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Original Research

Towards a Distinct Sleep and Behavioural Profile of Fetal Alcohol Spectrum Disorder (FASD): A Comparison between FASD, Autism and Typically Developing Children

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Abstract

Background: The term Fetal Alcohol Spectrum Disorders (FASD) describes a range of neurodevelopmental conditions, the direct result of prenatal alcohol exposure. FASD encompasses a range of behavioural, cognitive and sleep patterns that are sometimes indiscernible from other neurodevelopmental conditions, one in particular being Autism Spectrum Disorders (ASD). This study aimed to provide a comparison of behavioural, cognitive, affect-related and sleep profiles in children aged between 6 and 15 years with diagnoses of FASD or ASD, in contrast to typically developing (TD) children. **Methods**: We compared 29 children with FASD, 21 children with ASD and 45 typically developing (TD) children on parental-reported questionnaires measuring behaviour and executive functioning: the Child Behaviour Checklist (CBCL), the Spence Children's Anxiety Scale (SCAS) and the Behaviour Rating Inventory for Executive Function (BRIEF). Additionally, parents completed the Children's Sleep Habits Questionnaire (CSHQ), and children wore actigraphy watches while sleeping to objectively capture their sleep habits. The three groups were compared using ANCOVA, controlling for age effects. **Results**: Children with FASD scored significantly higher than the other two groups on the CBCL subscales of attention problems, somatic complaints, social problems, delinquency, and aggressive behaviour, as well as the panic subscale of the SCAS. Children with FASD also scored higher on all measures of the BRIEF than the ASD and TD groups, indicating greater problems with working memory and more difficulty shifting between tasks, planning, organising, inhibiting their behaviour and exercising emotional control. Nocturnal sleep duration in children with FASD was reported as one hour less than TD children and 46 minutes less than children with ASD per night. **Conclusions**: The findings in this study highlight several syndrome specific features (shorter sleep duration, executive functioning difficulties, and higher levels of social and behavioural problems and panic) that potentially contribute to the unique phenotype of FASD. Whilst this research highlights the need for further work in this area, initial clinical screening for FASD should take such data on discernible characteristics, particularly the syndrome specificity of the BRIEF, into consideration.

Keywords: FASD; prenatal alcohol exposure; ASD; Autism; sleep; syndrome specificity

1. Introduction

Fetal Alcohol Spectrum Disorders (FASD) develop due to prenatal alcohol exposure (PAE) and are estimated to be present in 2.4–4.8% of school aged children in Western Europe, Canada, and the USA [1–3]. The prevalence of sleep problems in children with FASD ranges from 55% to 85% and specifically includes sleep onset delays, increased sleep fragmentation and early waking [4–6]. Pesonen and colleagues [7] found in a sample of 289 children, that the 51 children whose mothers consumed more than 12 gm alcohol per week during pregnancy had an increased likelihood of reduced sleep efficiency and sleep duration. High levels of sleep problems in FASD have been linked with alterations to gene expression in hypothalamic neurons which regulate the circadian rhythm [8]. PAE can also cause structural changes to the cerebellum, which plays a role in homeostatic regulation involved in Non- Rapid Eye Movement (NREM) sleep [9,10]. Additionally, abnormal melatonin secretion in FASD may contribute to either delayed sleep phase (17% participants), advanced sleep phase (8% participants) or otherwise abnormal melatonin onset (54% participants [11]). To illustrate this a recent study found via subjective measures and polysomnography (PSG) that 55% of children with FASD had reduced Rapid Eye Movement (REM) and more night-time arousals, compared to 20% of typically developing (TD) children [12].

Children with FASD present with a range of behavioural and cognitive difficulties, such as challenges with working memory and organisational difficulties, challenging daytime behaviour, impulsivity, hyperactivity and inattentiveness [5,13]. Behavioural, executive function and psychological outcomes (e.g., anxiety) present in children with FASD may be exacerbated by sleep difficulties, as demonstrated in the broader literature with children with Autism Spectrum Disorders (ASD) and typically developing children [14,15]. Sleep difficulties in children with ASD have also repeatedly been linked with challenging daytime behaviour [16,17]. Whilst clearly distinct, many

Table 1. Demographics table.

		FASD (n = 27)	ASD (n = 20)	TD (n = 45)	F (df)	p	η^2
Age (years)	Mean:	9.87 †	8.84	8.12	8.70	<0.001	0.03
	SD:	2.31	1.73	1.28	(2,89)		
Sex (Male/Female)		15/12	16/4	23/22	2.52 (2,89)	0.05	0.03
SES (1/2/3)		2/19/6	5/14/1	6/30/9	2.43 (2,89)	0.09	0.009

Participants' demographic information within each diagnostic group, detailing the distribution of age, sex and socioeconomic status and the results of between-group univariate ANOVA tests for each demographic variable † indicates where the FASD group means were significantly higher than TD and ASD.

of the pathologies of ASD and FASD overlap. Bishop [18] found 34% of children with PAE in a sample of 29 showed social withdrawal and repetitive behaviours commonly seen in children with ASD. It was also found that children performed differently when interacting with peers, internalizing, and in areas of non-verbal communication [18].

