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Co-occurring Psychiatric Disorders in Preschool and Elementary School-Aged Children with Autism Spectrum Disorder

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Abstract We employed a clinical sample of young children with ASD, with and without intellectual disability, to determine the rate and type of psychiatric disorders and possible association with risk factors. We assessed 101 children (57 males, 44 females) aged 4.5–9.8 years. 90.5 % of the sample met the criteria. Most common diagnoses were: generalized anxiety disorder (66.5 %), specific phobias (52.7 %) and attention deficit hyperactivity disorder (59.1 %). Boys were more likely to have oppositional defiant disorder (OR 3.9). Higher IQ was associated with anxiety disorders (OR 2.9) and older age with agoraphobia (OR 5.8). Night terrors was associated with parental psychological distress (OR 14.2). Most young ASD children met the criteria for additional psychopathology.

Keywords Autism · Autism spectrum disorder ·
Psychopathology · Child behavior problems · Prevalence

Introduction

Autism spectrum disorder (ASD) is now known to occur in more than 1 % of the population (Baio 2012; Baird et al. 2006). Coupled with life-course persistence and significant psychosocial impairment, ASD causes a high levels of social and economic burden (Knapp et al. 2009). Recent studies have demonstrated that additional psychiatric disorders commonly occur in children with ASD with many

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studies reporting aggregated rates as high as 70–90 % (de Bruin et al. 2007; Leyfer et al. 2006; Mattila et al. 2010; Mukaddes and Fateh 2010; Simonoff et al. 2008). These rates are four to six times higher than those reported in the general population (Costello et al. 2003). They are also higher than in those found in many studies of children with intellectual disability (ID), e.g., Dekker and Koot (2003). In ASD, common co-occurring disorders in late childhood include attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD) and anxiety disorders, with emergence of depression and obsessive compulsive disorder in adolescence/adult life (Mazefsky et al. 2008; Simonoff et al. 2008; Skokauskas et al. 2010; van Steensel et al. 2013).

While there is a substantial literature in older children, adolescents and adults describing the prevalence and correlates of co-occurring psychiatric disorders in ASD, the topic has received less attention among preschool and elementary schoolchildren. However, diagnostic tools are now available for this age group, including questionnaires such as the 1.5–5 years old version of the Child Behavior Checklist (Ivanova et al. 2010), the Infant Toddler Social-Emotional Assessment (Carter et al. 2003), and diagnostic interviews such as the Preschool Age Psychiatric Assessment (PAPA) (Egger et al. 2006). Furthermore, recent studies support the use of current diagnostic concepts of psychopathology in younger children. Egger and Angold found similar architecture for common psychopathology when comparing preschool and older children and adolescents (Angold and Egger 2007; Sterba et al. 2007). Lecavalier used factor analysis and demonstrated the validity of DSM-IV syndromes in 3–5 year-old children with ASD (Lecavalier et al. 2011).

There have been two approaches to evaluating psychopathology in ASD: first, standardized measures designed for and evaluated in the general population and, second, bespoke instruments in which the mode of inquiry and/or criteria for symptom endorsement have been specifically modified for use in ASD populations. An advantage of the former approach is the ability to make direct comparisons with the general population, both about prevalence rates and risk/protective factors. However, researchers have raised a number of concerns about the suitability of standardized measures. When used directly with people with ASD rather than informants, their understanding and ability to provide accurate responses should be considered; typically developing younger children will give inaccurate responses rather than volunteer they do not understand questions (Breton et al. 1995). Furthermore, subtle distinctions between core symptoms of autism and those related to other psychopathology may not be well-differentiated in instruments designed for the general population. Leyfer et al. (2006) highlight that their

Autism Comorbidity Interview (ACI-PL), based on the Kiddie-SADS, includes probes and definitions designed to make such distinctions, e.g., between lack of social interest and social avoidance. Similarly, Mazefsky et al. (2008) showed that using a diagnostic interview with modified criteria reduced the rate of additional psychopathology in ASD.

We chose the PAPA in the present study because we thought it provided the best compromise between the two methods. As only parents are interviewed in this age group, there is no need to consider whether probes are understood by participants. There remains a broader concern about access to the mental state of younger children with poorer communication skills, but this applies to all interview measures. The PAPA was designed for use with parents of younger children with limited verbal skills and therefore relies more heavily on behavioral examples. We are unaware of any published studies using the PAPA in populations with autism but have applied its sister instrument, the Child and Adolescent Psychiatric Assessment (CAPA) in parent interviews of older children with ASD (Simonoff et al. 2008). The availability of general population norms for the PAPA allows direct comparison to findings in the general population, which is not possible with autism-specific measures such as the ACI-PL or BISCUIT (Matson et al. 2011).

In this study we describe the prevalence of parent-reported DSM-IV disorders in a clinical sample of children with ASD aged 5–9 years. We examine the role of several well-recognized risk factors for psychopathology in the general population, including sex, ID, parental psychological distress family socioeconomic position and ethnic minority status. We also explore the relationship of psychopathology to the child's age and autism severity.

Methods

Participants

The eligible population for the study was all children born between September 2000 and August 2004 (4–8 years at recruitment) with an ASD diagnosis and living in either of two London boroughs (Bromley and Lewisham, outer and inner London respectively). The Social Communication Questionnaire Lifetime version [SCQ; Rutter et al. (2003)] was used to measure ASD symptoms. Clinical diagnosis was established following a multidisciplinary neurodevelopmental and social communication assessment led by a single community pediatrician for each borough. The teams used multi-source information (parents, teachers, social workers), observation of the child (at clinic or at home and/or school) and structured assessments such as the Autism

Diagnostic Interview-Revised (Le Couteur et al. 1989), the Developmental, Dimensional and Diagnostic Interview (Skuse et al. 2004), the Diagnostic Interview for Social and Communication Disorders (Wing et al. 2002) and the Autism Diagnostic Observation Schedule (Lord et al. 2000). All cases who, in the subsequent research assessment, had an SCQ score below 10 (n = 7) were considered by the lead pediatrician who reviewed the clinical notes to confirm the ASD diagnosis.

