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Temperament Profiles in Preschool Attention-Deficit/Hyperactivity Disorder

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Abstract

Background

Attention-deficit/hyperactivity disorder (ADHD) is a heterogeneous disorder. Temperament may explain some of the heterogeneity underlying ADHD and improve clinical characterization. This study aimed to identify temperament-based profiles in preschoolers with ADHD and investigate their clinical correlates.

Methods

153 children aged 3 to 5 years (47–71 months) with a diagnosis of ADHD participated in an 8-week randomized controlled trial and subsequent 4-year follow-up study in Brazil (NCT02807870). Temperament was assessed using the Child Behavior Questionnaire-Short Form (CBQ-SF). Community detection analysis was applied to identify subgroups based on baseline lower-order temperament dimensions. Analysis of variance and logistic regression models were adopted to establish the clinical correlates of these subgroups.

Results

Three temperament-based subgroups were identified: (1) extroverted, characterized by lower fear and shyness as well as higher impulsivity; (2) irritable, characterized by lower soothability and smiling/laughter as well as higher anger, discomfort, fear, sadness, and shyness; and (3) mild, characterized by lower levels of anger, activity level, approach, high-intensity pleasure as well as higher levels of soothability, attentional focus and inhibitory control. At baseline, the mild subgroup showed lower ADHD symptom severity, irritability, and disruptive behavior, whereas the irritable subgroup had a higher rate of oppositional defiant disorder, irritability, and disruptive behaviors. In the 4-year follow-up, the irritable subgroup showed higher odds of anxiety disorders than the mild subgroup, after adjustment for sex (OR = 2.77, 95% CI [1.15, 6.70]).

Conclusions

Temperament-based clustering identified clinically interpretable ADHD subgroups in preschool children. These profiles may provide a framework for characterizing ADHD heterogeneity.

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by persistent patterns of inattention and/or hyperactivity-impulsivity that are inconsistent with the developmental level and that cause impairment in functioning in multiple settings [1]. The prevalence of ADHD is estimated at ~ 5% in childhood and adolescence [2]. ADHD is associated with early emotional

dysregulation, poor academic adaptation, and family and peer relationship difficulties that may persist into adolescence and adulthood [2]. In preschool children, typically defined as younger than 6 years, it is estimated that ~ 2.1% of children may have an ADHD diagnosis [3]. Preschool ADHD frequently presents with prominent emotional dysregulation, oppositionality, and emerging executive dysfunction [4]. It shares early risk markers with school-age ADHD [5] and shows substantial developmental continuity, with longitudinal evidence indicating that symptoms and impairment often persist into school age at clinically significant levels [6].

The ADHD population is highly heterogeneous in clinical profile, with differences in symptom presentation, comorbidity, cognitive characteristics, and treatment response. Therefore, reducing phenotypic heterogeneity may improve the understanding of symptom specificity, etiological mechanisms, clinical prediction, and personalized treatment [7]. One promising framework to describe early ADHD heterogeneity is temperament. In Rothbart's psychobiological model, temperament refers to constitutionally based individual differences in reactivity and self-regulation [8, 9]. This model is relevant to ADHD because the disorder is associated with difficulties with self-regulation and, in specific subgroups, elevations in reactivity, such as negative affect and surgency/extraversion [10]. Temperament can therefore provide a developmentally informed formulation of emotional patterns beyond core ADHD symptoms [8, 11].

Preliminary data-driven reports have provided consistent signals of the importance of temperament to map the heterogeneity of ADHD. For instance, Karalunas et al. [11] identified three temperament-based subgroups in school-aged children with ADHD: mild, with relatively normative emotional functioning; surgent, with higher approach motivation and positive affect; and irritable, with elevated negative affectivity. The subgroups were distinguished by peripheral physiology, neural connectivity, and clinical outcomes after 1 year. Subsequently, Karalunas et al. [12] confirmed the distinctiveness of these profiles across independent samples, with moderate stability over 2 years and described the irritable group as having greater clinical severity and possible adverse prognosis. Goh et al. [13] further replicated these three temperament-based ADHD subgroups and described similarly meaningful differences in clinical presentation and comorbidity. More recently, Blanken et al. [14] also identified a three-group model. However, no distinct irritable group emerged. Specifically, two groups showed similarly elevated neuroticism but differed in agreeableness and openness, while one group resembled a mild profile. Differences in sample characteristics, the measurement instrument used, and the underlying theoretical model may explain the distinct profiles. Altogether, these studies support temperament-based subtyping as a promising framework for improving ADHD clinical description.