In children with ASD, sleep difficulties can be associated with symptoms typically found in children with attention deficit hyperactivity disorder (ADHD), including hyperactivity and inattention [14]. Similarly, poor sleep has been linked to problems with verbal fluency, problem solving, inhibition, attention, and memory formation in TD children [19,20]. Sleep problems are common in children with ASD and proposed contributing factors include anxiety or attachment issues around bedtime, atypical circadian functioning due to dysfunction in translation and transcription mechanisms for genes linked to the sleep and internal timing process and irregular melatonin regulation [21–23]. As sleep profiles have been widely studied in both ASD and TD groups, comparing these with FASD will clarify any distinctiveness in FASD's sleep and behavioural profile not yet established elsewhere.

To provide further insight into the understanding of phenotypic characteristics in FASD, this study aimed to provide a comparison of behavioural, cognitive, affect-related (anxiety), and sleep profiles between the three groups (children with FASD, children with ASD and their typically developing peers).

2. Materials and Methods

2.1 Participants

Ninety-five caregiver and child dyads participated in the study. Children were aged between 6 and 15 years old (M = 8.6 years old) and were diagnosed with either ASD (21 children, 4 females); or FASD (29 children, 13 females) and 45 had no diagnosis (22 females). Full demographic data of the parent-child dyads is shown in Table 1. Children with FASD were notably older than children with ASD and TD. FASD tends to be diagnosed later due to waiting lists, reduced societal awareness and the fact that there is only one dedicated FASD diagnostic clinic in the UK. This is likely to explain the increased age in the FASD volunteer cohort shown in Table 1. All children met the following eligibility criteria as reported by the parents; (1) a diagnosis of FASD or ASD by a healthcare professional or no clinical neurodevelopmental diagnosis (TD group); (2) be aged between six to fifteen years old, inclusive. Children in the ASD group were not eligible if they reported a co-occurring neurodevelopmental condition. All participants with a diagnosis were asked to provide details of the clinic and clinician who made the diagnosis. Participants with FASD were invited to participate directly from the UK FASD clinic where diagnosis had been established. As diagnostic criteria for FASD typically overlaps with other conditions, children in the FASD group were ineligible if they also reported co-occurring ASD but no other conditions affected their eligibility. Other conditions that co-occurred in the FASD group included ADHD, Sensory-Processing Disorder and Conduct Disorder.

2.2 Procedure

Recruitment involved a multi-channel approach comprising of advertisements through online ASD forums, the UK FASD Network mailing list and a school in West London. Parents completed multiple online questionnaires. To collect objective sleep data children were then invited to wear an actigraphy watch for one week on their non dominant wrist. Children in the TD group wore the watch consistently for seven days and nights. Children in the FASD and ASD groups wore the watch at bedtime and caregivers removed them in the morning. This was done to mitigate any discomfort caused to children with FASD and ASD for whom wearing the watch for the full duration of the study could trigger sensory issues. Actigraphy data were collected during term time, ensuring sleep data reflected a normal school week. Children wore a CamNTech Motionware Actiwatch 8 (CamNTech, 2019). Actigraphy were set to default 'medium' sensitivity level and sampled at 50 Hz, collecting samples in one-minute epochs of data. Ethics for the study were approved by the UCL Institute of Education Research Ethics Committee.

2.3 Questionnaires

All families were asked to complete the following validated questionnaires along with the background demographic details in Table 1. Screening tools were used to confirm that children in FASD and ASD groups met diagnostic thresholds. Socioeconomic status (SES) was measured by asking caregivers questions about their ethnic origin, educational qualifications, and the job titles of all adults in the household. Based on their answers, they were given a National Statistics Socio-economic Classification score of 1, indicating managerial, administrative or professional occupations and/or higher education; 2, indicating intermediate occupations and A-levels or equivalent; or 3, indicating routine or manual occupations, or unemployed with some schooling [24]. The modal SES score was 2. The distribution of these scores is detailed in Table 1.

2.3.1 Autism Symptoms

The Childhood Autism Rating Scale, Parents Version (CARS; [25]) was used to test the severity of ASD symptoms. This is a 15-item screening questionnaire using a seven-point Likert Scale, ranging from typical to atypical behaviour. A score of 33 or higher indicates possible ASD for research purposes [26]. Categories include: relating to people, imitation, emotional responsiveness, body use, object use, adaptation to change, visual responses, listening responses, taste, smell, touch responses, fear or nervousness, verbal communication, nonverbal communication, activity levels, intellectual responsiveness and general observations. CARS has been shown to demonstrate moderate to good sensitivity, specificity (81.4% and 78.6% respectively) and good internal consistency (Cronbach's Alpha = 0.79).

2.3.2 FASD Symptoms

Severity of FASD symptoms was tested using the Neurobehavioral Screening Tool (NST; [27]) which is a ten-item binary checklist with questions examining whether children meet common neurobehavioral characteristics of FASD, although these are not always typical of children with FASD. Scores above 8, plus confirmed PAE indicate a FASD diagnostic evaluation should be carried out [27]. Categories included: acting young, lying and cheating, lacking guilt after misbehaving, difficulty concentrating, impulsivity, hyperactivity, displays of cruelty, stealing at home, and stealing outside the home. The NST has low sensitivity but high specificity (62% and 100% respectively) and is a widely used screening mechanism for FASD in children.

