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Detecting Autism Spectrum Disorders in the General Practitioner'S Practice

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Abstract It takes considerable time before Autism Spectrum Disorders are diagnosed. Validated diagnostic instruments are available, but not applicable to primary healthcare. By means of a case–control study we investigated whether there were differences in presented complaints and referral patterns between children with ASD ($n = 49$) and a control group of children without ASD ($n = 81$). Children with ASD were often presented as crybabies and often showed feeding problems. They visited the GP's surgery more often with anxiety disorders, enuresis, and sleeping disorders. They were referred more often to physiotherapists and speech-therapists and had tympanostomy tubes and tonsillectomies more often. Depression in the parents of children with ASD was remarkably prevalent.

Keywords Autism Spectrum Disorders · Detecting · General practitioner · Presented complaints · Referral patterns

Introduction

In the Netherlands, there are about 11,000 young people with Autism Spectrum Disorders (ASDs). ASD is not as rare as is commonly thought (Land and Schoemaker 2005) and, right from the birth of the child with ASD, this affects

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the entire family (Delfos 2003), which is a physical, emotional, and financial burden (Ghanizadeh et al. 2009; Hall and Graff 2010; Twoy et al. 2007).

Classic autism is currently detected at about three years of age (Barbaro and Dissanayake 2009), Asperger's syndrome and PDD-NOS tend to be diagnosed later with a mean age of, respectively 7.2 and 3.9-year-old (Barbaro and Dissanayake 2009) because there are fewer symptoms to alert parents and professionals that development is impaired. And the complex nature of these disorders and the current lack of consistent and reliable genetic or biologic diagnostic markers, make diagnosing challenging. There is consensus that de disorder has prenatal onset, thus there is considerable delay before children with ASD are diagnosed (Baron-Cohen et al. 2006). Investigations have shown that it is possible to diagnose Asperger's Syndrome and PDD-NOS before the age of 3, so it is the recognition that is the problem, and not a late onset (McConachie et al. 2005; Mulvihill et al. 2009).

Diagnostics and treatment are inextricably bound up with each other. Autism cannot be cured, but the children's, parents', and families' quality of life can be considerably improved with the right treatment approach (Berckelaer-Onnes 2004; Howlin et al. 2009; Reichow 2009; Sheinkopf and Siegel 1998). Early intervention is the best response to ASD: the earlier treatment is started, the more favourable treatment outcomes are (Howlin et al. 2009; Reichow and Wolery 2009; Rhoades et al. 2007; Sheinkopf and Siegel 1998). The younger the child, the better the opportunities are to move the young child toward a more typical developmental trajectory because of plasticity of the young brain. Also, the onset of secondary, compensatory behaviors may be prevented of minimized (Dawson 2008; Mundy et al. 2009). Although most children with ASD show problems before 12 months, there is a cohort of children who appear to develop typically after 12 months of life (Werner and
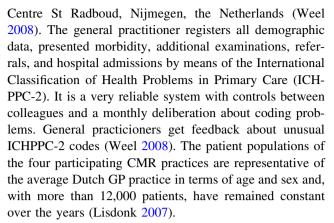
Dawson 2005; Goldberg et al. 2003). They reach appropriate language and social skills milestones, but then progressively lose these skills mainly in language, followed by social skills (Werner and Dawson 2005; Goldberg et al. 2003). Previous studies have found that regression in ASD occurs most often between 12 en 24 months of age (De Giacomo and Fombonne 1998; Rogers and Di Lalla 1990). This regression occurs in approximately 20 to 49% of children with ASD, with these different percentages as an outcome of the different diagnostic status of the child (Kurita 1985; Hoshino et al. 1987; Siperstein and Volkmar 2004). If the intervention will take place before this 'drop off', the impact on development will be even greater. Diagnosis, moreover, is often a great relief to parents, for they are aware very early on that something is the matter with their child without being able to pinpoint it exactly (Howlin and Asgharian 1999). Early diagnosis, therefore, is a source of relief to parents and a source of greater satisfaction with healthcare providers (Goin-Kochel et al. 2006).