The primary care services and local autism support groups identified 447 eligible children fulfilling the criteria; this number represents 1.38 % of the estimated population in 2010 for this age and geographical area (Large and Ghosh 2006).

Procedure

In the first phase of the study all eligible families were mailed information about the study, including an invitation to participate, consent form and a return envelope. Non-responders were subsequently contacted by phone. Responses were received from 362 (81 %) (see Fig. 1). Of these, 277 parents (62 %) completed the Developmental Behavior Checklist (Einfeld and Tonge 2002), the Profile of Neuropsychiatric Symptoms (Santosh et al., in press)


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┌─────────────────────────────────────────────────┐
│                 Target population                 │
│ Children with an ASD diagnosis, born September    │
│ 2000 - September 2004, living in two London       │
│ health districts                                  │
│ N=447 (160 Bromley, 287 Lewisham)                 │
│ 85.0% male                                        │
└─────────────────────────────────────────────────┘
┌─────────────────────────────────────┐
│         Response to invitation         │
│ No response = 85 (19.0%)               │
│ Return undelivered = 6 (1.3%)          │
│ Opt out = 50 (11.2%)                   │
│ Consent to participate =306 (68.5%)    │
└─────────────────────────────────────┘
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│         Parent questionnaires completed           │
│ N = 277 (62.0%)                                   │
│ (82.0% male, 18.1% female)                        │
└─────────────────────────────────────────────────┘
┌──────────────────────┐   ┌──────────────────────┐
│ IQ assessments        │   │ Teacher questionnaires │
│ completed             │   │ completed              │
│ N = 258 (93.1%)       │   │ N=228 (82.0%)          │
└──────────────────────┘   └──────────────────────┘
┌──────────────────────┐
│ Selected for in depth │
│ interview             │
│ N= 131                │
└──────────────────────┘
┌──────────────────────┐
│ PAPA Interview        │
│ N= 101                │
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Fig. 1 Sample selection and response rates

and the Social Communication Questionnaire, lifetime version, as well as a questionnaire on family demographic characteristics, described below. A cognitive assessment was undertaken, usually in the child's school, and teachers were asked to complete parallel behavior questionnaires.

The second phase of the study aimed to assess psychopathology in more detail. A sample of 131 children was selected from the 277 participants. All participating girls (n = 50) were invited, in order to provide a sufficiently large female sample for comparisons according to sex. A stratified random sample of boys (N = 81) was selected to include equal numbers of boys on each of the following characteristics (1) IQ (<70/≥70); (2) residing in the two London boroughs; (3) child's age (4.5–6.7/6.8–9.9 years) and (4) SCQ (<21/≥22). The mean time gap between the two phases was 373 days (SD 135, range 64–697).

Measures

Child Characteristics

Autism symptom severity was determined using the parent-reported SCQ, lifetime version; the published cut-off of ≥22 was used to split the sample into two groups.

IQ was measured in 258 cases by two study psychologists trained in the cognitive assessment of children with ASD and using one or more of the following tests, depending on the child's age and developmental level: the Mullen Scales of Early Learning [MSEL; Mullen (1997)], the Wechsler Preschool and Primary Scale of Intelligence [WPPSI-III-UK; Wechsler (2004)], and the Wechsler Intelligence Scale for Children [WISC-IV-UK (Wechsler et al. 2004)]. The British Picture vocabulary Scales were used to assess receptive language in 240 children (Dunn et al. 1997). Parents were also asked to provide an estimate of their child's 'functional age' (see Supplementary Appendix for details of questions). In 197 cases where both direct measure and estimate were available, the mean test-based IQ was 72.8 (SD = 27.4), parent-derived estimate 68.9 (SD = 23.2) with a correlation of 0.71 ($p < 0.001$). Therefore, in 15 cases where tested IQ was not available, the parent-derived estimates were substituted; in 4 cases neither measure was available.

DSM-IV symptoms and disorders present in the last 3 months were assessed using the electronic version of the Preschool Age Psychiatric Assessment (PAPA), a semi-structured, parent-reported interview for preschool children aged 2–5 years (Egger and Angold 2004). Interviews with the main caregiver were conducted in person, in most cases in the family home, and audio-taped. The majority of interviews were conducted by a specialist trainee (equivalent to clinical fellow) in Child and Adolescent Psychiatry (FS, N = 88 interviews) and the rest by two research
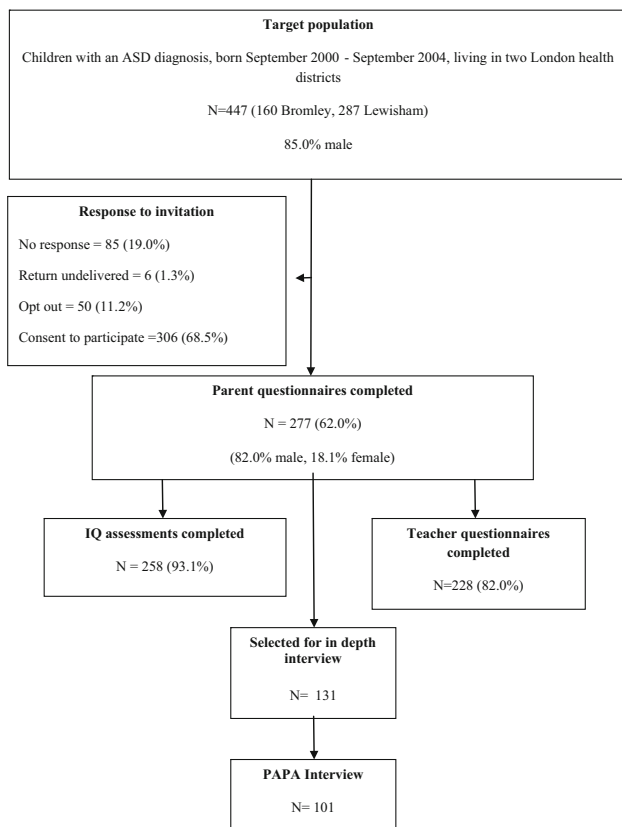
psychologists with specialist autism experience. All interviewers attended a 2 day training course on the PAPA. Validation of interview administration and coding was performed by the trainer (from Duke University) at an early stage in the study. Subsequently, specific coding issues were discussed on an ad hoc basis both with the US trainer and ES (who is author of the sister instrument, the CAPA). Weekly meetings with the principal investigator (GB) reviewed any specific questions. These included decisions about whether items met PAPA criteria for additional psychopathology or were more appropriately considered symptoms of ASD. The detailed PAPA symptom criteria were used rigorously but in an agnostic fashion to endorse individual symptoms. Standardized algorithms previously developed and reported were used to determine diagnoses (Egger et al. 2006). In the case of ADHD, the criterion excluding the diagnosis in the presence of ASD was waived.

