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Comparison of Neurological and Cognitive Deficits in Children With ADHD and Anxiety Disorders

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Abstract

Objective—To compare the neuro-cognitive profiles among initial clinic referred medication naive sample of children with anxiety disorders (ANXs) and ADHD in a youth sample.

Method—Three groups of patients, ANX ($n = 40$), ADHD ($n = 48$), and ANX + ADHD ($n = 33$), aged 7 to 12 years, were compared with respect to their Physical and Neurological Examination for Subtle Signs (PANESS) and cognitive measures (digit span, digit symbol, Trail Making Test [TMT]-A and TMT-B, Stroop test).

Results—ADHD group performed worse than the other two groups with regard to soft signs and cognitive test performance; ANX + ADHD were impaired relative to ANX but better than ADHD. Significant differences were found for gait and station problems, overflows and timed movements, TMT error points, and Stroop interference scores. ADHD patients had more difficulty in warding off irrelevant responses and lower speed of time-limited movements.

Conclusion—This clinical evaluation study suggested that ANX and ADHD seem to have significantly different neuro-cognitive features: Poorest outcomes were observed among children with ADHD; rather than problems of attention, inhibitory control deficits were the most prominent differences between ANX and ADHD; and the presence of ANX appears to have mitigating effect on ADHD-related impairments.

Keywords

anxiety; ADHD; PANESS; Stroop; TMT

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Introduction

ADHD and anxiety disorders (ANXs) are highly important youth mental disorders and often co-occur. ADHD is endorsed between 4% and 10% of the children (Skounti, Philalithis, & Galanakis, 2007). Despite being a well-studied disorder, its neurological-cognitive correlates remain unclear. ANXs are even more prevalent among children and affect up to 20% of the pediatric population (Greenberg et al., 1999). A developmental approach is particularly relevant to ANXs as they are among the first psychiatric disorders to manifest. For instance, whereas the mean age of onset for depression is 29, the mean age of onset for ANXs is 11 (Kessler et al., 2005). To date, there have been few studies exploring the impact of “pure” ANXs on cognitive test performance (Degnan & Fox, 2007). However, numerous studies have investigated cognitive functions in individuals with ADHD. Current models of ADHD suggest that it is best characterized as a disorder of impaired executive functions or reduced inhibition control (Nigg, 2001). By contrast, it has been suggested that ANXs are associated with increased control of inhibition (Degnan & Fox, 2007; Oosterlaan & Sergeant, 1998). Approximately 25% to 50% of all children with ADHD exhibit co-occurring ANXs with significant impact on cognitive test performance (Schatz & Rostain, 2006), but no consistent data were established about this impact (Vloet et al., 2010). It is conceivable that ANXs comorbid with ADHD may represent a different subtype because in the comorbid condition, ANXs might be secondary to the difficulties that may arise through ADHD in school or social activities. Data from the Multimodal Treatment Study of children with ADHD indicate that co-occurrence of ADHD + ANX seems indeed to be a distinct subtype with consequent implications for etiology, assessment, and treatment. In turn, attentional problems may also be developed secondary to ANXs (Jarrett & Ollendick, 2008).

Abnormalities on motor examination have afforded valuable insights into developmental disorders. Measures of motor function are more quantifiable and reproducible than measures of complex social behavior. Basic motor skills are assessed using a standardized motor examination for children, the Physical and Neurological Examination for Subtle Signs (PANESS; Denckla, 1985). The study of relationship between soft signs and psychiatric disorders in children has mostly been restricted to some disorders including ADHD, autism spectrum disorders (ASDs), obsessive compulsive disorder (OCD), Tourette’s disorder, schizophrenia, and there have been few reports on motor problems in “pure” ANXs (Emck, Bosscher, Beek, & Doreleijers, 2009; Erez, Gordon, Sever, Sadeh, & Mintz, 2004; Skirbekk, Hansen, Oerbeck, Wentzel-Larsen, & Kristensen, 2012). There is an extensive literature demonstrating an increased prevalence of motor impairment in children with ADHD, and a consistent motor finding in children with ADHD is excessive motor overflow (Pasini & D’agati, 2009). Excessive overflow in ADHD is correlated with impaired response inhibition (Mostofsky & Simmonds, 2008; Vitiello, Stoff, Atkins, & Mahoney, 1990), a finding that has been implicated as a core deficit of the disorder (Barkley, 1990). The earlier *minimal brain dysfunction* term included soft signs or motor problems as a signal of neurological dysfunction, and some authors have argued that these signs ought to be included in the diagnostics of ADHD (Cardo, Casanovas, de la Banda, & Servera, 2008). The relationship between pure ANXs and motor impairment has attracted little attention, and very limited data exist when compared with ADHD. Some studies emphasize the finding of balance

problems in connection with ANXs (Erez et al., 2004; Stins, Ledebt, Emck, van Dokkum, & Beek, 2009); others suggest a similar profile of motor impairment as ADHD (Skirbekk et al., 2012).

In neurodevelopmental disorders, comorbid conditions are more the rule than the exception. Although comorbidity is a general issue in psychiatry, when compounded with anxiety, where there are 11 different disorders, namely, separation anxiety disorder (SAD), selective mutism, specific phobia (SpP), social phobia (SoP), panic disorder, agoraphobia, generalized anxiety disorder (GAD), substance/medication-induced anxiety disorder, anxiety disorder due to another medical condition, other specified anxiety disorder, unspecified anxiety disorder, in addition to other cross-class comorbidities. We note here a clarification of our use of the broad term ANXs. Previously, the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev.; DSM-IV-TR; American Psychiatric Association, 2000) listed 13 separate ANXs including OCD and posttraumatic stress disorder (PTSD) in the ANX class. But our ANX sample will not include OCD and PTSD, an approach that is consistent with the new *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*; APA, 2013) proposal for the ANX category. Furthermore, with respect to the challenges posed in terms of sample selection and heterogeneity in clinical cross-sectional studies, we undertook careful diagnostic discrimination of the ADHD and ANX groups and refer to the ANX + ADHD as the combined group where the two conditions co-occur.