Nevertheless, ADHD temperament-based subtyping remains a recent concept with limited evidence base. Notably, to the best of our knowledge, the evidence is limited to children and adolescents aged 6 to 12. The developmental stage should be considered when identifying subtypes, given that ADHD is associated with maturational changes across development [15]. To address this gap, we sought to identify and characterize temperamental clusters in a sample of preschoolers with ADHD who originally participated in a randomized controlled trial and its subsequent follow-up study, comparing the results

with profiles reported in the literature. Through leveraging this rich phenotypic data collected throughout 4 years, we aimed to investigate whether the temperament-based profiles may help identify higher risk of comorbid disorders across development.

METHODS

Participants were recruited from the MAPPA study, an 8-week randomized clinical trial conducted at the Institute of Psychiatry, Hospital das Clínicas, University of São Paulo Medical School, São Paulo, Brazil (NCT02807870). A total of 153 participants were randomized 1:1:1 to methylphenidate + educational intervention (n = 51), placebo + behavioral parent training (n = 51), and placebo + educational intervention (n = 51) [16].

Subsequently, patients were referred to clinical services in the community and were naturalistically followed up for 4 years with annual assessments to investigate psychiatric disorders, ADHD trajectories and other psychiatric symptoms. Of all eligible patients, 121 (79%) were assessed in the 4th year and an additional 17 (11%) provided data on the third year, totaling 138 (90%) patients for this follow-up study analysis.

This study was approved by the Institutional Review Board (IRB) of the Clinical Hospital of the School of Medicine, University of São Paulo, under the Certificate of Presentation for Ethical Appreciation (CAAE) number 11581412.7.0000.0068. Written informed consent was provided separately by the parent or primary caregiver. This study is a secondary analysis and was not pre-registered independently. The research questions, subgroup identification approach, and clinical correlate analyses were formulated after completion of the primary trial, and the temperament-based clustering reported here was not specified in the original trial protocol.

Participants

The sample consisted of 153 children with ADHD (84% male) aged 47 to 71 months (mean [standard deviation] 60.45 [7.60]). ADHD and comorbid diagnoses were based on the semi-structured interview Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL [17]) conducted by a child and adolescent psychiatrist. Inclusion criteria included moderate to severe symptoms, defined as parent ratings of 32 or greater on the Swanson, Nolan, and Pelham-IV scale (SNAP-IV [18]), and school or daycare registration. Children were not eligible if they had IQ below 70; affective, psychotic, or autism spectrum disorders; psychotropic medication use during the previous 30 days; a major clinical condition such as unstable epilepsy or cardiovascular disease; a history of neurological disorder or head trauma with loss of consciousness; or if their parent or caregiver was unable to understand the study objectives and instructions.

Assessments

Temperament. Temperament was assessed using age-appropriate Rothbart temperament scales describing three higher-order domains: negative affectivity, surgency/extraversion, and effortful control [9, 19]. The validated questionnaire Child Behavior Questionnaire-Short Form (CBQ-SF) was used, rating typical behavior during the previous 6 months using a Likert-type scale. Items measure different lower-order temperament dimensions distributed across the three higher-order domains [20]. The negative affectivity domain is represented by anger/frustration, discomfort, falling reactivity/soothability, fear, and sadness. The surgency/extraversion domain is represented by activity level, approach/positive anticipation, high-intensity pleasure, impulsivity, and low shyness. The effortful control domain is represented by attentional focusing, inhibitory control, low-intensity pleasure, perceptual sensitivity and smiling and laughter.