2.3.3 Child Anxiety

Spence Children's Anxiety Scale (SCAS; [28,29]) is a 38-item questionnaire which was used to measure frequency of symptoms of Diagnostic Statistical Manual (DSM) anxiety disorders. It is aimed at children aged 6–16 and uses a four-point Likert Scale with responses ranging from Never (0) to Always (3). Subscales include panic, separation anxiety, physical injury, social phobia, obsessive compulsive, generalised anxiety, and a total calculated across all subscales. Scores of 31 or higher are considered clinically relevant. The SCAS has high internal validity with a Cronbach's Alpha score of 0.996 in this sample.

2.3.4 Child Daytime Behaviour

The Child Behaviour Checklist (CBCL; [30]) is a 118-item questionnaire which was completed by parents and screens for the possibility of psychological disorders in school-age children. It gives a list of statements summarising common behavioural problems and uses a three-point Likert Scale ranging from 1 (sometimes true) to 3 (often true). Clinical scores are determined as 64 or above [31]. There are eight syndrome scales which include withdrawn/depressed, anxious/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behaviour (hereafter, delinquency), and aggressive behaviour. The total for each subscale, plus additional questionnaire items which did not fit into the subscales are combined to form a total score. The CBCL had a Cronbach's Alpha of 0.994, demonstrating high internal validity in this sample.

2.3.5 Child Executive Functioning

The Behaviour Rating Inventory for Executive Function (BRIEF; [32]) is an 83-item questionnaire which was used to assess executive functioning skills in home and school environments. Eight subscales are categorised as either metacognitive or behaviour regulation scales. The metacognitive scales include working memory, planning/organising, organising materials (ability to order spaces such as desks and backpacks), monitoring (ability to check work and assess ones' own performance), and initiation (ability to independently generate ideas and strategies or initiate an activity). The behaviour regulation scales include shifting (ability to move freely between activities or situations), inhibition, and emotional control. A 'total' is also calculated which is a composite of all clinically relevant scales (inhibition, shifting, emotional control, working memory and planning/organising). Clinical scores are determined as 65 and above. The BRIEF is widely used with high internal validity and consistency, a Cronbach's Alpha of 0.996 in this sample.

2.3.6 Child Sleep

The Children's Sleep Habits Questionnaire (CSHQ; [33]) is a 33-item questionnaire which was filled out by parents to assess their child's sleeping habits. It includes a three-point Likert Scale with options ranging from 'rarely' (0–1 times per week) to 'usually' (5–7 times per week). Scores are considered clinically relevant at 41 or above. Questions assess problems around bedtime routines, indica-

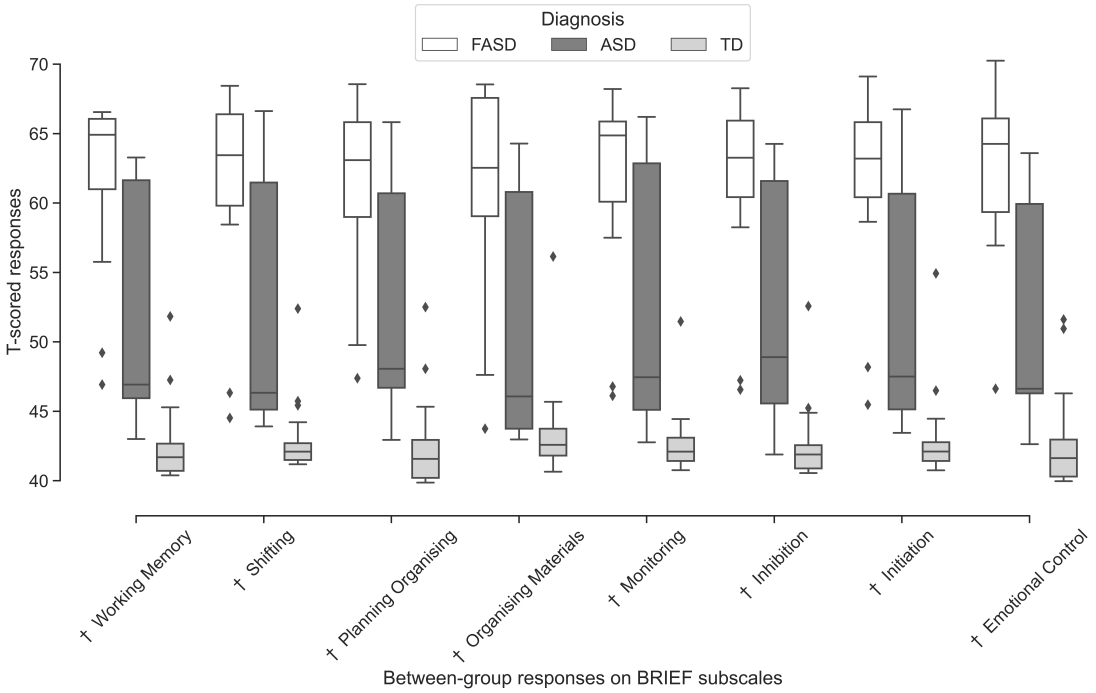

Fig. 1. Syndrome Specific Items in the Executive Function Questionnaire. A box plot showing T-scored responses to the BRIEF subscales, demonstrating the difference between groups in responses to this questionnaire. † indicates where the FASD group means were significantly higher than both TD and ASD.

tions that the child is not sleeping a normal amount, or that the child is waking during the night. Items are grouped into subscales: bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night waking, parasomnia, sleep disordered breathing, daytime sleepiness. The CSHQ has high internal validity and a Cronbach's Alpha of 0.999.