Given previous findings (Degnan & Fox, 2007; Oosterlaan & Sergeant, 1998; Pasini & D'agati, 2009; Vloet et al., 2010), it seems reasonable to predict that (a) different patterns will be found in both neurological and cognitive measures among the three study groups, (b) the soft signs among children with ADHD will be characterized by excessive overflow and the soft signs among children with ANXs will be characterized by balance and impersistence problems, (c) highest inattention and impulsive pattern will be recorded in the ADHD group, and (d) the co-occurrence of ANXs will have a positive influence with milder neuro-cognitive problems detected among children in the ANX + ADHD group.

Accordingly, we hypothesized that children with ANXs would show different neuro-cognitive patterns from children with ADHD that can be detected with objective tools not taking long in daily practice. No prior studies, to our knowledge, have examined the difference of both neurological and cognitive functions among three groups (ANX, ADHD, ANX + ADHD) in a pediatric sample. Therefore, although we expected some specific soft signs and cognitive dysfunctions as mentioned in the previous paragraph, data to generate more specific hypotheses are insufficient.

Method

Participants

Participants were consecutively recruited from a general child adolescent psychiatry outpatient unit at the Turgut Özal University. All participants underwent an extensive child psychiatric examination conducted by an experienced child and adolescent psychiatrist, and diagnosis was mainly based on *DSM-5 criteria* (APA, 2013) and made by the first author (P.Y.).

The inclusion criteria were children between 7 and 12 years and diagnosed to have ADHD combined presentation (previously named combined subtype) or ANX based on *DSM-5* criteria. In addition to *DSM-5* criteria, the structured parent interview, Kiddie–Schedule for Affective Disorders and Schizophrenia (SADS)–Lifetime Version (*KSADS-PL*) that has substantially overlapped properties with *DSM-5* ANX criteria except OCD and PTSD, and broad band rating scales (Child Behavior Checklist [CBCL] and Teacher Report Form [TRF]; Achenbach, 1991a, 1991b) were used to confirm ADHD, ANXs, and other mental disorders. Comorbidity was systematically registered. Children with comorbid ADHD and ANXs were also included in the study as a third group. Special attention was given to create three relatively homogeneous groups. So ANX + ADHD cases were deliberately separated by establishing comorbidity between ADHD and ANXs in these participants.

All patients were diagnosed for the first time and had never been evaluated for psychiatric disorders or treated with psychopharmacological medicine. The parents could choose to opt out of the study, but none of the parents refused to participate.

Exclusion criteria for both groups were identification of any medical or neurological disorders with obvious neuropathology (e.g., epilepsy, cerebellar disease, neurodegenerative disease); sensorial deficits (e.g., color blindness); psychosis, Tourette's disorder, OCD, major mood disorder including major depression, severe mood dysregulation (SMD), and bipolar disorder; ASD, intellectual disability (which previously was named as mental retardation), eating disorder, substance-abuse disorder; and history of head trauma, presence of any major pathological physical findings (e.g., high fever, joint immobility or tenderness, abnormal blood pressure or pulsation), or neurological findings (e.g., pathological reflexes, nystagmus, obvious tremor, rigidity) that influence neurological soft signs examination and/or cognitive test performance. Learning disorders (LDs), disruptive behavior disorder (DBD) including oppositional behavioral disorder and conduct disorder, speech disorders, behavioral sleep problems, and nocturnal enuresis were no exclusion criteria, due to the lack of evidence that they will alter identified neuro-cognitive features of ANXs or ADHD.

Children who were referred or who applied for excessive anxiety/worry and/or hyperactivity/inattentiveness were included only if their final diagnosis was assigned by the child psychiatrist based on mental examination and KSADS of participants, and after the decision of prominent clinical impairment with Clinical Global Impression of Severity (CGI-S) score (Guy, 1976). From an initial sample of 63 ANX children and 87 ADHD children, 29 were later excluded in view of other presenting co-occurring conditions (13 had intellectual disability, 5 had OCD, 3 had major depression, 2 had SMD, 2 had Tourette's disorder, 2 had high fever and joint immobility, and 2 had abnormal major neurological findings which were ataxia, nystagmus, and rigidity). A total of 121 children were included in the final study. The ANX sample ($n = 40$) included 21 boys and 19 girls with a ($M \pm SD$) age of 9.7 ± 1.7 . The ADHD sample ($n = 48$) included 34 boys and 14 girls with a mean age of 8.8 ± 1.7 . The ANX + ADHD combined sample ($n = 33$) included 23 boys and 10 girls with a mean age of 9.4 ± 2.3 . In the ANX group, 22 (55%) had GAD, 33 (82.5%) had social phobia, 34 (85%) had specific phobia, and 6 (15%) had SAD. In the ANX + ADHD group, 27 (81.8%) had specific phobia, 23 (69.7%) had social phobia, 13 (39%) had GAD, and 5 (15%) had SAD. Expectedly, a majority ($n = 48$, 65.7%) of children ($n = 73$) met criteria for

at least one other ANXs; moreover, a significant number of them ($n = 42$, 57.5%) had three or more comorbid ANXs. In the two ADHD and ANX + ADHD groups, all participants met criteria for ADHD combined presentation (previously named as combined subtype). The degree of severity of symptoms was similar in all groups, as determined by CGI-S score 4 criteria. The Hollingshead Index (1975) was used to assess socioeconomic status (SES) for each child in the study (Hollingshead & Redlich, 2007). Participants in all groups were primarily from the middle-class socioeconomic backgrounds. There were no significant group differences in age, gender, SES distribution, or lateral preference. The number of comorbid disorders was comparable among the three study groups. As expected, externalization problems were most intense in the ADHD group, whereas ANX group had more internalization problems as assessed by the CBCL and TRF. Sample characteristics are presented in Table 1.

The study was approved by Turgut Özal University School of Medicine institutional review board. All the children and their caregivers were given verbal information. Data collection was mostly incorporated in routine clinical work. Informed consent was verbal, as is customary, given the literacy level as parents.