Parental Characteristics

The Kessler Psychological Distress Scale (K-10) was used to measure parental psychological distress (Kessler et al. 2002). The K-10 includes questions about cognitive, behavioral, emotional and psychophysiological symptoms that are elevated among people with a wide range of different mental disorders. The 10-item questionnaire has good internal consistency; a score ≥ 24 indicate nonspecific psychological distress and was the cut-off for a binary variable. Parental education was dichotomized according to whether either parent had attained GCSEs (equivalent to a high school diploma) or higher. Families were characterized according to whether there was at least one parent who was employed; ethnicity was classified as white or other.

The study was approved by Guy's Hospital Research Ethics Committee (Approval Number 08/H0804/37).

Data Analysis

Data reduction and analysis used Stata 11 (StataCorp 2009). Inverse probability weights were generated to account for the study design, in which all females were included (and therefore assigned a probability weight of 1) while boys were selected according to IQ, residence, age and autism severity. All the prevalence rates and other statistics presented in this paper reflect the overall ASD population from which the sample was drawn. Wald test statistics (adjusted t and F tests) and p values were calculated using the linearization version of the robust parameter covariance matrix as implemented by the *svy* procedures of Stata 11. Logistic regression was used for binary outcomes.

Results

A total of 101 families (77 % of the invited group) took part in the interview stage. This included 57 boys and 44 girls with a mean age of 6.7 years. Table 1 summarizes the sample characteristics. Comparison between the participating and non-participating children showed that participating children had lower SCQ scores but otherwise were similar in terms of child and family characteristics. On the basis of measured IQ (and not including adaptive function criteria), 56 % had IQs in the normal range, 13 % mild, 10 % moderate ID, 15 % severe and 6 % profound ID.

Table 1 Comparison between characteristics of children and parents invited to in-depth stage

	Geographical area			Comparison of participated versus declined		
	Lewisham	Bromley	p	Declined	Participated	p
Total number (females)	87 (36)	44 (14)		30 (6)	101 (44)	
Mean age at stage 1 (SD, range)	6.7 (1.2, 4.5–9.3)	6.8 (1.1, 4.7–9.1)	0.59	6.7 (1.1, 4.9–9.0)	6.7 (1.1, 4.5–9.3)	0.81
Mean IQ (SD, range)	61.5 (28.0, 19.0–114.0)	77.8 (25.1, 19.0–120.0)	0.001	69.1 (30.4, 19.0–114)	66.4 (28.0, 19.0–120)	0.65
BPVS (SD, range)[b]	82.0 (15.1, 40–112)	93.8 (18.4, 40–120)	0.004	85.8 (16.6, 41–106)	86.1 (17.2, 40–120)	0.95
SCQ (SD, range)	19.6 (7.2, 3–42)	23.7 (6.9, 6–36)	0.002	24.3 (7.3, 9.0–42.0)	20.0 (7.0, 3.0–34)	0.006
Parental ethnicity white N (%)	27 (31)	37 (84)	0.000	12 (40)	52 (51.5)	0.27
Parent employed N (%)	53 (64.6)[a]	34 (77.2)	0.14	15 (60)[a]	73 (73.3)	0.27
Parent GCSEs or higher N (%)	45 (54.9)[a]	24 (54.5)	0.97	13 (52)[a]	56 (55.4)	0.76

SCQ Social Communication Questionnaire, *BPVS* British Picture Vocabulary Scales, GCSEs are equivalent to a high school diploma

[a] 5 missing values, [b] 27 missing values, 7 because of inability to access test

Prevalence

Table 2 shows the weighted 3-month prevalence rates for DSM-IV psychiatric disorders overall and stratified by child characteristics. It reveals that 90.5 % [95 % confidence intervals (CIs) 84.2, 96.7 %] of the sample had at least one psychiatric disorder. The prevalence of emotional disorders was 80.0 % (CIs 72.0, 88.1 %) and of behavioral disorders 28.7 % (95 % CIs 18.2, 39.2 %). The most common emotional disorders were GAD [66.5 % (95 % CIs 57.0, 76.0 %), followed by specific phobias [52.7 % (95 % CIs 40.2, 65.2 %)]. Social anxiety occurred in 15.1 % (95 % CIs 6.2, 24.0 %) and somewhat surprisingly, agoraphobia in 18.0 % (95 % CIs 9.2, 26.7 %). Major depressive disorder was present in 14.6 % (95 % CIs 6.0, 23.2 %). ADHD occurred in 59.1 % (95 % CIs 47.3, 70.9 %). ODD was present in 28.7 % (95 % CIs 18.2, 39.2 %) while conduct disorder was present in only 2.0 % (95 % CIs 0.6, 1 %), all of whom also met criteria for ODD.

Aggregation Among Psychiatric Disorders

The pattern of overlap amongst ADHD, ODD/CD and emotional disorders is shown in Fig. 2. Both ODD and ADHD rarely occurred in isolation from other disorders, in contrast to emotional disorders which presented without ADHD or ODD in 26.5 % of cases (weighted). In terms of the *number* of co-occurring disorders, 11.5 % of the sample had one, 28.5 % had two and 51.4 % three or more disorders. Multiple anxiety disorders frequently co-occurred; 75.6 % of cases that had any anxiety disorder met criteria for at least two diagnoses, with GAD and specific phobia the most common combination, occurring in 24.3 %. In evaluating the number of co-occurring disorders overall, when anxiety disorders are collapsed to a single diagnostic entity, 24.9 % of the sample had one diagnosis, 31.8 % two and 34.2 % three or more diagnoses.