2.4 Data Analysis

Data were analysed and visualised using SciPy, Statsmodels, Pingouin and Seaborn packages in Python. Missing data were imputed through multiple imputations by chained equations using the Python Miceforest package. One child in the ASD group and two in the FASD group were excluded from final analysis due to non-completion of the questionnaires. Variables were T-scored at the participant level. Normality was established using the Shapiro-Wilk test and homogeneity of variance assessed using Levine's test. One-way between-group univariate ANOVA tests were used to assess differences between groups on demographic variables with etq squared (η^2) given to show effect size. To provide a comparison of behavioural, cognitive, affect-related (anxiety), and sleep profiles between the three groups between-group differences in questionnaire responses were tested across the FASD, ASD and TD groups using multivariate analysis of variance (MANOVA). Where significant results were observed, one-way between-group univariate Analysis of Covariance (ANCOVAs) were used to determine which variables showed a group effect, using age as a covariate to account for the significant difference in age between groups, with partial eta squared (η_p^2) presented to reflect effect size. Alpha was set at 0.05. Bonferroni correction and the Games-Howell test were used to control for multiple comparisons. Influential outliers were identified using Cook's Distance and removed. Outliers were considered influential if Cook's D was greater than 4/n, where n is the total number of data points. Where outlier removal altered the significance of a result, results are marked "OR".

3. Results

Children's anxiety, daytime behaviour, executive functioning and sleep were compared across the three groups.

3.1 Demographics

One-way ANOVAs found between-group differences in age, $F(2,89) = 8.70$, $p < 0.001$, $\eta^2 = 0.03$, but not in sex, $F(2,89) = 2.52$, $p = 0.09$, $\eta^2 = 0.05$, or SES $F(2,89) = 2.43$, $p = 0.09$, $\eta^2 = 0.009$ in this sample of 92 children. Children with FASD (M = 9.87 years, SD = 2.31 years) were significantly older than children with ASD (M = 8.34 years, SD = 1.73 years; $t(44.98) = –2.54$, $p = 0.04$), and TD children (M = 8.12 years, SD = 1.28 years; $t(35.51) = 3.54$, $p = 0.003$). However, children with ASD and TD were not significantly different in ages ($t(28.31) = 0.483$, $p = 0.874$). There were significantly more boys than girls in the ASD group, but this

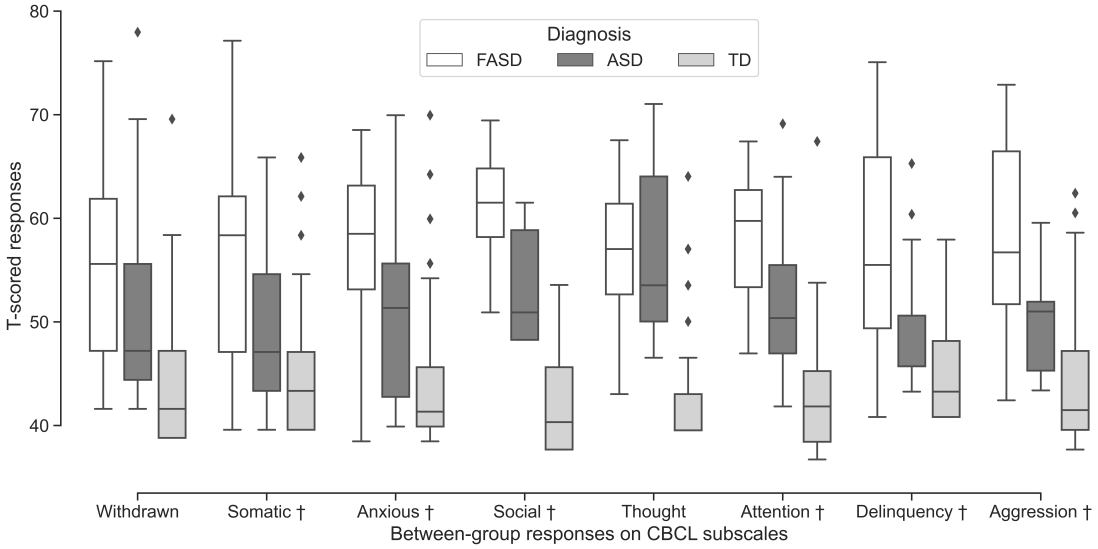

Fig. 2. Syndrome Specific Items in Behavioural Questionnaire. A boxplot showing the difference in responses between ASD, FASD and TD groups on the CBCL subscales. † indicates where the FASD group means were significantly higher than both TD and ASD.

was not found in the FASD or TD groups – reflected in Table 1. All groups reported more participants in intermediate occupations than in the other two SES categories.

3.2 Group Differences in Executive Function

MANOVA found responses to the questionnaires were significantly different among the diagnostic groups: BRIEF: $F(16,164) = 16.82$, $p < 0.001$, Wilk's $\Lambda = 0.143$; CBCL: $F(18,162) = 9.19$, $p < 0.001$, Wilk's $\Lambda = 0.245$; and SCAS: $F(14,166) = 3.69$, $p < 0.001$, Wilk's $\Lambda = 0.582$. Individual ANCOVAs are shown in Table 2 with Bonferroni corrected p values, partial eta squared (η_p^2) representing effect size, and the results of pairwise comparisons.