Instruments

Neurological measures

PANESS: This scale measures salient components of balance, speed-related skills, and motor function including lateral preference, gaits, motor persistence, coordination, overflow, dysrhythmia, and timed movements (Denckla, 1985). Five primary outcome variables were used in the current study (see Denckla, 1985; Larson et al., 2007, for detailed administration and scoring procedures):

1. *Total gaits and stations*, which includes total axial (gait, station, and balance tasks) performance errors and total involuntary movements (i.e., tremor, choreiform, and abnormal posture). The number of steps incorrectly performed on heel-walk, toe-walk, everted-walk, tandem forward, tandem backward plus suboptimal category performance group numbers on balance, and hopping are all summed up.
2. *Impersistence score*, which includes balance-related tasks and calculated as adding any numerals from “sustention item,” “tongue protrusion item,” and “eyes closed” item for a grand total of impersistence score. This summary variable was especially added to evaluate balance and coordination problems that were mentioned in previous studies (Erez et al., 2004; Stins et al., 2009) of ANX group.
3. *Total overflow* includes the total number of abnormal-for-age movements observed during gaits and timed movements. Calculated as the sum of all overflow occurring with gaits, timed limb movements, and tongue wiggles.
4. *Total dysrhythmia* includes the total number of timed motor examination trails in which the child failed to maintain steady rhythm for the duration of the task. Calculated as adding all left and right “dysrhythmia-*d*” notations put on

examination form during coordination examination including hopping, tongue wiggling, and all the timed limb movements.

5. *Total speed of timed movements* was measured from timed activities, including all 13 repetitive and patterned movements and tongue wagging. There were no normative data for the PANESS timed movements scores for Turkish children at the time of this study. Besides, as the cooperation and attention of the child to the task is important, aggregate global scores may be more reliable than individual items. So, we preferred to use raw data (seconds) to figure out comparisons for speed of timed movements.

Cognitive measures: The neuropsychological test battery consisted of Stroop, Digit Symbol, and Digit Span subtests of the Wechsler Intelligence Scale for Children–Revised (WISC-R) and Trail Making Test (TMT)-A and TMT-B.

Stroop Color-Word Test: This measures the ability to shift perceptual set with the changing demands to inhibit a habitual behavior pattern and to behave in an unusual way. This test consisted of three conditions: (a) color naming, (b) word reading, and (c) color-word interference. In the color naming condition, participants were asked to name, as quickly as possible, the color (red, green, or blue) of 126 dots, arrayed randomly in 9 columns and 14 rows on a sheet of white paper and scanned left to right and then top to bottom. On the word reading condition, participants were asked to read, as quickly as possible, an equal number of similarly arrayed words (“red,” “green,” or “blue”) printed in black. In the color-word reading condition, participants were asked to name a similar array of words written in incongruent colors as quickly as possible. The time of completion of each task was recorded in seconds. Stroop interference score was calculated as $C - ([A \times B] / [A + C])$ (Golden, 1976). Defects in these abilities result in perseveration, stereotypic behavior, and difficulty in controlling behavior. These functions are mainly frontal lobe functions. Higher interference score indicates worse performance. Stroop Test also assesses information processing rate, and parallel processing of attended and non-attended stimuli, and attention (MacLeod, 1991).

Digit Span and Digit Symbol subtests of WISC-R: The WISC-R consists of 10 subtests that assess verbal and performance abilities. Reliability and validity studies of the Turkish form have been conducted (Savaşır & Şahin, 1978). Although the WISC-R is a relatively outdated form of the test, it is widely used, and we do not have updated forms translated into Turkish. The digit symbol test consisted of presenting the participant with a sheet with numbers associated with symbols. The participant needed to identify and verbalize the number that should be placed in the space provided. The Digit Span Test is a widely used measure of attention and working memory that requires participants to immediately recall digit sequences of increasing length, both in forward and backward way.

TMT-A and TMT-B: The basic task is connecting a series of stimuli (numbers expressed as numerals) in a specified order as quickly as possible. The score is the number of seconds required to complete the task and the number of errors during TMT-B. TMT-A consisted of presenting the participant with a sheet that contained an ascending sequence of numbers

within circles. The patient needed to connect the numbers in ascending order as fast as possible while the examiner recorded the time (Spreen & Strauss, 1998). In TMT-B, the patients had to alternate between numbers and letters in a specified order, which taps mental tracking ability. TMT performance is heavily influenced by attention. The test takes 5 to 12 min. Higher scores in these two tests indicate bad performance. Time to complete served as a measure of speed, and the number of errors in TMT-B served as a measure of set-shifting.

Additional measures

KSADS-PL: This is a semi-structured diagnostic interview designed to assess current and past episodes of psychopathology in children and adolescents according to *Diagnostic and Statistical Manual of Mental Disorders* (3rd ed., rev.; *DSM-III-R*; APA, 1987) and *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*; APA, 1994) criteria (Kaufman et al., 1997). The Turkish form showed adequate validity and reliability (Gökler et al., 2004).

CBCL: The CBCL/6-18 includes 20 competence items and 118 problem items (Achenbach, 1991a; Achenbach & Rescorla, 2001). Broad-band internalizing, externalizing, and total symptom scales were examined (*T* scores have a mean of 50 and *SD* of 10). The test–retest reliability of the Turkish form was .84 for the total problems, and the internal consistency was adequate (Cronbach's $\alpha = .88$; Dumenci, Erol, Achenbach, & Simsek, 2004).

TRF: The TRF/6-18 includes items for rating academic performance, 4 adaptive characteristics, 118 specific behavioral/emotional problems, and 2 open-ended items such as those on the CBCL (Achenbach, 1991b; Achenbach & Rescorla, 2001). Broad-band internalizing, externalizing, and total symptom scales were examined (*T* scores have a mean of 50 and *SD* of 10). The test–retest reliability of the Turkish form was .88 for the total problems and the internal consistency was adequate (Cronbach's $\alpha = .87$; Erol & Simsek, 2000).

