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Validation of the diagnosis of autism in general practitioner records

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Abstract

Background

We report on the validity of the computerized diagnoses of autism in a large case-control study investigating the possible association between autism and the measles, mumps and rubella vaccine in the UK using the General Practitioner Research Database (GPRD). We examined anonymized copies of all relevant available clinical reports, including general practitioners' (GP) notes, consultant, speech therapy and educational psychologists reports, on 318 subjects born between 1973 and 1997 with a diagnosis of autism or a related disorder recorded in their electronic general practice record.

Methods

Data were abstracted to a case validation form allowing for the

identification of developmental symptoms relevant to the diagnosis of pervasive developmental disorders (PDDs). Information on other backgro features was also abstracted. A subset of 50 notes was coded independ reliability estimates for key clinical characteristics.

Results

For 294 subjects (92.5%) the diagnosis of PDD was confirmed after revie these, 180 subjects (61.2%) fulfilled criteria for autistic disorder. The me a PDD diagnosis in the GPRD database was 6.3 years (SD = 4.6). Consis estimates, the proportion of subjects experiencing regression in the cou was 19%. Inter-rater reliability for the presence of a PDD diagnosis was agreement on clinical features such as regression, age of parental recogn language delay and presence of epilepsy was also good (kappas ranging

Conclusions

This study provides evidence that the positive predictive value of a diagr the GPRD is high.

Background

Of 32 epidemiological surveys of autism and pervasive development diso recent review [1], 13 were published within the last 5 years. Increased r field of neuropsychiatry has led to a refinement of the definition of autisr combination of qualitative impairments in language/communication, in so patterns of play behaviours and interests. Improved operationalisation o within nosographies has occurred (American Psychiatric Association, 199 Organization, 1992), in parallel with the development of more precise dia as the Autism Diagnostic Interview [2] and the Autism Diagnostic Observ There has also been an increasing concern by the public about this group in part, by concern that the rates of PDD may have increased in recent d cause of the increase may be due to the side effects of vaccination [7-9] young infants to neurotoxins such as methylmercury or thimerosal [10].

The investigation of risk factors for autism in epidemiological surveys has size of many studies. The median number of cases identified in the 32 su children [1]. Some investigators examined the effects of specific environ large samples of subjects obtained from educational or hospital services computerized databases obtained through research networks of general General Practitioner Research Database (GPRD) [14], the Doctor Indepe in the UK [15], national registers [16] and memberships of consumer ass problems with the use of these databases because of uncertainties abou diagnosis of the cases. Often there is no information on specific clinical ch allow identification of subgroups of individuals within the same diagnosti with autism who have regressed in the course of their development), pre hypotheses proposing an association between subtypes of PDDs and sp

To test the hypotheses of a link between autism and exposure to combir rubella vaccines, or to other infectious agents, we designed a study base the GPRD database in the UK [19,20]. The research protocol included eva diagnoses in the GPRD database by obtaining clinical reports on a sub-sa in the study. We report the results of this validation study on a subset o based on the reports in the medical files of the general practitioners thr were identified.

Methods

The General Practice Research Database

The GPRD (previously called the VAMP (Value Added Medical Products) R
in 1987 and is now held on behalf of the Department of Health by the Me
[21]. It consists of the computerised general practice medical records for
the United Kingdom. The electronic record includes demographic informa
details of every consultation with a general practitioner, all prescribed dr
given, and details of referrals to hospital or specialist services. It is poss
practitioners copies of hospital letters regarding specific patients (in anor
not all participating general practices provide this service.

Practices in the GPRD originally used a modification of the Oxford Medical
coding system to record diagnoses [22]. Through the 1990s an increasin
changed to the READ coding system, which is now used throughout the U
Health Service [23].

Selection of cases and data obtained

Of patients with a recorded diagnosis of PDD in the GPRD, including prev
registered, 446 were registered with 203 general practices willing to pro
records. For 80 of these patients, records were not available as the pati
registered with the general practitioner. We obtained complete case reco
hospital clinic letters and specialist reports for 318 (87%) of the remainir

Abstraction of clinical data

The case validation form included a section on socio-demographic data, a
level of language and of educational status, together with estimates of a
learning disabilities. The assessment of learning disabilities was based o
data and, when not available, on a best estimate of intellectual functioni
bands after review of all the available information. A section on health co
occurrence of epilepsy, of treatments with psychoactive drugs, of associa
body measurements of head circumference, weight and height, of dysmo
report of any significant non-autistic symptom in the course of the develo
as: gastrointestinal symptoms, infections, sleeping difficulties or immune
Symptoms were rated as being either reported or not reported since infc
detailed coding (based on severity of the symptom, age of onset and of
for most cases where symptoms were reported. A section on pregnancy
incidence of maternal illness and infection during pregnancy, the mode of
birth weight and birth order. A section on the early development of the c
milestones (coded as normal versus delayed), the age of first words and
an age in months or as an approximate age band), language delay (defi
occurring until after 24 months of age or phrase speech not occurring un
age), any regression or loss of skill at any point in the course of develop
the type of skill lost. For those cases with some regression/loss of skills,
provided by the rater on whether the developmental pattern was sugges
regression/loss of acquired skills as opposed to fluctuating development
skill acquisition. As age on onset of first symptoms is a key diagnostic cri
operationalised in three different ways. First, we recorded the age at wh
recognized signs of developmental delay or variation in their child and th
first triggered their concerns. Second, we recorded age at the date of the
concerns about a developmental problem in the child (e.g. a referral lette
specialist to gain an opinion). Third, rater's assessment of age of onset
judgment of age of first symptom onset, irrespective of actual parental a
recognition of these symptoms at the time. Specific or global developme
identified in the first and second-degree relatives, along with specific me
autoimmune) and psychiatric disorders.