Pairwise comparisons showed higher scores in FASD group in comparison to the ASD and TD groups on all BRIEF subscales (See Fig. 1). Of all variables that exhibit specificity for FASD, The BRIEF subscales appear to provide the best differentiation between FASD from ASD and TD. The clinical threshold for the BRIEF was a score of 65 or higher. FASD response means were higher than this on all measures excluding the organising materials scale, indicating on all but that one scale, children with FASD are more likely to score within the clinical range.

3.3 Group Differences in Daytime Behaviour

Children with FASD scored significantly higher than TD children and children with ASD on the CBCL's attentional problems scale, somatic complaints scale, social problems scale, delinquency scale, and aggressive behaviour scale, as well as receiving a higher total score. The mean score for total CBCL was 22 (SD = 18.7) in the TD group and 52 (SD = 14.5) in the ASD group. Both are lower than the clinical score of 64. The FASD group's mean was above the clinical level at 82.2 (SD = 22.6), suggesting clinically significant behavioural problems assessed using the CBCL are more prevalent in children with FASD. Responses to the CBCL subscales are plotted in Fig. 2.

3.4 Group Differences in Anxiety

Children in the FASD and ASD groups were not significantly different on CBCL subscales assessing thought problems, anxiety/depression, and withdrawal, but both groups scored higher than TD children. ANCOVAs found significant group effects on the panic, obsessive compulsive, and separation anxiety subscales of the SCAS and the total score, but no other subscales. The FASD group was found to score more highly than the other two groups on generalized anxiety but when controlling for age there was no significant group difference. The mean score for total SCAS in the TD group was 23.1 (SD = 15.1). The mean in the ASD group was 31.2 (SD = 15.3) – just surpassing the clinical threshold of 31. The FASD mean was 42.9 (SD = 14.4). Children with FASD scored significantly higher than the other two groups on the panic scale, yet the ASD and TD groups did not differ from one another. FASD also scored higher than the TD group on the scale measuring separation anxiety, but there was no difference between FASD and ASD on this scale. The difference between FASD and TD groups on both measures were significantly different only after the removal of outliers. Group differences on the subscales of the SCAS are plotted in Fig. 3.

3.5 Between-Group Differences in Child Sleep

There were no significant group differences in sleep fragmentation assessed by actigraphy ($F(2,83) = 6.37$, $p = 0.12$, $\eta_p^2 = 0.13$).

Total sleep time was found to be different between groups ($F(2,83) = 7.15$, $p = 0.03$, $\eta_p^2 = 0.15$). Sleep du-

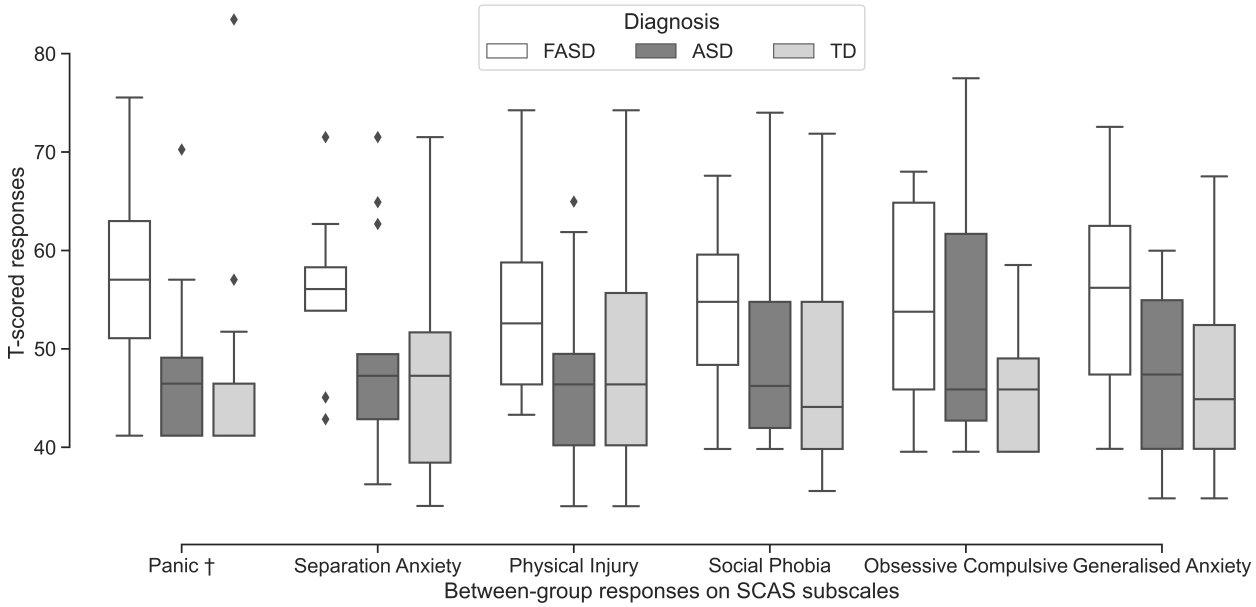

Fig. 3. Syndrome Specific Items in Psychological Questionnaire. A boxplot showing the difference in responses between ASD, FASD and TD groups on the SCAS subscales. † indicates where the FASD group means were significantly higher than both TD and ASD.