Diagnosing ASD proceeds in accordance with clear guidelines, using validated diagnostic instruments like the ESAT, ITC, CHAT and M-CHAT (Barbaro and Dissanayake 2009; Baron-Cohen et al. 1992; Dumont-Mathieu and Fein 2005; Gaag and Van Berckelaer-Onnes 2000). However, these instruments are mainly used in secondary or tertiary healthcare, and before children end up there, they will have gone through lengthy procedures involving considerable delay (Goin-Kochel et al. 2006). Primary health practitioners are not specifically trained to detect autism early and the disorder is relatively rare. There is a wide variety in symptomatology and presentation (Berckelaer-Onnes 2004). Also, most sets of criteria emphasise abnormalities in social and communicative development, both of which are difficult to assess before the age of 3. So as to reduce this delay in diagnostics, we investigated whether there are characteristic complaints that children with ASD present to the GP. As detection is an important task of the GP, an improved detection profile at the GP's practice may accelerate diagnostics. The Continuous Morbidity Registration (CMR) project, a database with prospectively collected long-term morbidity data, gave us the possibility to compose a cohort of children with ASD and a control group (Weel 2008). We framed the following research question:

Is there a difference in complaints presented in the general practice and in referral patterns between children with ASD and children without ASD?

Method

This study is a case–control study, making use of the CMR of the primary healthcare department at University Medical Centre St Radboud, Nijmegen, the Netherlands (Weel 2008). The general practitioner registers all demographic data, presented morbidity, additional examinations, referrals, and hospital admissions by means of the International Classification of Health Problems in Primary Care (ICH-PPC-2). It is a very reliable system with controls between colleagues and a monthly deliberation about coding problems. General practicioners get feedback about unusual ICHPPC-2 codes (Weel 2008). The patient populations of the four participating CMR practices are representative of the average Dutch GP practice in terms of age and sex and, with more than 12,000 patients, have remained constant over the years (Lisdonk 2007).

We used the CMR to select all patients up to 25 years of age who were diagnosed with ASD from 1985 until 2009. Upon consultation the Medical Ethics Committee region Arnhem-Nijmegen stated that ethical approval was not necessary because of the non-invasive and anonymous character of the study. In the CMR, the diagnosis of ASD is made in accordance with the DSM IV criteria (American Psychiatric Association, 1994). The patient files, supplemented with specialist correspondence if appropriate, were used to collect the following data.

Background Data

Date of birth, sex, socio-economic status, the family situation of the child (lives with father and mother, father or mother or other), and the total number of children. Socio-economic status was defined as high, middle, or low based on education and profession (Weel 2008). The parents' files were used to register any present psychiatric issues: schizophrenia/psychosis; anorexia nervosa/conversion disorder; phobia/anxiety disorder/obsessive–compulsive disorder; depression; personality disorder/behavioural disorder; addiction; pervasive development disorder.

Morbidity

The morbidity we examined was selected for its possible relation with ASD as described in the literature (Ashwood and Van de Water 2004; Cohly and Panja 2005; Gillott and Standen 2007; Jyonouchi et al. 2008; Krakowiak et al. 2008; Simonoff et al. 2008; Sterling et al. 2008; Sukhodolsky et al. 2008), such as problems in pregnancy (preeclampsia; eclampsia; premature birth; apgar score), feeding problems and crybaby (colic). Premature birth is defined as birt before the 37th week of pregnancy (Goldenberg et al. 2008). The definition of a crybaby (or colic) is the condition of a healthy baby in which it shows periods of intense, unexplained crying lasting more than 3 h a day, more than 3 days a week for more than 3 weeks (Wessels 1954). We also recorded psychiatric issues (psychosis; anorexia

nervosa; conversion disorder; phobia, anxiety, and or obsessive–compulsive disorder; depression; personality disorder; addiction; sleepproblems; enuresis; encopresis; trichotillosis), atopy, and traumata (fractures; luxations/ distortions; wounds/injuries; intoxications). All diagnoses were defined in conformity with the diagnostic criteria as used in the CMR (Weel 2008). The morbidity had to be present before the diagnosis of ASD.