CGI-S of illness: The CGI is rated on a 7-point scale, with the Severity of Illness scale using a range of symptoms from 1 to 7 (0 = *not assessed*, 1 = *normal, not at all ill*, 2 = *borderline mentally ill*, 3 = *mildly ill*, 4 = *moderately ill*, 5 = *markedly ill*, 6 = *severely ill*, and 7 = *among the most extremely ill patients*; Guy, 1976).

Procedure

The semi-structured proforma containing information regarding demographics, educational and socioeconomic status, family history, birth and developmental history was used for all participants. The CBCL questionnaire was filled in by parents, which led to a total of 98 cases. The TRF questionnaire was filled in by teachers, which led to a total of 75 cases. Neurological functions were assessed by the research fellows (Meryem Gül Teksin Bakır, İle Akta, Fatma Betül Ayvaz) using PANESS. Examiners were blind to the patient's diagnostic status at the time of the assessment and during scoring. After didactic training, 10 random patients were evaluated with PANESS. Those examinations (conducted on patients not included in this study) were rated by three raters (research fellows) to obtain a reliability estimate ($r = .85$) and each PANESS was administered by one of the raters. In the cognitive

assessment part, all participants were tested individually in a quiet room. The evaluation was performed using digit span, digit symbol, TMT-A, TMT-B, and Stroop by a trained psychologist (.P.S.) who was blind to the diagnosis of cases. Each participant received all the assessments in the same standardized order (PANESS first, then cognitive tests). A 10-min rest break was given between PANESS and cognitive tests, with the assessment lasting for 50 to 60 min. As both the PANESS and cognitive tests are short and fun, no fatigue was noted in the participants during evaluation.

Statistical Analysis

Statistical analysis was completed with the Statistical Package for Social Sciences (SPSS18). Group differences with respect to sample characteristics were assessed by Pearson's chi-square (χ^2) test (for gender, lateral preference, and comorbidity patterns) and ANOVA (for age, SES, CBCL, and TRF scores).

Because normative values for PANESS and some cognitive tests used in this study (TMT-A and TMT-B, Stroop) have not been measured on Turkish children, raw scores were used for their analysis.

Normality of data was checked using the Kolmogorov–Smirnov test. To identify group differences, all normally distributed neurological and cognitive outcomes were evaluated using ANOVA for each dependent variable, with groups as independent variables (ANX, ADHD, ANX + ADHD). In the case of significant F values, post hoc comparisons with Tukey or Dunnett's C , according to homogeneity of variance, were performed. Outcomes not normally distributed, verified by Kolmogorov–Smirnov test (total dysrhythmia, left dysrhythmia, right dysrhythmia, left overflow, digit span, digit symbol, TMT-B error), were analyzed by Kruskal–Wallis test, and if significant, pairwise comparisons using Mann–Whitney U test. Partial eta-squared (η_p^2) coefficients were calculated to measure effect size (.01 is small, .06 is medium, >.14 is large). We decided not to adjust for multiple testing to avoid Type II errors.

Pearson correlation coefficients were also computed among all dependent variables (five PANESS summary scores, six cognitive test results), and .10, .30, and .50 are interpreted as small, medium, and large coefficients, respectively.

For all analyses, a statistical threshold of $p < .05$ (two-tailed) was used to determine significance, with $p < .1$ considered a trend.

Results

There were no statistically significant differences in demographic characteristics, lateral preference, and comorbidity pattern among ANX, ADHD, and ANX + ADHD sample, and no significant differences were found in the distribution of ANX type between the two ANX and ANX + ADHD groups (Table 1). Therefore, in subsequent analyses, there was no need to control for these characteristics. The externalizing scores on both CBCL and TRF were significantly higher for the ADHD group than for the ANX group. However, there was no

statistically significant difference in the total, externalizing, or internalizing scores of CBCL and TRF between the ADHD group and the combined ANX + ADHD group.

Significant group differences were found for gait and station problems— $F(2, 93) = 4.05, p = .02$; overflows—total $F(2, 93) = 4.48, p = .01$; right $F(2, 93) = 4.17, p = .02$; left $\chi^2(2, 96) = 9.39, p = .02$; timed movements—total $F(2, 93) = 4.51, p = .01$; right $F(2, 93) = 3.40, p = .04$; left $F(2, 93) = 5.23, p = .007$ in neurological measures (Table 2), and TMT-B error points, $\chi^2(2, 96) = 10.28, p = .006$, Stroop interference scores, $F(2, 85) = 9.43, p = .000$, in cognitive measures (Table 3) among groups.

Then, first follow-up tests were conducted to evaluate pairwise differences for total gait and stations, total overflows, total timed movements, and Stroop interference scores. There were significant differences in the means of total overflows between the ANX group and ADHD group ($p = .007$), and between the ANX group and ANX + ADHD combined group ($p = .042$), but no significant differences between ADHD alone group and ANX + ADHD combined group. The ADHD group had higher overflow movements. Although children with ADHD alone had significantly ($p = .01$) slower timed movements than children with ANXs, there were no significant differences in other pairwise comparisons of this neurological soft sign. In the Stroop interference scores, there were significant differences between the ANX and ADHD groups ($p = .001$), and between the ANX + ADHD and ADHD groups ($p = .002$), but no significant differences between the ANX and ANX + ADHD groups. The results pointed to reduced Stroop test performance among participants in the ADHD group compared with the other two groups. As assessed by η_p^2 , the most strong relationship was found between Stroop interference scores and diagnosis, with 18% of the variance in Stroop scores explained by diagnosis ($\eta_p^2 = .182, p = .000$).

Second follow-up tests were conducted to evaluate pairwise differences for TMT-B error numbers that were not normally distributed. Mann–Whitney U post hoc tests revealed that participants in the ADHD group significantly made mistakes in TMT-B test ($p = .01$) compared with children in the ANX group, and made more mistakes than the ANX + ADHD combined group ($p = .06, ns$). The ANX group and the ANX + ADHD group did not differ significantly from one another. All post hoc comparisons were depicted in Table 4.