Clinical correlates. Irritability was assessed using the Affective Reactivity Index (ARI) reported by parents, a brief seven-item dimensional measure designed to quantify irritability in children over the previous 6 months [21]. Preschool (from 3 to 5 years and 11 months) and school-age (above 6 years old) versions of the Multidimensional Assessment Profile of Disruptive Behavior (MAP-DB) were used to assess disruptive behaviors [22, 23]. Dimensional domains include temper loss, aggression, noncompliance, low concern for others, punishment insensitivity and sneaky (this last domain only presented in school-age version); caregivers rate items according to the child's frequency of specific disruptive behaviors over the previous month. Intelligence quotient (IQ) was assessed using the Wechsler Preschool and Primary Scale of Intelligence [24]. Attentional and cognitive performance was evaluated with the Conners Kiddie Continuous Performance Test, Second Edition (K-CPT 2), a computerized continuous performance task used to assess sustained attention, response inhibition, reaction time, omission errors, commission errors, and related attentional indices in young children [25]. Global psychological, social, and functional impairment was assessed with the Children's Global Assessment Scale (CGAS), a clinician-rated measure of overall child functioning across home, school, and peer contexts, ranging from 0 to 100 [26]. Overall clinical severity was rated using the Clinical Global Impression (CGI) scale, a clinician-rated global index of illness severity and clinical change widely used in psychiatric research [27]. During the naturalistic follow-up, at each annual assessment, ADHD and comorbid diagnoses were based on the K-SADS-PL; ADHD severity was measured using the SNAP-IV scale, evaluated by independent raters based on parent interviews; Irritability and disruptive behaviors were measured by ARI and MAP-DB.

Data Analysis

Community detection. Community detection, a well-known clustering method in complex networks, was used to identify subgroups of densely connected individuals within a network of people from our sample [28, 29]. Specifically, we used standardized baseline CBQ-SF temperament subscales and computed Spearman's rank correlation coefficient for each pair of individuals to produce a child-by-child correlational matrix [30]. We used this correlational matrix as input into the Rubinov and Sporns method from the Brain Connectivity Toolbox to obtain the subgroups [31]. To identify the communities, we applied a weight-conserving modularity algorithm that starts with each node in its own community and iteratively joins communities whose conjunction produces the largest increase in modularity (Q) until Q

reaches its maximum. The value of Q was interpreted as the level of segregation between identified communities. Because modularity-based community-detection algorithms are heuristic and may yield run-to-run variability, we repeated the algorithm 10 times and assigned each participant to the community in which they were most frequently classified, thereby obtaining a single stable partition. This procedure follows the general rationale of consensus clustering approaches to reduce algorithmic instability [32]. To verify the internal validity of the identified subgroups, we compared the subgroups for differences in the CBQ-SF subscales at the baseline.

Clinical correlates. We assessed the clinical correlates by comparing diagnostic and symptomatic features, cognitive performance, and functional outcomes across groups at baseline and the latest available point from the follow-up (year 4 and, if not available, year 3) in separate analyses. For continuous variables, we used analysis of variance (ANOVA) to test mean differences among multiple groups [33]. When significant differences were observed in temperament subscales across clusters, Tukey's Honest Significant Difference (HSD) test was used to conduct *post hoc* pairwise comparisons between cluster means while accounting for multiple comparisons [34]. For follow-up categorical variables, we fitted weighted binary logistic regression models using anxiety disorders (including specific phobias, separation anxiety, social anxiety and generalized anxiety disorder) and depression (disorder) as dependent variables. A minimum of ten outcome events per predictor variable was adopted as the criterion for stable parameter estimation in the logistic regression models, following established recommendations for binary outcomes in small-to-moderate samples [35]. The mild subgroup was used as the reference category. We estimated a model including temperament subgroups and sex.

RESULTS

Community detection

Community detection analysis identified three temperamentally distinct subgroups of relatively similar size (number of participants [percentage]: 52 [34%], 49 [32%], and 52 [34%]) (Figure 1). The modularity quotient (Q = 0.49) indicated strong community structure, reflecting substantially greater within-group than between-group temperament similarity [28, 29]. Analysis was repeated across 10 runs of the modularity algorithm, and the final stable solution was based on the modal group assignment across runs.