Referrals

Referrals (before diagnosis) to neurologists, paediatricians, physiotherapists/ergotherapists, speech therapists, social workers, and Ear, Nose and Throat (ENT) doctors. The ENT referrals concerned the placement of tympanostomy tubes or tonsillectomy. The referrals had to be made before diagnosis.

We constructed a control group in order to compare the results in children with ASD with children without ASD. The control group was put together from the same four CMR practices at double the size of the research population and was matched with the ASD group for age, sex and practice. The CMR recording is based on the Dutch healthcare system, where all patients are registered with a GP and all access to primary and secondary care is via the GP. The control group was to have no codes for any pervasive development disorder, conduct disorder, learning difficulties and other psychiatric diseases, since these codes are likely to proceed to the diagnosis ASD. We compared the ASD group with the control group for psychiatric morbidity (phobia, anxiety, and/or obsessive–compulsive disorder, sleeping disorders and enuresis), atopy, traumata, and referrals to paediatricians, physiotherapists/ergotherapists, speech therapists, social workers, and ENT doctors. The date of diagnosis in the ASD group served as the comparison date for the controls. The controls had to be present in the practice at the time the ASD group was diagnosed with ASD. Next we compared the psychiatric problems of the parents of the children in the ASD group with the psychiatric problems of the parents in de control group. The psychiatric problems had to be present before or at the date of diagnosis of ASD in the ASD group.

The CMR data we obtained, were analysed with the aid of an SPSS programme to compute percentages, means, and standard deviations. We calculated odds ratio's with confidence interval to compare the ASD group with the control group. A p value below 0.05 or a confidence interval not containing 1, are considered as statistical significant. Because data about apgar score, feeding problems, cry babies, (pre)eclampsia and pre-term birth are not recorded by ICPC-coding in the CMR, we therefore, retrieved these data from the correspondence with specialists. We used the official definition while searching

through the correspondence in order to make the results reliable. Because we made a control group using the CMR it was not possible to compare these data with controls: we compared the data with known prevalence's in literature. Risk factors for ASS were analyzed in a multivariate logistic model to assess the independent predictors of ASS.

Results

Background Data

For characteristics of the research and control group see Table 1. The research population consisted of 49 children. There was no non-response or drop-out. The mean age at diagnosis was 8.74 (SD = 3.54) for boys and 9.17 (SD = 4.12) for girls. 7 Children were diagnosed with Asperger's Syndrome, the rest were diagnosed with PDD-NOS. There were no children with classic autism. Most children were living with both their biological parents (65.3%) and were the eldest child (63.3%) in a family of two (42.9%). At the time of this study, mean age of the boys was 14.1 (SD = 4.4) and that of the girls was 13.4 (SD = 4.2). Mean age of the father at the time of the child's birth was 34.5 years (SD = 5.4); mean age of the mother was 31.9 (SD = 4.2). The files of 40.0% of the mothers and 31.0% of the fathers recorded psychiatric problems (Tables 2, 3). Depressions were significant higher in both fathers (19.0% vs. 2.9%; Odds ratio 7.85; 95% CI 1.71 to

Table 1 Demographics study population $n = 49$ and control group $n = 81$

	Study population (%)	Controls (%)
Gender		
Male	42 (85.7)	69 (85.19)
Female	7 (14.3)	81 (14.81)
Socio-economic status		
Low	11 (22.4)	23 (31.08)
Middle	22 (44.9)	30 (40.54)
High	7 (14.3)	21 (28.38)
Unknown	9 (18.4)	0 (0.00)
Caretakers		
Father and mother	32 (65.3)	67 (82.7)
Father or mother	10 (20.4)	7 (8.6)
Other	7 (14.3)	2 (2.5)
Unknown	0 (0)	5 (6.2)
Total number of children		
1	9 (18.4)	5 (6.2)
2 or 3	35 (71.4)	65 (80.2)
4 or 5	5 (10.2)	4 (4.9)
Unknown	0 (0)	7 (8.6)