Secondary Analyses

Figure 1 visually represents the relationship between variables. To determine the relationship between measures, correlation coefficients were computed among PANESS summary scores and cognitive test results. Using the Bonferroni approach to control for Type I error across 55 correlations, a p value of .000 ($.05 / 55 = .00009$) was required for significance. The results of the correlational analyses were depicted in Table 5. Twelve of the 55 correlations were statistically significant and were greater than or equal to .32. Higher PANESS scores correlate within each other. Also, higher TMT-B scores correlate with higher TMT-B error scores, $r(94) = .44, p = .000$, and higher TMT-A scores, $r(94) = .42, p = .000$. However, most of the correlations between PANESS scores and cognitive test results were not significant except for correlations between TMT-A and three summary scores of PANESS (total gait and stations, $r(94) = .57, p = .000$; total overflows, $r(94) = .40, p = .000$; total timed

movements, $r(94) = .55, p = .000$). In general, these results suggest that if participants show soft neurological soft signs in one area, they tend to show impairments in other areas of PANESS examination, and tend to complete TMT-A test in a longer time.

Discussion

This study was undertaken to compare neuro-cognitive profile among ANX alone, ADHD alone, and ANX + ADHD comorbid patients. All patient samples matched for gender, age, SES, lateral preference, and comorbidity pattern. Both soft signs examination and cognitive test battery were used to compare the three pediatric patient groups. To the best of our knowledge, this is the first time such data have been reported.

Our analyses replicate certain findings in the literature, while clarifying other issues. First, our findings generally support the notion that ADHD is associated with greater disruption in neuro-cognitive performance, reminiscent of the fact that it used to be called “minimal brain dysfunction” (Cardo et al., 2008). In almost all parts of neurological soft signs examination, patients with ADHD had worse performance. Same pattern was detected in cognitive measures. ADHD participants had most impaired results in almost all cognitive tests. Overall, patients with ADHD alone exhibited the most impaired neuro-cognitive profile, consistent with previous observations (Barkley, 1990; Cardo et al., 2008; Mostofsky & Simmonds, 2008; Nigg, 2001; Tseng, Henderson, Chow, & Yao, 2004; Vitiello et al., 1990).

Second, our study revealed that the comorbid ANX + ADHD group seems to represent an intermediate form, mean lesser disturbed than ADHD but more disturbed than the ANX group. Our first hypothesis that different neuro-cognitive patterns will be found among the three groups was confirmed by these results. These results also confirmed our other hypothesis that the presence of ANXs might have a positive impact on ADHD-related impairments. The ADHD group presented with the most severe gait and station problems, excessive overflows, slowness in timed movements, mistakes in TMT-B test, and Stroop performance, followed by the ANX + ADHD group, whereas the ANX + ADHD group performed similar to ANX group in most measures, except for more overflows and worse Stroop performance. The observation that the participants in the ANX + ADHD combined group exhibited milder impairments than those in the ADHD alone group but more so than those in the ANX alone group aligns with previous studies that reported better inhibitory control (Manassis, Tannock, & Barbosa, 2000; Pliszka, 1992), less attentional problems (Vloet et al., 2010), and better treatment response (Jensen et al., 2001) among children with ANX + ADHD when compared with those with ADHD alone.

With regard to balance and persistence problems, we suggested greatest impairment in ANXs. Of interest, PANESS impersistence scores did not differ among groups. So our second hypothesis was only partially supported with the findings of most excessive overflow movements in ADHD, but there were not many balance and impersistence problems in ANX participants. On the contrary, ADHD groups (both alone and combined) had more impersistence than ANX group, but the finding did not reach statistical significance. Some studies (Mao, Kuo, Yang, & Su, 2014) have reported that the balance ability of children with ADHD were less proficient than that of normal controls, although others (Erez et al., 2004;

Stins et al., 2009; Tseng et al., 2004) have emphasized the finding of balance problems in connection with ANXs. Based on Erez et al.'s (2004) and Stins et al.'s (2009) studies, we might have expected patients with ANXs to display more balance, impersistence, gait, and station problems. This was not the case in this study. Although the present data failed to support the hypothesis that ANX patients have more balance problems, we found more (statistically nonsignificant) dysrhythmic movements in ANX participants. Yet, with the exception of dysrhythmia being associated with ANXs (dysrhythmic movements were highest in ANXs), other neurological soft signs were most notable in ADHD participants. Balance and rhythm are closely related, and dysrhythmia might be interpreted as a sign that participants with ANXs may exhibit problems belonging to this domain. According to previous studies, using PANESS, dysrhythmia seems to differentiate children with ADHD and Asperger syndrome (AS) from controls (Cole, Mostofsky, Larson, Denckla, & Mahone, 2008; Jansiewicz et al., 2006; Pasini, D'Agati, Pitzianti, Casarelli, & Curatolo, 2012). It is plausible that deficits found on PANESS were broadly affected by the selected comparison groups. Studies comparing different groups showed that ADHD participants performed faster on timed activities compared with AS participants (Pasini et al., 2012), but slower compared with controls (Cole et al., 2008). One possible explanation is that some neurologically subtle signs may be more disorder specific, such as slowness related with AS or overflow related with ADHD, and might be able to distinguish patient groups, whereas others may be quite non-specific to most neurodevelopmental disorders. Likewise, impairments in rhythm and balance might be widespread and nonspecific signs. Presence of nonspecific signs can only differentiate patients from controls, not from other patient groups. As our study lacked a normal control group, we cannot speculate regarding this issue.