When comparing the baseline temperament scores across subgroups (Figure 2 & Table 1), group 1 (labeled extroverted) showed lower fear and shyness as well as higher impulsivity (all $p < .001$); group 2 (labeled irritable) showed lower soothability and smiling/laughter (all $p < .001$), as well as higher anger, discomfort, fear, sadness, and shyness (all $p < .001$); and group 3 (labeled mild) showed lower anger, activity level, approach, and high-intensity pleasure (all $p < .001$) as well as higher soothability, attentional focus, and inhibitory control (all $p < .001$).

Clinical correlates

The three groups were similar in age, but the sex distribution differed across subgroups (p = .011), with the extroverted group showing a lower proportion of males than the other groups (Table 2). IQ and K-CPT 2 scores did not differ significantly between groups, nor did baseline CGAS scores. ADHD symptom severity varied significantly by subgroup. The mild group showed lower SNAP-IV total, inattentive, and hyperactive-impulsive scores than both extroverted and irritable groups (all p < .001). Comorbid oppositional defiant disorder differed significantly across groups (p = .003), with the highest prevalence in the irritable group (57.1%) and the lowest in the mild group (25%). Conduct disorder and anxiety disorders had higher numerical prevalence in the irritable group compared with both other subgroups, but without statistical significance (p = .111 and p = .113, respectively). Irritability, measured by the ARI, showed a graded pattern across groups, with highest scores in the irritable group, intermediate scores in the extroverted group, and lowest scores in the mild group (p < .001). Preschool MAP-DB dimensions also differed across subgroups. The irritable group showed higher low concern for others than the mild group (p = .016) and higher aggression than both the extroverted and mild groups (p < .001). Temper loss, noncompliance, and punishment insensitivity were significantly lower in the mild group than in both the extroverted and irritable groups (all p < .001) (Table 2).

Follow-up data indicated that children in each of the three temperament-derived subgroups did not differ significantly in CGAS or CGI scores at ages 7 to 9 years (Table 3). The mild group continued to have lower SNAP-IV total scores than both extroverted and irritable groups (p = .002), as well as lower inattentive (p = .018) and hyperactive-impulsive symptoms (p = .002). Compared with the other groups, the irritable group continued to have a higher comorbidity rate over time (p = .016) and had a higher presence of conduct disorder at any time point (p = .039). The irritable group also showed higher ARI scores than the mild group (p = .014). In the weighted logistic regression model adjusted for sex, the irritable subgroup showed significantly higher odds of anxiety disorders compared with the mild subgroup (β = 1.02, SE = 0.45, *p* = 0.023), corresponding to approximately 2.77-fold higher odds of anxiety (OR = 2.77, 95% CI [1.15, 6.70]) (Figure 3 & Table 4). The extroverted subgroup did not differ from the mild subgroup (β = 0.10, SE = 0.44, *p* = 0.827), and sex was not significantly associated with anxiety (β = −0.18, SE = 0.49, p = 0.718). Depression was not analyzed because only 7 of the 138 participants included in the follow-up analysis met criteria for this diagnosis, yielding too few outcome events for stable parameter estimation in a weighted logistic regression model adjusted for subgroup and sex.

DISCUSSION

This study investigated a clinical sample of 153 preschool children with ADHD and identified three temperament-based subgroups that were clinically distinct and informative of clinical outcomes 4 years later. Community detection analyses revealed an extroverted profile, characterized by lower levels of fear and shyness and higher levels of impulsivity; an irritable profile, characterized by lower levels of soothability and smiling/laughter and higher levels of anger, discomfort, fear, sadness, and shyness; and a mild profile, characterized by lower levels of anger, activity level, approach, and high-intensity pleasure and higher levels of soothability, attentional focus, and inhibitory control. These subgroups were not differentiated by cognitive impairment or functional severity. However, differences were observed in

ADHD symptomatology, ODD comorbidity, irritability, and disruptive-behavior scores. Additionally, the irritable subgroup showed higher odds of anxiety disorders at the 4-year follow-up.

These findings support the view that temperament-based phenotyping can capture clinically relevant heterogeneity within ADHD [7, 11–13]. The three profiles observed in our study resemble temperament-based ADHD subgroups previously described in school-aged samples [11, 12]. Our study expands these findings to preschool children.