ration measured by actigraphy was significantly shorter in FASD (M = 7:27 hours) than TD (M = 8:34 hours; t(56.77) = –4.50, $p = 0.001$) and ASD (M = 7:46 hours, t(38.03) = 3.007, $p = 0.013$) groups. Children with FASD had an average of 46 minutes less sleep per night than children with ASD. TD had an average of 13 minutes more sleep than ASD and an average of 60 minutes more sleep than children with FASD. This study did not find any significant differences between groups on the CSHQ measure of sleep disordered breathing (F(1,84) = 1.23 $p = 1$, $\eta_p^2 = 0.03$). The number of awakenings during the night measured using actigraphy also did not differ between groups (F(2,84) = 0.3348, $p = 1$, $\eta_p^2 < 0.001$). Nor did sleep onset latency (F(2,84) = 0.78, $p = 1$). Sleep efficiency was found to show a group effect (F(2,84) = 19.90, $p < 0.001$), with FASD (M = 66.53%, SD = 10.0), reporting significantly lower efficiency than TD children (M = 79.73%, SD = 6.91, t(34.61) = –5.77, $p = 0.001$). Children with ASD (M = 71.03%, SD = 6.79) reported significantly lower efficiency compared to TD children (t(32.25) = –4.48, $p = 0.001$) but no difference when compared with FASD (t(40.68) = 1.71, $p = 0.21$).

There was a significant difference in parent-reported sleep onset delay measured by the CSHQ (F(2,85) = 11.30, $p < 0.001$, $\eta_p^2 = 0.21$), with FASD (M = 2.640, SD = 1.29) and ASD (M = 2.053, SD = 0.86) groups reporting higher scores than the TD group (M = 1.378, SD = 0.68; t(31.32) = 4.463, $p = 0.001$ and t(28.37) = 3.072, $p = 0.013$). No difference was found between FASD and ASD in sleep onset delay (t(41.03) = –1.792, $p = 0.19$).

Night waking was found to be distinct between groups (F(2,83) = 12.44, $p < 0.001$, $\eta_p^2 = 0.23$), as was daytime sleepiness (F(2,81) = 10.07, $p < 0.001$, $\eta_p^2 = 0.20$). Children with FASD reported the highest scores for night waking (M = 5.92) and daytime sleepiness (M = 11.17), followed by ASD (M = 4.83, M = 9.13, respectively), and lastly TD (M = 4.31, M = 8.71, respectively). Effect sizes for CSHQ differences were all notably smaller than those seen when assessing group differences found in the BRIEF, CBCL and SCAS responses.

4. Discussion

To provide a comparison of behavioural, cognitive, affect-related (anxiety), and sleep profiles between groups, five key findings are presented. Firstly, children with FASD scored significantly higher than children with ASD and TD children on scales measuring attentional problems, somatic complaints, social problems, delinquency, aggressive behaviour, panic, and separation anxiety.

Attentional problems, delinquency and aggression are amongst the more commonly reported externalised behaviours in children with FASD, often being reported by caregivers. Our findings demonstrated that children with FASD scored higher on measures of attentional problems, delinquency and aggression than children with ASD and TD children. This may be partially explained by the selection criteria, as the NST, used to diagnose FASD, included questions surrounding the child's history of disobedience, stealing, lying and bullying others [27]. However, a meta-analysis of 65 studies comparing children who have experienced PAE with children with ADHD on measures including the CBCL found externalizing behaviours such as aggression and delinquency were consistently present following PAE across a range of assessment criteria [34]. The NST showed a particularly high specificity and sensitivity

Table 2. ANCOVA table for questionnaires.