Considering existing data, we cautiously expected ADHD patients to manifest more impulsive, inattentive responses, and errors in cognitive tasks. Indeed, ADHD participants exhibited worse performance in almost all measures, and significant differences were found in TMT-B error numbers and Stroop interference scores. ADHD participants made significantly more mistakes than ANX participants but not more than the ANX + ADHD participants, with impulsive, disinhibited cognitive response style. Their significantly worse Stroop performance than the other two groups suggests that when ADHD co-occurs with ANXs, impulsive responses ameliorate but attention problems still continue. This suggestion is consistent with the review of Schatz and Rostain (2006), and their conclusion that ANXs may partially inhibit the impulsivity seen in ADHD. But our findings about ANX participants has not completely accorded with the other idea in this review that higher levels of anxiety were correlated with sluggishness, which means slower reaction time and lesser frequency of mistakes. This hypothesis might be mainly related with inattentive subtype of ADHD, which was not investigated in our study. Some researchers have posited that anxiety may inhibit impulsivity while making attentional tasks worse (Brown, 2008; Pliszka, 1989). However, in the present study, ANX + ADHD participants were not more inattentive than ADHD only participants. The presence of anxiety seems to prevent impulsive responses but does not lead to more attentional impairments seen in ADHD.

When considered together, the cognitive tests, TMT-A and TMT-B scores ($r = .42, p = .000$), TMT-B scores and TMT-B errors ($r = .44, p = .000$), and TMT-B errors and Stroop interference scores ($r = .34, p = .000$) correlated significantly in the total sample, namely,

positive correlations were observed between TMT and Stroop tests. Larger response time in TMT tasks and higher interference problems in Stroop test scores were associated significantly with a greater number of errors performed in TMT-B.

Errors made during the TMT-B test are likely to present problems in the inhibition of the prepotent impulse. Friedman and Miyake (2004) posture that the Stroop interference score is a measure of behavioral inhibition (i.e., proponent response inhibition), in that fluently reading the color name is a salient process that requires the effective inhibition of irrelevant information (colors of the ink the words written in). TMT-A measures mainly simple attention, fine motor skills, and visual skills. TMT-B and Stroop tests are more related with focused attention and interference control. Digit span and digit symbol tests are influenced considerably by visual and auditory memory skills. In all these tests, only TMT-A, a relatively simpler test compared with the others, was correlated with some PANESS scores. Children with higher TMT-A scores tended to have more problems in PANESS, and as seen in Table 5, we could conclude that the variance of 33% of gait and station problems (.572), 16% of excessive overflow movements (.402), and 30% of the slowness in timed movements (.552) were accounted for by their linear relationship with their TMT-A scores.

With respect to attention functions, it has been suggested that intrusive worries and hypervigilance to threat cues associated with ANXs often manifest as symptoms of inattention (Jarrett & Ollendick, 2008), which can complicate differentiation of test results. A recent study by Jarrett, Wolff, Davis, Cowart, and Ollendick (2012) compared cognitive test performance of three groups (ANX, ADHD, ANX + ADHD) and found separate attentional difficulties in ANXs and ADHD. Although symptoms of inattention are hallmarks of both ANXs and ADHD, inattention in ANXs may be functionally diverse than inattention in ADHD, given differences in neuro-cognitive correlates.

It is important to note that no significant relationship with other measures and no significant differences among groups were found with respect to digit span and digit symbol. Although raw scores were used in the other tests, for digit span and digit symbol, standardized scores were examined. To assess the effect of the standardized scores, we ran group comparisons and correlation analyses using raw scores of all tests. Again, all previously nonsignificant comparisons remained nonsignificant, and no significant correlations were found with respect to digit span and digit symbol. So the lack of difference cannot be attributed to the type of scores used for analyses. These tests might be considered as distinct from others as they involve both memory and internal visual scanning processes. Participants must remember visual or auditory information. Memory component of digit span and digit symbol might make them less sensitive to the subtle attentional differences among groups. Failures on these tests may be the result of different factors that form response inhibition issues, and they may be considered measures of storage, rather than of the processing component of attention. It is also possible that some measures may not have been sensitive in detecting more subtle differences between patient groups and those comparisons using healthy controls may have yielded disparate outcomes.

Participants with ADHD demonstrate significant deficits in reaction time in tasks requiring rapid inhibition of nonrelevant movements for a consistent motor performance. Most striking

differences were found as to complete tempore in time-limited movements (longer times needed to complete in the timed movements part of PANESS), to difficulty in warding off irrelevant stimulus and movements (more overflows, gait and station problems in the related parts of PANESS, and more mistakes in TMT-B and higher interference scores in Stroop task). The lack of a group difference in relation to digit span, digit symbol test scores, and PANESS impersistence scores might be due to the their occurrence in both disorders and this is consistent with the previous findings of attention problems and imbalance in ADHD and ANXs (Ghanizadeh, 2011; Jarrett & Ollendick, 2008; Jarrett et al., 2012; Konicarova, Bob, & Raboch, 2014). Consistent with the previous studies (Pasini & D'agati, 2009; Vitiello et al., 1990; Mostofsky & Simmonds, 2008), only the tasks requiring inhibitory control produced significant differences among groups, confirming the suggestions that ADHD is best characterized as a disorder of reduced inhibition control (Barkley, 1990; Nigg, 2001) and ANXs are associated with increased control of inhibition (Degnan & Fox, 2007; Oosterlaan & Sergeant, 1998), and leading to the idea that imbalance and inattentiveness may not be sensitive enough to capture diminished capacity in these patient groups. Similar to Manassis, Tannock, Young, & Francis-John's study (2007), we did not replicate earlier findings of greater impairment in ANX + ADHD than in "pure" ADHD (Pliszka, 1989, 1992), and we found that pure ADHD was the most impaired group. In sum, the first notable finding in the current study is that the ADHD alone group has significantly greater impairments both in neurological and cognitive measures. Second, the co-occurrence of ANXs is associated with milder impairments. Third, rather than problems of attention, inhibitory control deficits are the most prominent differences between ANXs and ADHD.

The present study aimed to further elucidate characteristic deficits in ANXs and ADHD based on their neurological and cognitive features precisely because the nature of such deficits may be relevant to the management of these patients. Accurate assessment is the first critical step in effective treatment planning. Motor and cognitive profile of youth might have meaningful contributions in assessment processes. For example, excessive activities such as unnecessary body movements and inability to suppress irrelevant interfering stimuli and responses can cause learning difficulties and poor motor skills, which may result in athletic, social, and academic failures; accidental injuries; low self-esteem; and increased risk of additional mental problems like depression. The clinical evaluation methods herein, conducted in a time-efficient way, can be easily incorporated into everyday practice, and results might have implications for individually tailoring the intervention accordingly. Besides their therapeutic implications, they also have important etiological connotations to clarify the nature of deficits in ANXs and ADHD, because they constitute direct and objective measures.