At follow-up, some baseline differences persisted while others attenuated or disappeared. The mild group continued to show lower ADHD severity, and the irritable group retained higher irritability and greater cumulative comorbidity burden, including higher conduct disorder rates across time. However, MAP-DB disruptive-behavior dimensions were no longer significantly different, suggesting possible convergence in parent-observed disruptive behaviors. Possible reasons for this convergence include developmental change and informant bias, or possibly treatment effects or reduced statistical power due to drop-out. Although there was a trend toward less stimulant prescription in the irritable subgroup, this finding should be interpreted cautiously. Stimulant treatment in ADHD has been shown to improve emotional dysregulation and irritability [36–38], so lower stimulant exposure in the irritable subgroup most likely reflects greater clinical complexity, comorbidity burden, tolerability concerns, or treatment-selection factors rather than poorer stimulant response [7, 39, 40].

The association between the irritable subgroup and anxiety is consistent with developmental models in which irritability is conceptualized as a transdiagnostic phenotype linking ADHD with both externalizing and internalizing outcomes [41, 42]. It is also consistent with longitudinal evidence suggesting that early irritability and negative affectivity can co-develop with anxiety and disruptive symptoms across childhood, reflecting overlapping pathways of emotional reactivity, threat sensitivity, and impaired affective regulation [43, 44]. The co-occurrence of anxiety disorders and higher conduct disorder in the irritable subgroup might be interpreted as a marker of this clinical complexity. Conduct disorder is highly heterogeneous, with emotionally reactive presentations, in which higher negative affectivity, irritability, threat sensitivity and reactive aggression may be prominent [45, 46]. Also, early onset of conduct disorder has been associated to a persistent course, higher exposure to risk factors, such as harsh and inconsistent discipline and parental psychopathology, and negative outcomes including higher frequency of convictions in adulthood. Within this framework, anxiety symptoms and conduct problems may coexist as partially overlapping expressions of broader affective and behavioral dysregulation, particularly in children with higher irritability and externalizing liability [45].

This study reinforces temperament as a possible tool for ADHD heterogeneity assessment and as a developmentally grounded strategy for clinical stratification. Nigg [7] argues that ADHD often functions as an early gateway phenotype for later externalizing and internalizing complications, and that temperament may serve as an early marker for identifying different developmental pathways. In this context, the mild group may represent a standard-care group due to reduced clinical severity and lower comorbid complexity compared with other profiles. Conversely, the irritable subgroup may represent a

particularly important clinical phenotype because of higher irritability, greater externalizing comorbidity and increased chances of anxiety disorders. Irritability is common in ADHD and is associated with later anxiety, depression, behavioral problems, suicidality, and impairment independent of comorbid diagnoses [41, 42]. Therefore, care for the irritable subgroup may require specific clinical planning with longitudinal monitoring for conduct problems [47, 48].

This study had strengths such as the use of a well-characterized clinical preschool ADHD sample, a data-driven community detection approach, developmentally appropriate Rothbart-based temperament measure and longitudinal follow-up integrating multiple outcomes for a broad clinical profile. Limitations include recruitment from a specialized clinical trial sample, which may reduce generalizability; drop-out across follow-up and reliance on the last available assessment for longitudinal comparisons for 90% of the sample; and the use of questionnaire-based temperament ratings with possible informant bias and no observational measures. The number of outcomes also increases the possibility of chance findings, and our observational longitudinal analyses cannot establish causal pathways. Future work should replicate these findings in larger, diverse, multisite preschool cohorts; investigate differences in neurobiological mechanisms; test whether temperament profiles predict differential response to behavioral and pharmacological interventions; and integrate temperament

with neurocognitive and contextual measures.

Conclusion

Temperament-based community detection identified three clinically interpretable profiles in preschool children with ADHD: extroverted, irritable, and mild. These profiles were associated with distinct baseline clinical characteristics and partially differentiated longitudinal outcomes. The mild group showed a less severe symptom and comorbidity profile, whereas the irritable group showed higher irritability, externalizing symptomatology, cumulative comorbidity over time and increased chances of anxiety disorders. Temperament-based profiling may therefore contribute to a more developmentally informed approach to ADHD heterogeneity and early clinical stratification.