		FASD M (SD)	ASD M (SD)	TD M (SD)	F (df)	p	η_p^2	FASD/ASD	FASD/TD	ASD/TD
CBCL	Withdrawn	5.9 (3.0)	4.6 (3.3)	1.9 (1.9)	17.06 (2,84)	<0.001	0.29	0.43	0.001	0.01
	Somatic	4.7 (2.2)	2.3 (2.2)	1.7 (2.1)	11.93 (2,85)	<0.001	0.22	0.003	0.001	0.56
	Anxious	13.3 (5.2)	9.5 (5.3)	3.9 (4.7)	24.07 (2,83)	<0.001	0.37	0.07	0.001	0.002
	Social	9.0 (2.2)	5.9 (1.8)	1.8 (1.7)	99.74 (2,81)	<0.001	0.71	0.001	0.001	0.001
	Thought	5.3 (2.2)	4.4 (1.8)	0.9 (1.4)	74.42 (2,81)	<0.001	0.65	0.37	0.001	0.001
	Attention	13.3 (3.8)	9.4 (3.7)	3.2 (2.9)	63.44 (2,82)	<0.001	0.61	0.009 OR	0.001	0.001
	Delinquency	7.0 (4.2)	3.2 (2.1)	1.6 (1.9)	28.17 (2,82)	<0.001	0.41	0.002	0.001	0.03
	Aggression	22.4 (8.9)	13.0 (6.2)	6.9 (6.7)	30.33 (2,83)	<0.001	0.42	0.001	0.001	0.004
	Total	82.2 (22.6)	52.0 (14.5)	21.5 (18.7)	68.23 (2,82)	<0.001	0.62	0.001	0.001	0.001
SCAS	Panic	6.0 (2.7)	2.4 (2.2)	1.2 (1.8)	30.79 (2,82)	<0.001	0.43	0.001 OR	0.001	0.14
	Separation Anxiety	9.4 (3.6)	7.1 (4.1)	5.6 (4.4)	8.94 (2,86)	00.01 OR	0.17	0.11	0.001	0.36
	Physical Injury	5.4 (2.7)	4.2 (2.6)	4.8 (3.2)	0.88 (2,84)	0.99	0.02	0.30	0.67	0.68
	Social Phobia	8.7 (3.6)	5.8 (3.1)	5.2 (4.5)	4.43 (2,83)	0.65	0.10	0.02	0.002	0.82
	Obsessive Compulsive	4.6 (2.6)	4.4 (3.7)	1.8 (2.1)	9.95 (2,85)	0.005	0.19	0.90	0.001	0.05
	Generalised Anxiety	8.1 (3.5)	4.9 (3.0)	4.8 (3.6)	5.63 (2,86)	0.22	0.12	0.009 OR	0.001	0.9
	Total	42.9 (14.4)	31.2 (15.3)	23.1 (15.1)	11.07 (2,84)	0.002	0.21	0.051	0.001	0.18
BRIEF	Working Memory	70.9 (13.7)	25.7 (16.4)	5.5 (6.4)	232.73 (2,78)	<0.001	0.86	0.001	0.001	0.003
	Shifting	76.0 (12.3)	20.9 (15.5)	4.5 (6.1)	310.58 (2,78)	<0.001	0.89	0.001	0.001	0.006
	Planning Organising	68.0 (13.2)	26.3 (14.5)	6.5 (6.9)	221.59 (2,79)	<0.001	0.84	0.001	0.001	0.001
	Organising Materials	60.6 (10.3)	14.5 (12.7)	5.9 (6.1)	247.25 (2,79)	<0.001	0.86	0.001	0.001	0.06
	Monitoring	67.4 (14.8)	22.9 (19.2)	4.9 (5.0)	169.44 (2,81)	<0.001	0.81	0.001	0.001	0.007
	Inhibition	68.1 (15.1)	24.9 (16.7)	5.0 (6.0)	193.45 (2,79)	<0.001	0.83	0.001	0.001	0.002
	Initiation	68.7 (9.1)	19.7 (15.8)	5.1 (6.5)	277.52 (2,79)	<0.001	0.88	0.001	0.001	0.01
	Emotional Control	70.6 (15.1)	33.3 (18.6)	7.0 (7.6)	165.11 (2,80)	<0.001	0.80	0.001	0.001	0.001
	Total	173.7 (29.2)	151.6 (38.2)	35.8 (29.0)	272.49 (2,81)	<0.001	0.87	0.01	0.001	0.001
CSHQ	Bedtime Resistance	8.40 (2.67)	8.83 (2.36)	8.75 (2.86)	0.03 (2,83)	0.99	0.000	0.83	0.86	0.90
	Sleep Onset Delay	2.64 (1.29)	2.05 (0.83)	1.38 (0.68)	11.30 (2,85)	0.002	0.21	0.19	0.001	0.01
	Sleep Duration	6.51 (1.57)	5.52 (1.58)	3.71 (1.10)	29.72 (2,84)	<0.001	0.41	0.13	0.001	0.001
	Sleep Anxiety	7.08 (2.04)	6.89 (2.16)	6.36 (2.03)	1.08 (2,84)	0.99	0.04	0.90	0.65	0.35
	Night Waking	5.92 (1.44)	4.83 (1.30)	4.31 (0.98)	12.43 (2,83)	<0.001	0.23	0.05	0.001	0.31
	Parasomnia	10.15 (2.53)	9.11 (2.02)	9.09 (2.17)	3.83 (2,84)	0.99	0.03	0.31	0.19	0.90
	Sleep Disordered Breathing	3.54 (0.84)	3.33 (0.75)	3.74 (0.97)	1.23 (2,84)	0.99	0.03	0.67	0.62	0.20
	Daytime Sleepiness	11.17 (3.17)	9.13 (1.96)	8.71 (2.00)	10.07 (2,81)	0.005 OR	0.20	0.05	0.005	0.75
	Total	52.72 (7.17)	47.56 (5.84)	40.29 (6.33)	29.44 (2,82)	<0.001	0.02	0.05	0.001	0.001

ANOVA and pairwise comparisons of subscales within the CBCL, SCAS, BRIEF and CSHQ questionnaires.

within this sample suggesting that it was particularly able to detect FASD in this sample of children with the condition. This may not generalise to all children with FASD, as Ronen and colleagues [35] reported specificity of the NST at 72–73% and sensitivity at 34–36%, much lower rates when comparing the NST against diagnosis in 151 children (40 with FASD). Due to the high prevalence of other conditions in the FASD group, this study would have been underpowered to assess the impact of each co-occuring condition on this outcome, however it is possible that the presence of Conduct Disorder in some participants may contribute to this finding. Problems with conduct in children with FASD relate particularly to difficulties in understanding social norms, however FASD also often occurs alongside negative SES outcomes including a range of environmental traumas. Traumatic past experiences, combined with neurological impairments associated with FASD, have been associated with higher levels of aggression, externalised behaviours and contact with the criminal justice system [36]. As such, it is important to further understand these features of FASD and develop interventions to improve long-term outcomes.