Limitations

1. The present study was limited with a small sample size, which precluded comparisons according to gender and age of children.
2. The normative data for PANESS and some cognitive measures (TMT, Stroop) for Turkish children were not available at the time when the study conducted.

3. There was no control group, and the study focused primarily on patients with ADHD and ANXs, which could limit the generalizability of the results. Thus, it is difficult to make connections to participants without diagnosable disorders.
4. One could speculate that results might be affected by comorbid learning disability (LD). But the proportion of comorbid LD was comparable among groups. In addition, when ADHD and LD co-occur, it seems likely that the soft signs are more related to ADHD than with LD (Patankar, Sangle, Shah, Dave, & Kamath, 2012).
5. ANXs have been considered as a whole group (further research studies might focus on differentiating subtypes of ANXs).
6. Although some investigators note that the most basic skills are mastered by age 7 (Larson et al., 2007), the age at which neurological subtle signs are expected to be absent or pathological has not been established yet, and it is usually preferable to measure neurological subtle signs after the age of 8. Thus, including 7-year-old participants in the present sample might be seen as another limitation.
7. A final limitation of the present study is that the narrow definitions of the study populations limit their generalizability. Some common comorbid disorders (e.g., OCD, tic disorders, mood disorders) were on exclusionary criteria for all groups. But these constricted inclusion/exclusion criteria were used to maximize both within-group homogeneity and the probability of detecting between-group differences. So the rationale was to study “core” features of these disorders.

Strengths

1. Comorbid cases of ANXs and ADHD were deliberately discriminated and three very distinctive groups had been constituted.
2. The degree of severity of symptoms was similar across all groups, implying that differences are unlikely to be due to symptom severity in one or the other group.
3. Participants were in a relatively narrow age range, and there were no statistically significant differences in demographic characteristics.
4. All participants were diagnosed for the first time and had no prior treatment with medications.
5. Both neurological and cognitive assessment had been used for comparison of groups. Multi-informant data collection was conducted.
6. The examination of neurological features and neurological and cognitive tests had been carried out “blind” to each other. More important, they were completely blind to patient’s diagnostic status.
7. Only tools and examination methods that were easy to use, did not take a long time, and could be easily incorporated in routine clinical work were used.

So the strengths of this report are as follows: well-characterized sample, reliance on the well-established neurological examination method and cognitive test battery, and findings

are of special interest for clinicians because study was designed in such a way as to replicate everyday clinical practice.

Conclusion

This study evaluated differences among patients with ANXs, ADHD, and comorbid ANX + ADHD using both soft neurological signs examination and cognitive test battery. We found significant differences with respect to gait and station problems, excessive overflow movements, slowness of timed movements, error numbers in TMT-B, and Stroop interference scores among three patient groups. The ADHD group represented a more severe presentation, and the ANX + ADHD group appeared to be clinically intermediate between the ADHD and ANX alone groups, on the basis of severity of soft neurological signs and cognitive test performances.

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Figure 1.
Relationships among PANESS summary scores and cognitive test results.
Note. PANESS = Physical and Neurological Examination for Subtle Signs.

Table 1

Demographic Variables

	ANX (n=40)	ANX+ADHD (n=33)	ADHD (n=48)	Test ^a	p
Age (years) (mean±SD)	9.7±1.7	9.4±2.5	8.8±1.7	$F_{(2,118)}=2.25$	.11
SES (mean±SD)	2.8±.6	2.8±.6	2.9±.7	$F_{(2,118)}=.49$	.61
Male/Female (n)	21/19	23/10	34/14	$\chi^2_{(2,121)}=3.74$	.15
Hand preference (right/left)	39/1	31/2	43/5	$\chi^2_{(2,121)}=5.77$	.22
General Lateral preference (right/left)	39/1	32/1	44/4	$\chi^2_{(2,121)}=1.93$	.38
Total comorbidity	40/17	33/17	48/27	$\chi^2_{(10,121)}=8.83$	.55
LD	40/13	33/11	48/17	$\chi^2_{(2,121)}=3.24$	.64
DBD ^a	40/2	33/2	48/5		
Others ^b	40/2	33/3	48/4		
CBCL internalization	58.17±8.1	56.22±11.7	52±10.1	$F_{(2,95)}=5.21$	.09
CBCL externalization	51.02±7.5	57.14±10.8	59.17±7.8	$F_{(2,95)}=2.34$	.02*
CBCL total	54.59±7.8	56.68±11.2	55.58±8.9	$F_{(2,95)}=.92$	.68
TRF internalization	54.95±10.7	56.82±11.2	52.72±9.3	$F_{(2,72)}=2.71$	.17
TRF externalization	52.12±9.4	55.08±11.5	59.87±8.7	$F_{(2,72)}=3.18$	.04*
TRF total	53.54±10	55.95±11.4	56.29±9	$F_{(2,72)}=1.47$	.73
GAD	40/22	33/13		$\chi^2(1, 73) = 1.76$	.18
SpP	40/34	33/27		$\chi^2(1, 73) = 0.44$	.83
SoP	40/33	33/23		$\chi^2(1, 73) = 0.26$	.61

	ANX (n=40)	ANX+ADHD (n=33)	ADHD (n=48)	Test ^a	p
SAD	40/6	33/5		$\chi^2(1.00207\ 3) = 0.00$	.10
3 or more comorbid ANXs	40/26	33/16			
	GAD + SpP + SoP + SAD = (2)	GAD + SpP + SoP + SAD = (1)			
	GAD + SpP + SoP = (20)	GAD + SpP + SoP = (12)			
2 comorbid ANXs	SAD + SpP + SoP = (4)	SAD + SpP + SoP = (3)			
	40/4	33/2			
	SpP + SoP = (4)	SpP + SoP = (2)			

Note. ANX = anxiety disorder; SES = socioeconomic status; LD = learning disorder; DBD = disruptive behavior disorder; CBCL = Child Behavior Checklist; TRF = Teacher Report Form; GAD = generalized anxiety disorder; SpP = specific phobia; SoP = social phobia; SAD = separation anxiety disorder.