Effects of Child Characteristics

Male sex was a risk factor for ADHD (OR 2.9, 95 % CIs 1.2, 6.9), ODD (OR 3.9, 95 % CIs 1.3, 11.8) and tic disorder (OR 5.5, 95 % CIs 1.1, 27.6). Higher IQ was associated with anxiety disorders as an aggregate group (referred to as *any anxiety disorder*) (OR 2.9, 95 % CIs 1.0, 8.1) but not with any specific one and not with other disorders. Older children were more likely to have anxiety disorders including GAD (OR 4.5, 95 % CIs 1.7, 11.8), separation anxiety (OR 5.5, 95 % CIs 1.5, 20.8) and agoraphobia (OR 5.8, CIs 1.6, 21.3). As a post hoc analysis, we explored the relationship of any anxiety disorder to the presence of language, defined by the first question on the SCQ (the child's ability to string a few words in a meaningful sentence) and found a non-significant trend for the presence of language to increase the probability of any anxiety disorder (OR 2.7, 95 % CIs 0.9, 8.5, *p* = 0.08).

Participants with more autism symptoms were more likely to have diagnoses of agoraphobia (OR 5.4, 95 % CIs 1.3, 22.7), ODD (OR 3.5, 95 % CIs 1.1, 10.6) and night terrors (OR 7.5, 95 % CIs 1.3, 42.1).

Effects of Parental Characteristics

Table 3 shows weighted rates of disorders by family characteristics. Night terrors were associated with both parental psychological distress (OR 14.2, 95 % CIs 2.4, 84.6) and parental unemployment (OR 8.9, 95 % CIs 1.4, 56.0). Lower parental educational level was associated with higher rates of any emotional disorder (OR 8.7, 95 % CIs 1.7, 43.0) and ODD (OR 4.5, CIs 1.3, 15.3) but with a lower rate of enuresis (OR 0.2, CIs 0, 1.0).

Discussion

This study is currently amongst the few to describe the prevalence and associated risk factors for psychiatric disorders among younger children with ASD. Virtually all (90.5 %) met criteria for at least one DSM-IV disorder. The aggregate rate is substantially higher than that for a similar age group in the general population, where rates of 12-16 % have been reported (Egger and Angold 2006; Wichstrom et al. 2012). Furthermore, rates among children with ID, albeit somewhat older, are reported to be 20–40 %, substantially lower than those in our present study (Dekker and Koot 2003). However the present findings are broadly in line with those reported in older children and adolescents with ASD (de Bruin et al. 2007; Leyfer et al. 2006; Mattila et al. 2010; Mukaddes and Fateh 2010; Simonoff et al. 2008). These high rates raise questions about diagnostic classification, its application in people with ASD, and the extent to which core autism symptoms may overlap with other psychopathology. Broadly there are three alternative explanations. First, the autism spectrum phenotype may include symptoms that are usually considered part of another disorder, such as difficulties with sustained attention or social anxiety. It was on this basis that DSM-IV excluded the diagnosis of ADHD in the presence of ASD; DSM-5 has removed this exclusion, taking an agnostic approach to the reasons for overlap, consistent with our approach in this study. However, it should be noted that ADHD medication may be less effective in children with ASD (Harfterkamp et al. 2012; RUPP Autism Network 2005; Simonoff et al. 2013a, b).

Second, ASD, or characteristics associated with it, may increase the risk of other symptoms/disorders. Hence, we

Table 2 Weighted rates (95 % confidence intervals) of disorders by child characteristics