The overall diagnostic rating of a child was made with two approaches, c
based on judgment of the rater. First, reports were searched for evidenc
symptoms for PDDs. A computer diagnostic algorithm using DSM-IV symp
Instead of using the typical DSM-IV algorithm (2 social symptoms, 1 com
symptoms, 1 repetitive behaviour symptom, together with at least 6 sym
possible), we generated an algorithm to take account of the uneven qua
subjects. The algorithm generated a PDD diagnosis when at least three
symptoms were scored, with the further constraint that there would be a
social domain and 1 symptom in either the communication/language or t
domain. This algorithm is consistent with that used in a recent survey us
review approach [5]. Second, when all the documentation had been revi
asked to make a global judgement regarding the presence or absence of
when present, to provide a diagnosis for the specific subtype of PDD wh
index of confidence in the rater's judgment about the PDD diagnosis was

Raters and inter-rater reliability

The two raters were a child psychiatrist (EF) and a psychologist (LH) bot
the field of autism. LH reviewed and coded all the files. In order to obtair
the rating procedure, a subset of 50 medical notes chosen at random an
was rated blindly by EF. Records that posed particular coding difficulties
consensus ratings were derived by the two raters at the end of the stud
eligible to be selected for the inter-rater reliability study. All ratings were
history of immunization.

Statistical analysis

All data were analyzed with SPSS and SAS with conventional chi-square
categorical variables and Student's t test for continuous variables. Inter-
measured with the kappa coefficient for categorical ratings and with the
coefficient (ICC) for continuous measures [24]. Throughout, a p value of
level of statistical significance. Missing data occurred at high rates for ma
the case validation forms and, as a result, we report both absolute and r

Results

Sample characteristics

Medical notes for 318 subjects were obtained. They varied in quality and
some children, GP records included several consultant reports, speech a
and educational psychology reports. For other children, the information a
sometimes the only available data consisting of one, or a few, letters be
consultants. A high proportion of records had missing data on parental a
and detailed psychometric assessment of the child and therefore the fre
variables are not described here. Of the 318 children whose medical forr
raters confirmed a diagnosis of PDD in 294 children (92.5%). Compared t
confirmed PDD diagnosis, children for whom the diagnosis was not confir
significantly fewer PDD symptoms (2.1 vs 6.2; $p < .001$), higher languag
80% vs 45%; p=.051), and more frequent parental concern arising for th
of 3 years (20% vs 2.9%; p=.024). No significant differences were found
birth year, presence of epilepsy or regression or in the average age at fi
database.

The main characteristics of the 294 children with a confirmed diagnosis o
1. The male/female ratio was 4.25:1. A third of the children had no phra
level was recorded (at a mean age of 7.9 years). About a third of childre
intellectual skills falling into the normal range. 55 (19%) children showed
regression and loss of acquired skills, and a further 34 had a developme

with an uneven and slow rate of acquisition of new skills as they grew u
and of epilepsy (18%) are consistent with those described in other surve
mean number and pattern of DSM-IV symptoms was consistent with the
autism, especially as symptoms of social deficits appeared to be reporte
1). The computer-based algorithm identified 237 (80.6%) of the 294 cas

Table 1. Characteristics of 294 Children with PDD

It was possible to allocate a more specific diagnosis to 217 of the 294 ch
autistic disorder in 180 children (82.9%), Asperger Disorder (AD) in 18 ch
PDDNOS (Pervasive Developmental Disorder Not Otherwise Specified) in
confidence level in the diagnostic subtype was generally high (high in 67.
and low in 13.1%). In the remaining 77 children (26.2%), the quality of t
the diagnosis of a specific PDD subtype. A comparison of the PDD childre
specific diagnosis showed that children without a PDD subtype were com
autism with respect to language level and intellectual functioning but clo
either PDDNOS or AD with respect to age at first electronic diagnosis and
Compared to both other groups, they had significantly fewer PDD sympto
reflecting the poorest quality of the notes that precisely precluded a fina
by raters.