Table 2 Mental health of fathers ($n = 42$) compared to the fathers in the control group ($n = 70$)

	Fathers of a child with ASD number (%)	Fathers in control population number (%)	Odds ratio's (95% CI)	p value
Depression	8 (19.0)	2 (2.9)	7.85 (1.71 to 56.66)	<0.01*
Phobia/anxiety/obsessive–compulsive disorder	3 (7.1)	0 (0.0)		0.05
Addiction: alcohol/drugs/other (tobacco excluded)	3 (7.1)	2 (2.9)	2.59 (0.37 to 22.59)	0.34
Personality disorder	1 (2.4)	0 (0.0)		0.38
Autistic spectrum disorder	0 (0.0)	0 (0.0)		
Schizophrenia/psychosis	0 (0.0)	1 (1.4)		0.63

* p value below 0.05 is considered as significant

Table 3 Mental health of mothers ($n = 45$) compared to the mothers in the control group ($n = 76$)

	Mothers of a child with ASD number (%)	Mothers in control population number (%)	Odds ratio's and (95% CI)	p value
Depression	16 (35.6)	9 (11.8)	4.05 (1.61 to 10.66)	<0.01*
Phobia/anxiety/obsessive–compulsive disorder	3 (6.7)	1 (4.0)	4.86 (0.50 to 131.50)	0.16
Personality disorder	2 (4.4)	0 (0.0)		0.14
Anorexia nervosa/conversion disorder	1 (2.2)	0 (0.0)		0.37
Autistic spectrum disorder	0 (0.0)	0 (0.0)		

* p value below 0.05 is considered as significant

56.6) and mothers (35.6% vs. 11.8%; Odds ratio 4.05; CI 1.61 to 10.66). There were no cases of anorexia nervosa or a conversion disorder in the group of fathers. In the group of mothers there was no registered addiction (alcohol, drugs, other, but no tobacco) and no schizophrenia or psychosis.

Morbidity

Preeclampsia and eclampsia occurred in 8.2 and 2.0% of the cases and 10.2% of the babies were premature. 12.2% of the babies were born preterm. All babies obtained Apgar scores over 7. More than one in four boys was diagnosed as a crybaby, and in girls this percentage was approximately one in two. More than a quarter of the girls had postparturition feeding problems (28.6%), for the boys this was 7.1%. There was a significantly higher prevalence of phobia, anxiety, and obsessive–compulsive disorders in the ASD group (16.3% vs. 0.0%; $p < 0.01$) (Table 4). Enuresis was also significantly more diagnosed (18.4% vs. 2.5%; Odds ratio 8.74; 95% CI 1.97 to 61.77) as were sleeping disorders (24.5% vs. 0.0%; $p < 0.01$), especially in girls (42.9%). Half the boys and a quarter of the girls had atopy, which was the same as in the control group. There were more luxations in the ASD group (20.4% vs. 3.0%; Odds ratio 6.57; 95% CI 1.79 to 31.13) wounds or injuries were reported by 76.2% of the boys and 57.1% of the girls,

which, however, was not significant compared to the control group (45.5%). Fractures and intoxications were not more prevalent than in the control group.

Referrals

Before the diagnosis of ASD was made, more than half the patients had been referred to a physiotherapist/ergotherapist (54.3% vs. 11.1%; Odds ratio 8.90; 95% CI 3.68 to 22.89) or speech therapist (45.7% vs. 6.2%; Odds ratio 11.99; 95% CI 4.27 to 38.94), and patients were often referred to both (Table 5). There were significantly more referrals to ENT doctors for tonsillectomy or tympanostomy tubes than in the control group (41.3% vs. 14.8%; 3.40; 95% CI 1.71 to 9.60).