DSM-IV disorders	Total sample (N = 101)	Sex			IQ			Age at assessment			Autism severity		
		Females (N = 44)	Males (N = 57)	Odds ratio	IQ < 70 (N = 57)	IQ ≥ 70 (N = 44)	Odds ratio	≤7.5 year (N = 47)	>7.5 (N = 54)	Odds ratio	SCQ ≤ 21 (N = 62)	SCQ > 21 (N = 39)	Odds ratio
Any DSM disorder	90.5 % (84.2–96.7)	81.8 % (70.1–93.5)	92.7 % (85.0–100.0)	2.8 (0.7–10.7)	87.3 % (77.3–97.3)	92.1 % (84.1–100.0)	1.7 (0.4–7.0)	89.5 % (77.8–100.0)	91.3 % (85.3–97.3)	1.2 (0.3–5.3)	88.0 % (78.9–97.1)	94.5 % (87.5–100.0)	2.4 (0.5–11.7)
Any DSM emo. dis.[a]	80.0 % (72.0–88.1)	68.2 % (54.1–82.3)	83.1 % (73.6–92.6)	2.3 (0.9–5.8)	68.6 % (55.1–82.0)	85.9 % (75.8–96.1)	2.8 (1.0–8.0)	70.1 % (54.2–86.0)	88.7 % (82.2–95.1)	3.3* (1.2–9.3)	78.8 % (66.9–90.8)	82.0 % (73.5–90.5)	1.2 (0.5–3.0)
Any anxiety disorder	78.9 % (70.7–87.0)	65.9 % (51.5–80.3)	82.2 % (72.6–91.8)	2.4 (0.9–6.0)	66.5 % (52.6–80.4)	85.2 % (75.0–95.4)	2.9* (1.0–8.1)	69.2 % (53.2–85.1)	87.4 % (80.5–94.3)	3.0* (1.1–8.5)	78.8 % (66.9–90.8)	79.0 % (69.7–88.2)	1.0 (0.4–2.5)
Agoraphobia	18.0 % (9.2–26.7)	13.6 % (3.2–24.0)	19.1 % (8.4–29.8)	1.5 (0.5–4.6)	10.3 % (3.0–17.5)	21.9 % (9.2–34.6)	2.5 (0.8–7.1)	6.4 % (1.7–12.6)	28.1 % (12.5–43.7)	5.8** (1.6–21.3)	8.4 % (0.0–17.7)	33.4 % (16.1–50.7)	5.4* (1.3–22.7)
Specific phobia	52.7 % (40.2–65.2)	50.0 % (34.8–65.1)	53.4 % (38.2–68.6)	1.1 (0.5–2.7)	45.6 % (29.4–61.5)	56.4 (39.4–73.4)	1.6 (0.6–4.0)	62.0 % (44.3–80.0)	44.6 % (27.3–61.9)	0.5 (0.2–1.4)	53.4 % (37.0–69.8)	51.5 % (32.5–70.6)	0.9 (0.3–2.5)
Panic disorder	3.1 % (0.0–7.5)	2.3 % (0–6.78.0)	3.4 % (1.2–8.7)	1.5 (0.1–20.4)	0 %	4.7 % (0.0–11.3)	–	0 %	5.9 % (0.0–14.0)	–	1.8 % (0.0–4.3)	5.3 % (0.0–16.0)	3.1 (0.2–39.8)
Social phobia	15.1 % (6.2–24.0)	11.4 % (1.7–21.0)	16.0 % (5.1–26.9)	1.5 (0.4–5.2)	5.3 % (0.0–13.7)	20.1 % (7.4–32.7)	4.5 (0.7–28.0)	8.0 % (0.1–16.0)	21.2 % (6.0–36.0)	3.0 (0.7–12.7)	12.9 % (2.4–23.3)	18.7 % (2.7–34.7)	1.6 (0.4–6.3)
Generalized anxiety dis.	66.5 % (57.0–76.0)	59.1 % (44.2–74.0)	68.4 % (57.1–79.7)	1.5 (0.7–3.4)	53.5 % (38.4–68.5)	73.2 % (60.8–85.5)	2.4 (1.0–5.8)	49.3 % (33.4–65.2)	81.5 % (71.0–92.0)	4.5** (1.7–11.8)	66.2 % (53.7–78.8)	67.0 % (52.6–81.4)	1.0 (0.4–2.5)
Separation anxiety	18.6 % (9.4–27.8)	15.9 % (4.8–27.0)	19.3 % (8.1–30.4)	1.3 (0.4–3.8)	9.9 % (0.1–19.8)	23.0 % (10.4–35.6)	2.7 (0.7–9.9)	6.8 % (0.0–13.7)	28.8 % (12.8–44.8)	5.5** (1.5–20.8)	20.0 % (8.3–31.9)	16.2 % (1.5–30.8)	0.8 (0.2–2.8)
Major depression	14.6 % (6.0–23.2)	4.5 % (0.0–10.9)	17.2 % (6.4–27.9)	4.3 (0.8–22.4)	6.3 % (0.0–18.1)	18.8 % (6.2–31.5)	3.4 (0.4–32.7)	7.8 % (0.0–17.5)	20.6 % (5.3–35.8)	3.0 (0.5–17.3)	15.4 % (4.8–26.0)	13.3 % (0.0–28.1)	0.8 (0.2–3.9)
Oppositional defiant dis.	28.7 % (18.2–39.2)	11.4 % (1.8–21.0)	33.1 % (20.2–46.1)	3.9* (1.3–11.8)	19.5 % (3.9–35.1)	33.3 % (19.7–47.1)	2.0 (0.6–6.5)	26.3 % (10.7–42.0)	30.7 % (16.6–44.8)	1.2 (0.4–3.5)	18.8 % (5.2–32.4)	44.7 % (28.3–61.1)	3.5* (1.1–10.6)
Conduct disorder	2.0 % (0.0–6.1)	0 %	2.6 % (0.0–7.6)	–	0 %	3.1 % (0.0–9.2)	–	0 %	3.8 % (0.0–11.4)	–	0 %	5.3 % (0.0–16.0)	–
ADHD	59.1 % (47.3–70.9)	38.6 % (23.9–53.4)	64.4 % (50.0–78.7)	2.9* (1.2–6.9)	60.7 % (44.1–77.4)	58.3 % (42.6–74.0)	0.9 (0.3–2.3)	56.6 % (39.1–74.1)	61.3 % (45.6–76.9)	1.2 (0.5–3.2)	53.5 % (37.0–70.0)	68.2 % (52.6–83.9)	1.9 (0.7–5.0)
Motor and Voc Tic dis.	17.4 % (8.1–26.7)	4.5 % (0.0–10.9)	20.7 % (9.2–32.3)	5.5* (1.1–27.6)	16.6 % (1.4–31.8)	17.8 % (6.2–29.5)	1.1 (0.3–4.2)	17.3 % (5.0–29.6)	17.5 % (3.8–31.3)	1.0 (0.3–3.7)	10.9 % (0.6–21.2)	28.0 % (10.3–45.7)	3.1 (0.8–12.7)
Encopresis	1.9 % (0.4–4.3)	4.5 % (0.0–10.8)	1.3 % (0.0–3.8)	0.3 (0.0–3.3)	2.7 % (0.0–6.5)	1.5 % (0.0–4.6)	0.6 (0.0–6.6)	4.2 % (0.0–9.3)	0 %	–	0.8 % (0.0–2.2)	3.9 % (0.0–9.7)	5.3 (0.4–67.4)
Enuresis	13.5 % (5.5–21.5)	16.0 % (0.0–0.27)	13.0 % (0.0–0.2)	0.8 (0.2–2.6)	22.2 % (6.5–38.0)	9.0 % (1.2–16.9)	0.3 (0.0–1.2)	20.7 % (7.8–33.7)	7.2 % (0.0–15.8)	0.3 (0.0–1.3)	11.8 % (2.3–21.4)	16.2 % (2.2–30.3)	1.4 (0.4–5.7)
Night terrors	4.9 % (1.1–8.6)	6.8 % (0.0–14.5)	4.4 % (0.0–8.7)	0.6 (0.1–3.0)	1.4 % (0.0–4.1)	6.7 % (1.3–12.0)	5.1 (0.6–45.0)	7.9 % (0.6–15.3)	2.2 % (0.0–5.3)	0.3 (0.0–1.6)	1.5 % (0.0–3.6)	10.3 % (1.1–19.5)	7.5* (1.3–42.1)

