. San Antonio, TX: Pearson/PsychCorp, 2002.
2. Wiig EH, Nielsen NP, Minthon L, Warkentin S. *AQT: Assessment of Parietal Function*. Svensk Version & Norsk Versjon. Stockholm, Sweden: Pearson/PsychCorp, 2003.
3. Wiig EH, Nielsen NP, Jacobson J. A Quick Test of Cognitive Speed: Patterns of age groups 15 to 95 years. *Percept & Mot Skills* 2007; 104:1067-1075.
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- Post-hoc analyses showed significant differences for **C**, **F**, and **CF** between (a) intake and after treatment with Methylphenidate, and (b) intake and after treatment with Atomoxetine, no significant differences between the after-treatment measures of processing speed.
- Two-tailed t-tests, assuming unequal variance, tested overhead (**O**) differences between intake and after medication with Methylphenidate ($t = 3.92$; $p = 0.0020$; $\eta^2 = 0.5616$), and then Atomoxetine ($t = 6.16$; $p = 0.0000$; $\eta^2 = 0.75$).
- Effect sizes (η^2) were small (0.22) for **C**, large (0.83) for **F**, medium (0.59) for **CF** and medium-to-large (0.75) for **O**.

Table 4. Individual **AQT** naming times and overhead (sec.) at intake without medication and after treatment with Methylphenidate and Atomoxetine.

| n | At Intake | | | | Methylphenidate | | | | Atomoxetine | | | | | |
|----|-----------|----|-----|----|-----------------|----|----|----|-------------|--------|----|----|----|----|
| | C | F | CF | O | Dosage | C | F | CF | O | Dosage | C | F | CF | O |
| 1 | 18 | 22 | 51 | 11 | RU 20 mg | 16 | 22 | 50 | 12 | 60 mg | 15 | 19 | 34 | 0 |
| 2 | 28 | 36 | 73 | 9 | R 10 mg | 24 | 30 | 48 | 6 | 80 mg | 20 | 22 | 39 | 3 |
| 3 | 29 | 40 | 74 | 5 | R 40 mg | 18 | 23 | 41 | 0 | 40 mg | 17 | 22 | 41 | 2 |
| 4 | 22 | 24 | 70 | 24 | R 30 mg | 18 | 19 | 48 | 11 | 100 mg | 18 | 19 | 43 | 5 |
| 5 | 25 | 32 | 67 | 10 | R 50 mg | 20 | 20 | 48 | 8 | 80 mg | 19 | 22 | 46 | 5 |
| 6 | 23 | 26 | 80 | 31 | M 30 mg | 20 | 26 | 74 | 28 | 40 mg | 19 | 19 | 51 | 13 |
| 7 | 27 | 29 | 80 | 24 | R 20 mg | 22 | 27 | 52 | 3 | 60 mg | 21 | 24 | 51 | 6 |
| 8 | 29 | 44 | 70 | 3 | R 10 mg | 23 | 27 | 55 | 5 | 40 mg | 23 | 25 | 53 | 5 |
| 9 | 22 | 28 | 81 | 31 | C 54 mg | 19 | 26 | 55 | 10 | 80 mg | 19 | 23 | 54 | 12 |
| 10 | 28 | 26 | 67 | 16 | R 20 mg | 26 | 25 | 53 | 2 | 60 mg | 26 | 25 | 54 | 3 |
| 11 | 25 | 26 | 67 | 16 | R 10 mg | 25 | 25 | 62 | 12 | 60 mg | 26 | 25 | 54 | 3 |
| 12 | 25 | 26 | 78 | 27 | R 40 mg | 28 | 28 | 51 | 5 | 60 mg | 23 | 27 | 56 | 4 |
| 13 | 39 | 42 | 100 | 19 | M 40 mg | 27 | 29 | 61 | 5 | 80 mg | 28 | 27 | 61 | 6 |

Conclusions

- The **AQT** additive model may provide sensitive quantitative measures for comparing and monitoring effects of pharmacological treatment of ADHD.
- **AQT** measurements indicate when subjects have reached stabilization and normal processing speed and efficiency.
- **AQT** dual-dimension processing speed and efficiency were significantly reduced before medication, but improved to near-normal levels after treatment with Methylphenidate.
- After stabilization of ADHD symptoms with Atomoxetine, all exhibited normal dual-dimension processing speed and efficiency, regardless of the degree of impairment before medication.
- **Fail criteria** for dual-dimension processing speed (> 60 sec) and efficiency ($> +6$ sec) at intake identified 12 and 11 patients respectively.
- **Fail criteria** for either the dual-dimension or overhead measures or both (> 60 sec / $> +6$ sec) identified all 13 patients at intake.
- Data were collected in an outpatient psychiatric practice, without external funding and procedures were limited by requirements to follow prevailing Danish psychiatric practice in a social medicine environment. Findings are therefore considered preliminary.