We calculated a multivariate analyse with the risk factors enuresis, luxations and referrals to the physiotherapist/ergotherapist, speech therapist and ENT doctors. We couldn't add the risk factors phobia, anxiety, and obsessive–compulsive disorders and sleep disorders in this multivariate model, because their were no children with these -conditions in the control group. After calculation the variables luxations, referrals to the physiotherapist/ergotherapist, speech therapist and ENT doctors were still risk factors for ASD ($p < 0.05$), but enuresis was not a risk factor any more ($p = 0.458$) (Table 6).

Table 4 Comorbidity of children with ASD ($n = 49$) and children without ASD ($n = 81$)

	Children with ASD number (%)	Children without ASD number (%)	Odds ratio's (95% CI)	p value
Phobia/anxiety disorder/ obsessive–compulsive disorder	8 (16.3)	0 (0.0)		<0.01*
Enuresis	9 (18.4)	2 (2.5)	8.74 (1.97 to 61.77)	<0.01
Sleep problems	12 (24.5)	0 (0.0)		<0.01*
Atopy	23 (46.9)	25 (30.9)	1.97 (0.94 to 4.14)	0.89
Fractures	4 (8.2)	8 (9.9)	0.81 (0.20 to 2.85)	0.77
Intoxications	4 (8.2)	2 (2.5)	3.48 (0.59 to 28.04)	0.17
Luxations/distortions	10 (20.4)	3 (3.0)	6.57 (1.79 to 31.13)	<0.01*
Wounds/injuries	36 (73.5)	46 (56.8)	2.10 (0.97 to 4.65)	0.06

* p value below 0.05 is considered as significant

Table 5 Referrals in children with ASD ($n = 46$[a]) and children without ASD ($n = 81$)

	Children with ASD number (%)	Children without ASD number (%)	Odds ratio's (95% CI)	p value
Physiotherapist/ergotherapist	25 (54.3)	9 (11.1)	8.90 (3.68 to 22.89)	<0.01*
Speech therapist	21 (45.7)	5 (6.2)	11.99 (4.27 to 38.94)	<0.01*
ENT doctors	19 (41.3)	12 (14.8)	3.40 (1.71 to 9.60)	<0.01*
Pediatrician			1.45 (0.69 to 3.07)	0.59

* p value below 0.05 is considered as significant

[a] 3 missing

Table 6 Multivariate analyses risk factors ASD (enuresis, luxations, referrals to the physiotherapist/ergotherapist, speech therapist and ENT doctors; missing phobia, anxiety, and obsessive–compulsive disorders and sleep disorders) in children with ASD ($n = 49$) and children without ASD ($n = 81$)

	Odds ratio's	95% CI	Significant
Enuresis	2.05	0.31 to 13.65	
Luxations	11.17	2.07 to 60.18	*
Physiotherapist/ ergotherapist	12.63	3.92 to 40.68	*
Speech therapist	7.07	1.87 to 26.67	*
ENT doctors	5.54	1.62 to 18.98	*

* p value below 0.05 is considered as significant

Discussion

With respect to problems in the pregnancy we find no striking differences between the ASD group en the general population. Preeclampsia occurred in the pregnancies of approximately 1 in 12 children. This is the same percentage as in the general population, were percentages between the 7.0 and 10.0% are reported (Vigil-De Gracia 2001). One pregnancy (2.0%) ended in eclampsia; this is slightly higher than the general population, where percentages range between 0.2 and 0.6% (Benedetto et al. 2011).

However, this was just one child. 12.2% of the children were pre-term, this is more than in the general population were the percentage is 6.2% (Cousens et al. 2010). It has been shown before that hypoxaemia and Apgar scores below 7 are a possible risk factor in the development of ASD (Kolevzon et al. 2007). In this research population all children had Apgar scores above 7. Post-partum there were more problems. The number of crybabies is one in tree (30.6%). This is a high percentage compared the prevalence between 3.0 and 20.0% in the general population (Hiscock and Jordan 2004; Long 2001).