* p < 0.05; ** p < 0.01

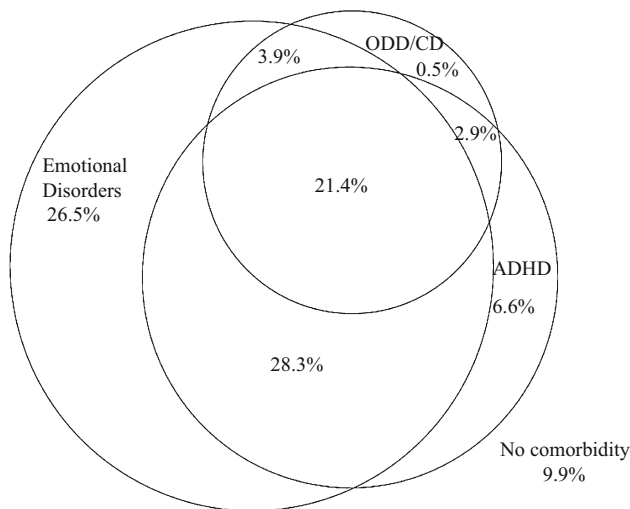[a] Any emotional disorder = major depression ± any anxiety disorder

Fig. 2 Pattern of overlap co-morbidities amongst children (Emotional disorder = depression + anxiety disorders)

have shown that cognitive rigidity in ASD is associated with anxiety (Hollocks et al. 2014). People with ASD experience higher rates of bullying (Montes et al. 2007; Rowley et al. 2012) and other adverse life events (Green et al. 2005) which may also increase their susceptibility to additional psychopathology. Finally, structured instruments for the general population may inadvertently miscode autistic symptoms to other domains of psychopathology. Thus, Mazefsky et al. (2012) demonstrated that using an interview in which symptom definitions are modified to account for ASD presentation led to a very substantial reduction in rates. In the present study, PAPA interviews were undertaken by researchers with extensive experience of ASD who were trained not to misattribute ASD symptoms to other psychopathology, but nevertheless high rates of psychopathology are reported. Other methods will be required to test these alternative models, including risk factor studies and clinical trials.

With respect to emotional disorders, we found anxiety disorders were very common both individually and in association with other disorders, with rates higher than those reported in older age ASD groups (Simonoff et al. 2008; Witwer and Lecavalier 2010). For the overall anxiety disorder category, as well as for some individual disorders, we found an association with higher IQ and older age. Studies in older ASD populations vary, with some reporting a similar relationship with higher IQ, others finding no association or one to lower IQ (Amr et al. 2011; Gadow et al. 2005; Simonoff et al. 2008; Sukhodolsky et al. 2008). In this study with younger children we speculate that more developed language, partly indexed by IQ, supports the communication of worries, so that parents are more aware of these emotions. Alternatively, higher IQ, as well as older age, may expose children to more anxiety-provoking

situations including greater interaction with peers. Finally, higher IQ/developmental level may allow them to engage in higher-order cognitions, such as worries about past events, the future, and self-efficacy, which are the hallmarks of anxiety disorders such as GAD. We note that separation anxiety, which largely involves observable behaviors, was associated with older age but not higher IQ. In this case, older children may have had more experiences of separation, including school attendance, which may have led to greater anxiety.

The rate of social phobia (15.1 %) is similar to that reported in late childhood by (Simonoff et al. 2008) but higher than that of others (Leyfer et al. 2006; Mattila et al. 2010; Mukaddes and Fateh 2010). It is uncertain at present whether this represents variation among populations, differences between instruments or chance variation. In our study interviewers were trained to distinguish social anxiety and avoidance from lack of social interest without evidence of anxiety.

The high rate of agoraphobia (18.0 %) is also noteworthy. Parental accounts indicated that children exhibited anticipatory anxiety and/or avoidance behavior in settings such as public transport or noisy shops. One explanation is that abnormal responses to high levels of sensory stimuli may be causative but this needs further exploration (Goldsmith et al. 2006; Green et al. 2010).

Finally the rate of depression in our study is higher than in the general population of the same age, with general population studies reporting rates of 2.1 and 2.0 % respectively (Egger and Angold 2006; Wichstrom et al. 2012).

Our rate of ADHD, 59.1 %, and its association with male sex, is consistent with other studies (de Bruin et al. 2007; Mukaddes et al. 2010; Witwer et al. 2012) although slightly higher than others (Leyfer et al. 2006; Simonoff et al. 2008). The rate of ODD (28.7 %) is strikingly similar to what we reported using the CAPA with older children as well as that in other studies (Leyfer et al. 2006; Simonoff et al. 2008; Witwer et al. 2012). The low rate of CD is expected and consistent with reports in older children (Simonoff et al. 2008, 2013a). We made diagnoses of ODD and CD irrespective of the child's intention to cause distress or harm to others. While this is in line with the diagnostic algorithms, many clinicians distinguish children on the basis of whether there is 'intentionality' in their behaviour. However, a lack of intention to cause distress may not be limited to those with ASD, e.g., children with ADHD. This further highlights that 'behavior that challenges' or 'challenging behavior,' which is common in ASD, does not conform to the structure of CD and should be considered separately (McClintock et al. 2003).