The mean age at first parental concern regarding their child's developme
9.8) in 142 children where a precise age could be estimated. Age of first
in medical records could be estimated in broad age bands in 207 subject
3 years in 201 subjects (97.1%). Onset of first symptoms was also deter
judgment, based on the medical records, in 91 subjects and was 12 mon
subjects where both a parental and a rater age of onset were available,
onset was significantly younger than the age at parental concern (12.1 r
paired t-test; p = 0.02). Finally, the presence of a PDD in a first-degree r
was reported in 7.8% of the sample, consistent with other surveys of PD

We compared children with an autistic disorder diagnosis with children w
(Table 2). The PDDNOS/AD group had significantly fewer language and in
were on average 2.3 years older than their autistic counterparts when re
database. Regression was less often reported in the PDDNOS/AD group.

Table 2. Comparison of Children with Autism or other PDD (N = 217)

Since regression and loss of skills is a clinical feature of potential interes
examined further the clinical correlates of regression. As regression was
PDDNOS/AD group and as these children were different from children wit
age at diagnosis and severity, we restricted this analysis to those childr
autistic disorder (Table 3). The regressive and non regressive groups dif
language level and intellectual functioning where children with regressio
functioning at the final assessment. They also had a significantly lower a
letter on file mentioning a developmental problem.

Table 3. Autistic Children with or without Regression (N = 179[1])

Trends over time in clinical features that are known to indicate autism se
for the autism group (Table 4). Birth years were grouped into 5-year inte
significant trend for decreasing levels of mental retardation and for an in
males, suggesting that clinical presentation became less severe over tim
birth cohorts made the interpretation of trend for phrase speech and for

interpret. Other clinical features, including regression, did not change sig

Table 4. Characteristics of 178[1] Children with Autism over five year interv

Interrater reliability

Interrater reliability was examined on the subset of 50 randomly selecte between the two raters was good for the presence/absence of a PDD in t and there were only 2 cases where raters originally disagreed. The agre DSM-IV symptoms was excellent (ICC = .92). PDD symptom scores for ea separately showed high intra-class correlations as well, with ICC values domain, .75 for the communication/language domain, and of .91 for repe agreement was also good to excellent on the presence/absence of langu of regression or loss of skills in the course of development (Kappa = .58) = .84), on overall language level (Kappa = .62), on estimate of intellectu levels (normal range, mild retardation, moderate to profound retardation the presence/absence of any developmental disorder amongst first degr = .74). Reliability was lower for regression due to the difficulty in differen developmental stagnation and to establish language level before the rep

Discussion

We have shown that the positive predictive value of a diagnosis of autis electronic health record of patients in the General Practice Research Dat than in a previous study where the diagnosis of autism was confirmed in a GPRD computer record of autism [25]. A high positive predictive value f recorded in the GPRD has been found for a range of other conditions. Fo cataract identified had their diagnosis confirmed by a review of hospital summaries [26] and a recorded diagnosis of myocardial infarction was co cases [27]. In our study, the diagnosis of PDD was confirmed by expert 92.5% of the cases. Amongst the unconfirmed cases were several recor which precluded a positive confirmation of the diagnosis. A North Londor disability register identified a similar proportion of confirmed cases (89%) validation [28]. The study design precluded an estimate of the sensitivity PDD, that is the percentage of children with a PDD who did not have this records. This would have required a much more extensive study.

The characteristics of the children with PDD were consistent with those autistic samples. Thus, for children with an autistic disorder from this stu was 4.3:1 (146/34) and the proportion of subjects without intellectual im these results compare well to respective figures of 4.3:1 and 30% derivi epidemiological surveys of autism [1]. Equally, the 7.8% risk of PDD in th in line with current estimates [29]. Similarly, the rate of 19% (24% in the regression in the course of the development are consistent with the rate 31.3%) or more recent ([31]: 25%; [4]: 15.6%) epidemiological surveys samples ([32]: 37.2%; [33]: 29.6%; [34]: 30%). The relatively wide rang across studies reflects the different definitions and methods of data colle studies. Therefore, on a range of indices, our sample characteristics wer including well characterized PDD children.

Within the PDD spectrum, a relatively small proportion was identified as Asperger Disorder. This would not have been surprising in earlier years, Asperger Disorder was not defined until 1992, and therefore many of the received a diagnosis that lead to ascertainment in the sample. However, increased, there were still few children with these diagnoses among the in the GPRD. This was unexpected: evidence from epidemiological surve

prevalence of PDDNOS is higher than that of autistic disorder [1,4]. This alternative explanations: first, a precise differentiation between autism possible in our study (maybe due to our particular mode of data collectio of children with atypical forms of autism in the autistic disorder group; se with atypical autism were not diagnosed as having a PDD at all; and thir a PDD diagnosis, the recording of diagnosed PDDNOS into GPRD is less c The fact that the severity of autism, as indicated by gender ratio, intelle decreased over time supports the first interpretation. It could be the cas trend also reflects a genuine change in the association between autistic retardation, possibly due to earlier diagnosis and intervention.

Conclusions

We conclude from this validation study that the positive predictive value autistic spectrum disorders or of the broad category of PDDs is good in t differentiation of PDD subtypes within this broad PDD class was, howeve

Authors' contributions

LH and EF coded all the medical notes. LM, EF and CC analyzed the data. part in study design, interpretation of the results and writing the paper. approved the final manuscript.

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