There are significantly more phobias, anxiety disorders, and obsessive–compulsive disorders. In the literature, ASD has also been linked with obsessive–compulsive disorders (Jacob et al. 2009). Kanner's hypothesis in 1943 was that characteristics like rigidity and repetitive movements were related to anxiety. It might also be the case that, due to the nature of the disorder, people with autism lack the skills to cope with stress or to recognize situations that might cause anxiety. Enuresis is also more prevalent in the ASD group, which has not been reported in the Detecting ASD in the GP's practice literature before. This might be explained by children with ASD being less receptive to instruction or by hypotonia of the pelvic floor muscles. Over a quarter of the children visited the GP with sleeping disorders, while there were no registered sleep problems in the controls.

In the literature, it is reported that children with ASD frequently have bowel problems. These bowel problems respond well to dietary adjustments (Jyonouchi et al. 2008). This has given rise to the theory that there may be a higher sensitivity to atopy among children with ASD. Though we have seen many post-parturition feeding problems in our study, atopy is not more prevalent than in the control group.

A large group of children with ASD presents one or several traumata, with significantly more luxations and distortions in the ASD group. In their study, Mint et al. reported motor apraxia in 34% and hypotonia in 51% of all children with ASD. Hypotonia might offer an explanation for the frequent occurrence of luxations and distortions in children with ASD.

Before being diagnosed with ASD, virtually all children were referred more than once. Motor apraxia might explain frequent referrals to physiotherapists. Verbal development retardation, which is inherent to ASD with the exception of Asperger's syndrome, may help to explain referrals to speech therapists. Parents of children with ASD more often report bronchial infections (Cohly and Panja 2005), which might help to explain the frequent referrals to ENT doctors.

A striking feature is the frequent occurrence of depression in families with a son or daughter with ASD. One in five fathers and one in three mothers were suffering from depression or suffered from depression in the past. This might be explained by the burden involved in raising a child with ASD, but, considering the congenital component in ASD (Jacob et al. 2009; Muhle et al. 2004; Santangelo and Tsatsanis 2005), one might also think of undiagnosed parental ASD.

An other glaring finding is that the age at diagnosis in the ASD group is rather late (8.74-year-old for boys and 9.17-year-old for girls), compared to the data we find in the literature (7.2-year-old for PDD-NOS and 3.9-year-old for Asperger's Syndrome). An explanation may be that the majority of children in our study group were suffering from PDD-NOS and Asperger's syndrome. Both diseases are difficult to diagnose, so a detecting profile for these diseases is needed and usefull. Another explanation can be that our age of diagnostics is determined by the GP who adds the code for ASD in the file of the patient. So there can be a delay: when the psychiatric diagnoses the ASD, it takes some time before this diagnosis reaches the GP, and thus, before he adds the code for ASD in the file of the patient. So this can be a restriction in our study.

Another restriction in our study is that we had to accept registration and diagnosis as these had been performed by GPs. However, the CMR registration is characterized by a high degree of validity and reliability as GPs regularly test each other for uniformity of registration (Weel 1995). Moreover, the study population was small, involving 49

patients. Because of the small population we were only able to discover large effects. However, these results will be of more use for clinical practice. It is a strength of this study that it involved no selective non-responses or drop-outs and besides the CMR data allow for a unique case–control study.

In conclusion children with ASD present more often as crybabies, especially girls. Girls also show more feeding problems. Children with ASD also report to the GP's surgery more often with anxiety disorders, enuresis, and sleeping disorders. There is a significantly higher prevalence of luxations. In addition, they are more often referred to physiotherapists and speech therapists and to ENT doctors for placement of tympanostomy tubes or for tonsillectomy. Lastly depression in the parents is also more prevalent than can be expected.

Taking our findings separately there is no strong evidence for the diagnosis ASD. Combined together nevertheless the characteristics can form important cues in detecting ASD. Our findings must be validated in a prospective study in order to develop a detection profile in the primary care. Given the fact that there is still a delay in diagnosing ASD a reliable and valid profile of symptoms in order to detect ASD is urgently needed.

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