With respect to tic disorders, the literature reports highly variable rates and ours lie in the middle; the present rate of

Table 3 Weighted rates (95 % CIs) of disorders by family characteristics

Disorders	K-10			Education			Employment			Ethnicity		
	Low (N = 71)	High (N = 26)	Odds ratio	GCSEs or above (N = 76)	Below GCSEs (N = 25)	Odds ratio	Parent employed (N = 72)	No parent employed (N = 29)	Odds ratio	Other (N = 49)	White (N = 52)	Odds ratio
Any DSM disorder	91.4 % (86.2–96.6)	86.5 % (68.6–100.0)	0.6 (0.1–3.0)	88 % (79.6–96.3)	98.1 % (94.4–100.0)	7.2 (0.8–65.3)	87.3 % (78.7–95.9)	98.4 % (95.2–100)	8.8 (1.0–79.0)	90.8 % (84.1–97.4)	94.7 % (89.1–100.0)	1.8 (0.4–7.6)
Any DSM emo. dis.[a]	81.4 % (71.9–90.9)	73.4 % (53.4–93.5)	0.6 (0.2–2.2)	74.7 % (63.9–85.5)	96.3 % (91.0–100.0)	8.7** (1.7–43.0)	78.9 % (68.8–89.1)	82.8 % (68.7–96.9)	1.2 (0.4–4.2)	79.4 % (69.0–89.6)	84.7 % (72.7–96.8)	1.4 (0.4–4.8)
Any Anx disorder	81.4 % (71.9–90.9)	70.7 % (50.4–90.9)	0.6 (0.2–1.9)	73.8 % (62.9–84.7)	94.4 % (88.0–100.0)	6.0* (1.5–23.5)	78 % (67.7–88.3)	81.1 % (66.7–95.6)	1.2 (0.4–3.9)	77.9 % (67.4–88.4)	83.8 % (71.6–96.0)	1.5 (0.5–4.6)
Agoraphobia	15.1 % (4.3–25.8)	26.9 % (6.0–47.8)	2.0 (0.5–9.1)	16.6 % (6.4–26.8)	22.1 % (2.7–41.5)	1.4 (0.4–5.6)	16.5 % (5.4–27.7)	21.5 % (3.6–39.3)	1.4 (0.3–5.7)	23.7 % (8.7–38.7)	13.2 % (1.8–24.6)	0.5 (0.1–1.9)
Specific phobia	54.4 % (39.4–69.4)	43.1 % (19.9–66.3)	0.6 (0.2–1.9)	47.2 % (32.5–61.9)	69.4 % (48.6–90.2)	1.4 (0.4–5.6)	50.1 % (35.3–64.9)	59.1 % (37.6–80.5)	1.4 (0.5–4.1)	54.2 % (37.3–71.2)	53.8 % (35.5–72.0)	1.0 (0.4–2.7)
Panic disorder	4.4 % (0.0–10.3)	0 %	–	4.2 % (0.0–9.9)	0.0 %	–	3.5 % (0.0–9.3)	2.2 % (0.0–6.6)	0.6 (0.0–8.4)	1.3 % (0.0–3.9)	5.1 % (0.0–13.4)	4.0 (0.3–56.7)
Social phobia	11.4 % (1.6–21.3)	17.6 % (0.0–37.0)	1.7 (0.3–8.8)	12.5 % (3.0–22.0)	22.9 % (0.2–45.6)	2.0 (0.4–10.0)	15.0 % (4.3–25.7)	15.3 % (0.0–32.6)	1.0 (0.2–5.1)	14.3 % (10.9–27.5)	16.6 % (3.1–30.2)	1.2 (0.3–5.4)
GAD	73.0 % (62.1–84.0)	47.0 % (23.7–70.3)	0.3 (0.1–1.0)	63.4 % (51.9–75.0)	75.9 % (55.9–95.8)	1.8 (0.5–6.2)	68.1 % (57.8–78.4)	62.5 % (41.5–83.5)	0.8 (0.3–2.1)	70.8 % (58.4–83.1)	65.6 % (50.2–81.0)	0.8 (0.3–2.0)
Separation anxiety	18.0 % (7.5–28.4)	19.0 % (0.0–38.5)	1.0 (0.3–4.5)	15.5 % (5.5–25.5)	28.0 % (5.0–51.0)	2.1 (0.5–8.7)	19.0 % (8.8–29.3)	17.4 % (0.2–34.7)	0.9 (0.2–3.3)	19.0 % (4.2–33.9)	19.0 % (5.6–32.5)	1.0 (0.3–3.9)
Major depression	16.9 % (6.0–27.8)	10.1 % (0.0–26.0)	0.5 (0.0–4.0)	15.3 % (5.7–25.0)	12.4 % (0.0–30.0)	0.8 (0.1–4.5)	17.6 % (6.7–28.5)	7.1 % (0.0–20.8)	0.4 (0.0–3.3)	17.5 % (3.3–31.6)	12.5 % (0.2–24.8)	0.7 (0.1–3.3)
Oppositional defiant dis.	23.0 % (9.8–36.2)	40.8 % (20.8–60.7)	2.3 (0.7–7.3)	20.5 % (8.5–32.4)	53.7 % (31.0–76.3)	4.5* (1.3–15.3)	25.2 % (11.7–38.6)	37.4 % (17.7–57.1)	1.7 (0.5–5.7)	22.1 % (7.0–37.2)	36.6 % (19.9–53.3)	2.0 (0.6–6.7)
Conduct disorder	0 %	8.2 % (0.0–23.9)	–	0 %	8.2 % (0.0–24.0)	–	0 %	7.1 % (0.0–20.8)	–	4.2 % (0.0–12.4)	0 %	–
ADHD	56.9 % (42.1–71.8)	61.6 % (40.7–82.5)	1.2 (0.4–3.5)	56.2 % (41.8–71.0)	68.0 % (47.4–88.4)	1.6 (0.5–5.0)	56.9 % (42.4–71.5)	64.6 % (45.3–84.0)	1.4 (0.5–3.9)	66.4 % (50.9–81.9)	54.9 % (37.0–72.6)	0.6 (0.2–1.7)
Motor and vocal tic dis.	18.6 % (7.1–30.0)	8.3 % (0–19.8)	0.4 (0.0–2.1)	14.0 % (3.8–24.0)	28.0 % (6.3–49.8)	2.4 (0.6–9.3)	21.5 % (9.8–33.3)	7.2 % (0.0–17.1)	0.3 (0.0–1.4)	18.0 % (3.3–33.0)	17.6 % (5.3–29.9)	1.0 (0.3–3.6)
Encopresis	0 %	5.9 % (0.0–14.8)	–	2.6 % (0.0–5.7)	0 %	–	2.0 % (0.0–5.2)	1.6 % (0.0–4.8)	0.8 (0.0–10.0)	0 %	4.0 % (0.0–8.9)	–
Enuresis	10.2 % (2.0–18.5)	21.1 % (1.1–41.0)	2.3 (0.5–10.4)	16.7 % (6.7–26.7)	3.8 % (0.0–9.0)	0.2* (0.0–10.0)	10.8 % (2.5–19.1)	20.3 % (2.1–38.4)	2.1 (0.5–8.6)	13.7 % (1.6–25.7)	14.0 % (3.2–24.9)	1.0 (0.3–3.9)
Night terrors	1.3 % (0.0–3.1)	15.7 % (1.5–29.9)	14.2** (2.4–84.6)	4.5 % (0.5–8.5)	6.0 % (0.0–15.1)	1.4 (0.2–8.8)	1.6 % (0.0–4.0)	12.9 % (1.1–24.7)	8.9* (1.4–56.0)	2.4 % (0.0–5.8)	7.5 % (0.5–14.6)	3.3 (0.5–20.7)