^a χ^2 = Pearson chi-square test and F = Fisher's exact test.

^b Others = Nocturnal enuresis, phonological disorder, behavioral sleep problems.

* Statistically significant p value.

Table 2

Neurological measures (PANESS summary scores)

	ANX (mean±SD)	ADHD (mean±SD)	ANX+ADHD (mean±SD)	η^2_{est}	p	p [†]
1) Total gait and stations ^a	5.03±3.2	8.25±5	6.96±5.1	F _(2,93) =4.05	.02*	.080
2) Impersistence ^a	.48±.9	.86±1	.86±.9	$\chi^2_{(2,106)}=3.96$	.14	.038
3) Total overflow ^a	8.3±5.7	14±9.1	13.5±9.2	F _(2,93) =4.48	.01*	.088
Right overflow ^a	3.69±2.8	6.5±4.7	5.8±4.2	F _(2,93) =4.17	.02*	.082
Left overflow ^a	3.48±3	6.2±4.4	5.7±4.2	$\chi^2_{(2,96)}=9.39$	.02*	.078
4) Total dysrhythmia ^a	6.3±2.4	5.9±3.2	5±3.6	$\chi^2_{(2,96)}=3.16$	.2	.033
Right dysrhythmia ^a	3±1.3	2.5±1.7	2.4±1.8	$\chi^2_{(2,96)}=2.85$	.24	.030
Left dysrhythmia	2.6±1.4	2.9±1.6	2.1±1.7	$\chi^2_{(2,96)}=5.28$	.07	.055
5) Total timed movements ^b	98.71±25.5	117.83±29.1	105.15±24.6	F _(2,93) =4.51	.01*	.088
Right timed movement ^b	46.99±8.5	53.71±13.8	47.55±11.8	F _(2,93) =3.40	.04*	.069
Left timed movements ^b	47.52±9.6	57.08±14.8	49.38±13.2	F _(2,93) =5.23	.007*	.102

Note. PANESS = Physical and Neurological Examination for Subtle Signs; ANX = anxiety disorder.

^a χ^2_2 = Kruskal–Wallis test and F = Fisher's exact test.^b Number of movements in raw scores.^c Time in seconds in raw score.

* Statistically significant p value.

Table 3

Cognitive Measures

	ANX	ADHD	ANX+ADHD	Test ^f	p	p ^g
<i>Digit Symbol^a</i>	9.48±2.4	10.29±2.5	9.4±2.5	$\chi^2_{(2,96)}=2.56$	.28	.027
<i>Digit Span^a</i>	13.26±5	12.19±3	15.69±12.5	$\chi^2_{(2,95)}=.17$	.92	.002
<i>TMT A^b</i>	63.1±23.8	80.9±43.2	75.2±45.9	$F_{(2,90)}=1.78$	.17	.038
<i>TMT B^b</i>	152.4±75	162.4±71	156.8±74	$F_{(2,91)}=.16$	.85	.004
<i>TMT B^c error</i>	2.17±2.8	4.68±3.9	3±3.3	$\chi^2_{(2,96)}=10.28$	.006[*]	.108
<i>Stroop Interference^d</i>	31.8±12.5	49.81±24.9	33.14±20	$F_{(2,85)}=9.43$	.000[*]	.182

Note. ANX = anxiety disorder; TMT = Trail Making Test.

^a χ^2 = Kruskal–Wallis test and F = Fisher’s exact test.

^b Standardized scores.

^c Raw scores, time in seconds.

^d Number of errors.

^e Calculated scores by $C - ([A \times B] / [A + C])$ formula described in the text.

^{*} Statistically significant p value.

Table 4

Post Hoc Pairwise Comparisons.

<i>Variables</i>	<i>Groups</i>			<i>Test</i>
	<i>ANX vs ADHD</i>	<i>ANX+ADHD vs ADHD</i>	<i>ANX vs ANX+ADHD</i>	
<i>Total gait and stations</i>	.006[*]	.67	.27	<i>Dunnet's C</i>
<i>Total overflows</i>	.007[*]	.042[*]	.99	<i>Dunnet's C</i>
<i>Total timed movements</i>	.01[*]	.14	.64	<i>Tukey HSD</i>
<i>TMT B errors</i>	.001[*]	.06	.39	<i>Mann-Whitney U</i>
<i>Stroop Interference</i>	.001[*]	.002[*]	.99	<i>Tukey HSD</i>

Note. ANX = anxiety disorder; TMT = Trail Making Test.

^aNumber of errors.^{*}Statistically significant p value.

Table 5
Bivariate Correlations Among the Soft Neurological Signs and Cognitive Test Results.

	Impersistence	Total gait and stations	Total overflow	Total dysrhythmia	Total timed movements	Stroop	TMT B errors	TMTB	TMTA	Digit symbol
<i>Total gait and stations</i>	.55*									
<i>Total overflow</i>	.21	.53*								
<i>Total dysrhythmia</i>	.16	.32*	.41*							
<i>Total timed movements</i>	.26	.44*	.44*	.38*						
<i>stroop</i>	.33	.28	.28	.10	.34					
<i>TMT B error</i>	.23	.10	.12	-.05	.15	.34*				
<i>TMTB</i>	.23	.22	.05	-.05	.12	.27	.44*			
<i>TMTA</i>	.29	.57*	.40*	.10	.55*	.30	.21	.42*		
<i>Digit symbol</i>	-.15	-.20	-.05	-.07	-.17	-.12	-.15	-.11	-.15	
<i>Digit span</i>	-.10	.02	.10	-.04	-.01	.05	.02	-.16	-.07	.39

Note. TMT = Trail Making Test.

* $p = .000$ for bivariate correlations.