Children with FASD scored higher on social problem scales than children in the ASD and TD groups. Our prediction was that children with ASD would demonstrate a higher number of social and communication difficulties than the other two groups (FASD and TD) [37]. Children with FASD are more likely to present with separation anxieties due to the higher likelihood of this population to experience foster care and frequent change in caregiver [38,39] which could be a possible explanation for this finding since these experiences may impact the ways in which children

with FASD relate to their peers or face problems when socialising.

A second key finding is that children with FASD demonstrated increased problems with working memory, shifting between tasks, planning, organising, monitoring their behaviour, inhibition, organising their materials and spaces, initiating tasks and emotional control. Children with FASD consistently showed more executive function problems than both other groups. Therefore, the BRIEF questionnaire used in this study to measure executive functioning could be a useful resource for identifying FASD in children. This supported previous recommendations that BRIEF should be considered alongside current diagnostic assessments when establishing the presence of FASD [40], as clinically elevated scores appear widely among FASD populations. This finding is also consistent with international reports of elevated BRIEF scores among children with FASD [41,42], suggesting the phenomenon persists cross-culturally. There was variation in the ASD responses to the BRIEF. Children with ASD had diagnoses ranging from 'mild' to 'severe' and came from both mainstream and special education, whereas those with FASD and TD were in mainstream education only. It is possible that this variety in severity of ASD symptoms among participants in that group is the cause of the variation in their responses. Future research may consider if symptom severity in ASD influences this association between the severity of ASD and variability in responses to questionnaires assessing executive function.

A third key finding is that children with FASD and ASD had higher levels of panic and separation anxiety than TD children. This supports findings by Mughal and colleagues [43] who found high levels of anxiety in children with FASD using the same questionnaire measures. Mughal *et al*. [43], also found an association between anxiety and sleep problems measured using the CSHQ which suggested a bi-directional relationship. It is expected that children with FASD would experience some level of separation anxiety as a high proportion of children with FASD experience foster care. Anxiety has also been widely associated with ASD, with up to 19% of children meeting the diagnostic criteria for separation anxiety, and up to 70% generalized anxiety [44].

A fourth key finding is that children with ASD averaged 13 minutes less sleep per night than TD children, and FASD children averaged one hour less per night than TD children. In the FASD population, this is consistent with the findings of Hanft and colleagues [45] who showed that children who experienced PAE spent less total time asleep but did not differ in the number of night-time awakenings or the proportion of time spent in sleep-wake states. Similarly, a large actigraphy study with 289 participants found that PAE was associated with shorter sleep duration [7]. Additionally, Chen and colleagues [4] had previously shown that children with FASD slept an hour less each night than their typically developing peers. This was one of only a small number of multi-method studies previously conducted and only five children in this study completed polysomnography, so the present findings support the notion that this phenomenon exists and is robust across greater numbers of children with FASD.

Elrod and Hood quantified these sleep time differences in children with ASD in 2015, finding that children with ASD slept an average of 32.8 minutes less per day than typically developing children. A similar reduction was reported by Díaz-Román and colleagues [46] in a meta-analysis assessing objective and subjective studies on sleep behaviour in ASD. Across eight studies and 247 participants who were assessed using PSG, children with ASD were found to have an average of 37.5 fewer minutes of sleep per night, indicating this phenomenon is consistent across methodologies. The same finding appears to be consistent over time, as a study assessing sleep duration at eight intervals from the age of eight months to 11 years found that children with ASD achieved between 17 and 40 minutes less sleep per night than typically developing children, independent of sex and ethnicity [47]. This is higher than the 13 minutes average observed in the present study and less than the reduction of sleep time reported in FASD.

Finally, sleep onset delay was significantly higher in children with FASD than in TD children. However, this increase was not specific to FASD as children with ASD also exhibited higher sleep onset delay. Actigraphy results did not reflect this relationship as there was no difference between groups in sleep onset latency. Sleep onset delay has been found to be previously over reported in parental subjective report [48,49].

5. Limitations

The use of caregiver reporting over objective data collection methods in this study may limit these findings. The measures for daytime behavioural difficulties are subjective and do not necessarily capture the full social and communication profile of ASD, as the focus is on social delinquency, or the disinclination to follow rules. Further, this study used a small sample which may limit the ability to generalise these findings more widely to the FASD and ASD populations.

6. Conclusions

This study is notable as its findings highlight several syndrome specific features (shorter sleep duration, executive functioning difficulties, and higher levels of social and behavioural problems and anxiety) that potentially contribute to the unique phenotype of FASD. As a small-scale study with interesting results indicating syndrome specificity, further research is much warranted.

Availability of Data and Materials

Data is provided with the submitted article.

Author Contributions

AAB contributed to formal analysis, data curation, visualisation, writing – original draft and writing – review and editing. RM contributed to conceptualisation, methodology, investigation, project administration, supervision, and writing – review and editing. DD contributed to conceptualisation, methodology, project administration, supervision, and writing – review and editing. EJH contributed to formal analysis, project administration, supervision and writing – review and editing. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

All participants gave full informed consent to take part in this research study. Ethics for the study were approved by the UCL Institute of Education Research Ethics Committee (Approval number 16683/001).

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Conflict of Interest

The authors declare no conflict of interest. Dagmara Dimitriou is serving as one of the Guest editors of this journal. We declare that Dagmara Dimitriou had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Gernot Riedel.

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