Abbreviations

ANOVA, analysis of variance; ARI, Affective Reactivity Index; CBQ-SF, Child Behavior Questionnaire-Short Form; CGAS, Children's Global Assessment Scale; CGI, Clinical Global Impression; K-CPT 2, Conners Kiddie Continuous Performance Test, Second Edition; K-SADS-PL, Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version; MAP-DB, Multidimensional Assessment Profile of Disruptive Behavior; SNAP-IV, Swanson, Nolan, and Pelham-IV scale.

Declarations

Funding

No funding was received to assist with the preparation of this manuscript.

Competing interests

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Ethics approval

This study was performed in line with the principles of the 1964 Declaration of Helsinki and its later amendments. The study was approved by the Institutional Review Board of the Clinical Hospital, School of Medicine, University of São Paulo (Certificate of Presentation for Ethical Appreciation – CAAE – no. 11581412.7.0000.0068).

Consent to participate

Written informed consent was obtained from the parent or primary caregiver of each participant.

Data availability

The data that support the findings of this study are not publicly available due to ethical restrictions and participant confidentiality requirements, as approved by the Ethics Committee of Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HC-FMUSP). The primary trial is registered at ClinicalTrials.gov (NCT02807870). Deidentified data may be made available upon reasonable request to the corresponding author, subject to institutional review board approval and execution of a data sharing agreement.

Author contributions

M.V.M.F. and G.V.P. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Conceptualization: [Guilherme Vanoni Polanczyk; Mauro Victor de Medeiros Filho]. Methodology: [Guilherme Vanoni Polanczyk; Luis Carlos Farhat; Mauro Victor de Medeiros Filho]. Formal analysis and investigation: [Mauro Victor de Medeiros Filho; Grover Enrico Castro Guzman] Writing – original draft preparation: [Mauro Victor de Medeiros Filho]. Writing – review and editing [all authors].

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Tables

Tables 1 to 4 are available in the Supplementary Files section.

Figures

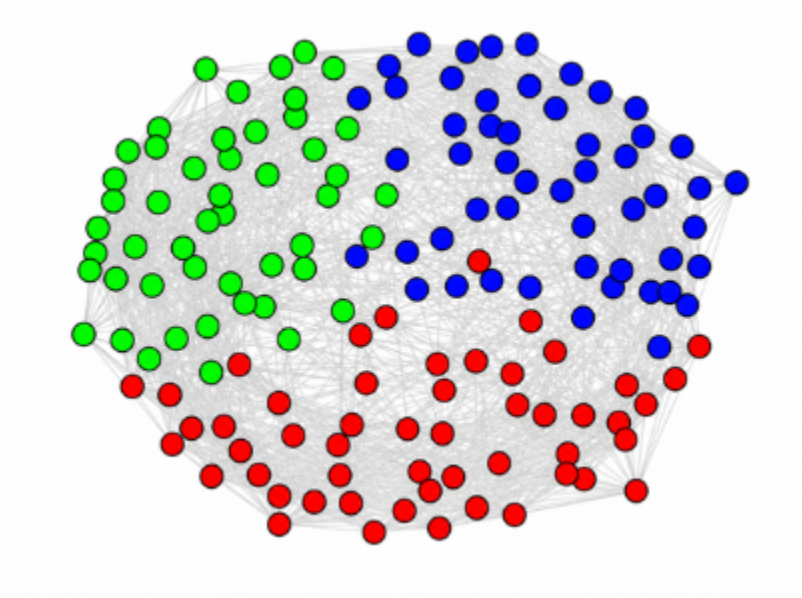


Figure 1

Spring-embedded visualization of temperament subgroups

Note. Nodes represent individuals and connecting edges indicate correlations between individuals. Group 1 (extroverted) with 52 [~34%] patients is represented by red nodes; group 2 (irritable) with 49 [~32%] patients by green nodes; and group 3 (mild) with 52 [~34%] patients by blue nodes. The modularity quotient was Q = 0.49.