* $p < 0.05$; ** $p < 0.01$

[a] Any emotional disorder = major depression ± any anxiety disorder

17.4 % is strikingly similar to the rate of 13.8 % that we reported in older children using the CAPA (Simonoff et al. 2008). Interview reports are not the optimal method for identification as, on the one hand, informants may not have noticed tics and, on the other, may confuse them with stereotypies and mannerisms in ASD. Finally, despite inherent methodological difficulties in the study of sleep disorders, we report rates for night terrors that are similar to previous studies for this age group of children with ASD (Krakowiak et al. 2008; Richdale and Schreck 2009; Williams et al. 2004). The reported association between ASD severity and parental psychological distress has been reported elsewhere (Doo and Wing 2006; Mayes and Calhoun 2009).

Co-occurrence Amongst Additional Psychiatric Disorders

The finding that most children with ASD meet criteria for multiple disorders fits with previous studies (de Bruin et al. 2007; Gjevik et al. 2011; Leyfer et al. 2006; Mattila et al. 2010; Mukaddes and Fateh 2010; Mukaddes et al. 2010; Simonoff et al. 2008). The extent of co-occurrence is higher than that reported in the general population. This may in part reflect issues about classification (Rutter 2011; Sterba et al. 2010). We also found high levels of co-occurrence among the three main domains of ADHD, ODD/CD and emotional disorders.

Risk Factors and Correlates of Psychiatric Disorders

This is one of the first studies to include a sufficient number of girls with ASD to evaluate sex differences. The only differences found were higher rates of ADHD and ODD in boys, findings mirroring those among typically developing children (Egger and Angold 2006). There is a relative absence of associations with age, bar those already described with respect to anxiety, but we note the limited age range of the present sample.

As with our previous studies we found that ID, a well-known risk factor for most psychiatric disorders in the general child population, was *not* associated with most additional disorders in this sample (Charman et al. 2011; Eisenhower et al. 2005; Simonoff et al. 2008). With respect to family characteristics, a similar lack of association to that reported here has been found in previous studies indicating that these factors may be less important in ASD than in typically developing children, possibly due to different causal pathways (Gadow et al. 2008; Gjevik et al. 2011; Simonoff et al. 2008). We failed to find associations between parental psychological distress and psychiatric disorders; this finding is at odds with several other studies (Davis and Carter 2008; Hastings 2003; Tehee et al. 2009)

but in line with our previous report in later childhood, where psychopathology was unrelated to parenting stress or maternal psychological distress (Simonoff et al. 2008). Many of the previous studies are of small sample sizes. Further, measures of 'parenting stress' often include items indexing characteristics of the parent–child relationship, which may be influenced by ASD symptoms and other psychopathology. In the present study, we measured parental psychological distress, rather than parenting stress, which may partially account for the differences. One large study demonstrated a link between parental psychopathology/psychological distress and the presence of ASD in contrast to typical development (Totsika et al. 2011) and an earlier meta-analysis demonstrated considerable inconsistency among studies but an overall relationship with parental psychopathology that was moderated by the child's level of functioning (Yirmiya and Shaked 2005). More research is needed to disentangle these relationships and understand the link to additional psychopathology as opposed to ASD characteristics.

Strengths and Limitations

Strengths of this study include its careful sampling method and the large proportion of females. To our knowledge, this is the first study of psychopathology in ASD to over-sample females allowing a better comparison across the sexes. This study uses community-based clinics providing universal diagnostic services and hence includes all children with an ASD diagnosis in the sampling frame. There are also several limitations. Children had clinical rather than research diagnoses of ASD. Although there were few differences between those participating and declining, the non-participating children had higher SCQ scores. Because SCQ scores were associated with social disadvantage, the sample may under-represent families with higher levels of psychosocial adversity as well as those with most severe autism symptoms. Another limitation is the use of an instrument, the PAPA, that has not been validated in populations with either ASD or ID. However, we believe that the careful methodology allows our findings to be compared to general population samples. As with a number of other studies, the use of parent-only assessments, such as the PAPA, limits the way in which 'pervasiveness' is defined for diagnoses such as ADHD. However, because the ADHD diagnostic algorithm requires parents to indicate knowledge of the child's behaviour in other settings (such as school), it is not clear whether this will increase or decrease the reported prevalence. We note that parents of children in this age group are usually closely involved in their children's activities outside the home and are likely to be able to report on their behavior in these other settings. This is a moderately sized sample, but because of the

exploration of moderating factors, some of the associations we report have wide confidence intervals and need to be interpreted with caution.

In summary, our study shows that the high rates of psychiatric disorders in ASD previously reported for older children and adolescents also occur in younger children. Many of these disorders have evidence-based interventions, at least for typically developing children. Therefore, clinical implications include the need to systematically assess for additional psychopathology at an early stage when children are diagnosed with ASD, as recommended in the UK (National Institute for Clinical Excellence Guidance 2012). There is also a need for validated screening and diagnostic tools for psychopathology for this population and this should be a high priority for future research. Finally, in the absence of effective treatment for the core symptoms of ASD, and with the knowledge that additional psychopathology persists in ASD, it is essential to develop an evidence base for treatment of co-occurring psychopathology (Simonoff et al. 2013a).

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