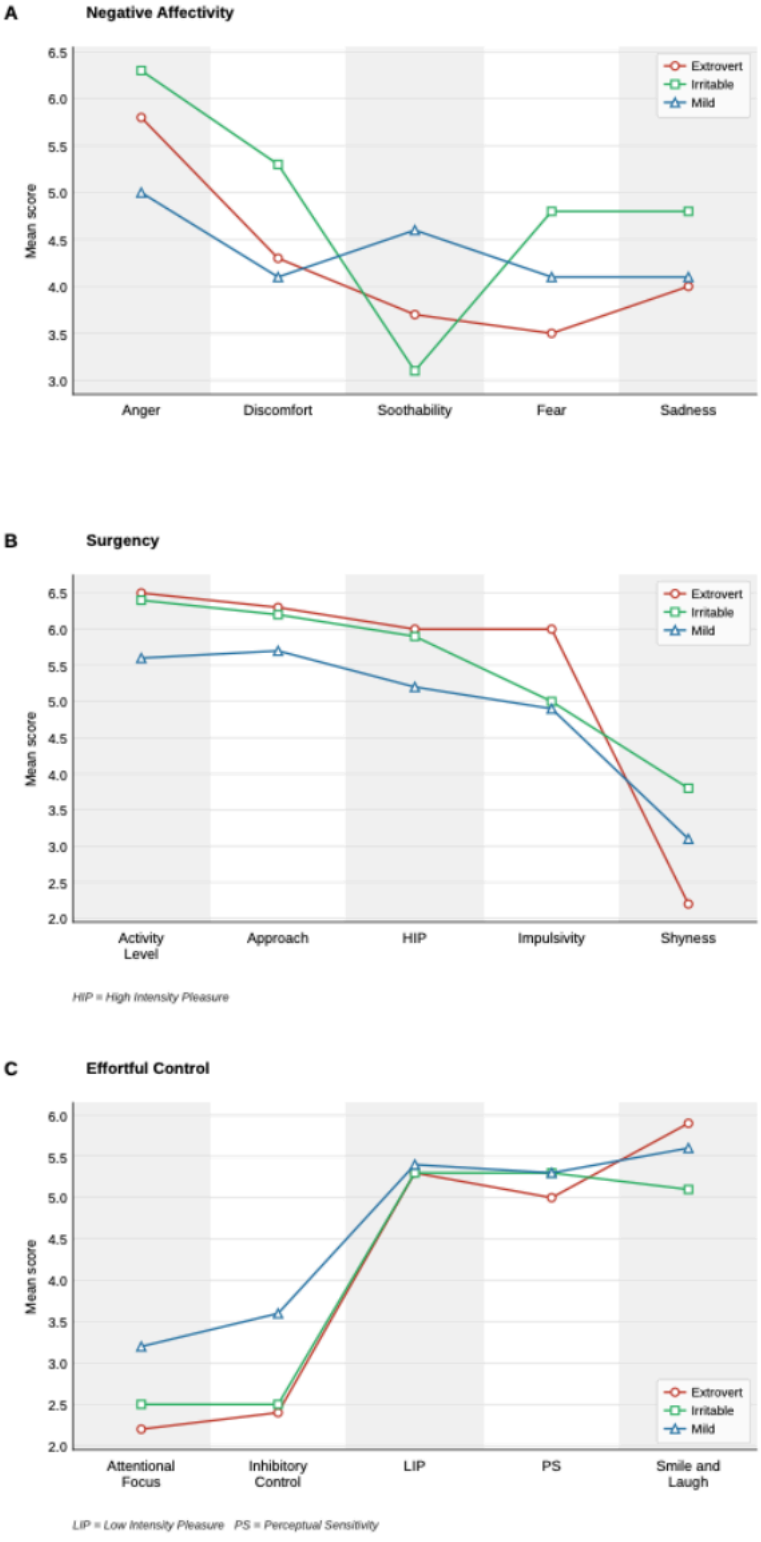


Figure 2

Temperament subgroup profiles



Figure. *Odds ratios (OR) with 95% confidence intervals (CI) for anxiety disorder diagnosis at 4-year follow-up. Weighted logistic regression model adjusted for sex; Mild subgroup as reference category. Filled diamond = statistically significant ($p < 0.05$); circle = non-significant. Dashed vertical line indicates OR = 1.00 (null effect). OR = Odds Ratio; CI = Confidence Interval.*

Figure 3

Odds ratios for anxiety disorders at 4-year follow-up

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1to4.docx