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The Italian Preadolescent Mental Health Project (PrISMA): rationale and methods

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Abstract

The Italian preadolescent mental health project (PrISMA – Progetto Italiano Salute Mentale Adolescenti) is the first Italian study designed to estimate the prevalence of mental disorders in preadolescents (10–14 years old) living in urban areas, and to analyse the demographic and biological correlates of emotional and behavioural problems. This paper describes the rationale, methods and the analysis plan of the project.

The design of the study used a two-stage sampling procedure, one screening stage of emotional and behavioural problems in a large sample of subjects attending public and private schools and a second stage of diagnostic assessment in a sample including all high scorers and a proportion of low scorers. In the screening stage, parents of preadolescents were asked to fill in the Child Behavior Checklist (CBCL), whereas in the second stage preadolescents and their parents were administered the Development and Well Being Assessment for the assessment of mental disorders together with the Strengths and Difficulties Questionnaire and two scales (C-GAS and HoNOSCA) designed to evaluate the functioning of the preadolescent in different areas. Genetic samples were collected during the screening stage, after parents gave their informed written consent. The findings of this study are expected to allow an adequate planning of interventions for the prevention and the treatment of mental disorders in preadolescence as well as efficient health services. Copyright © 2006 John Wiley & Sons, Ltd.

Key words: mental disorders, preadolescence, prevalence, genetic screening

Introduction

In the last decade the increase in epidemiological studies and the widespread use of diagnostic classification systems such as the DSM-IV (American Psychiatric Association, 1994) and the ICD-10 (World Health Organization, 1993) have considerably improved our understanding of mental disorders in late childhood and early adolescence.

A review of 52 studies covering a period of nearly 40 years (Roberts et al., 1998) showed that the prevalence of mental disorders ranges between 1% and 51% in males and females and that it increases with age, from 10.2% (range 3.6%–24%) before the age of 6, to 13.2% in preadolescence (range 1.4%–30.7%) up to 16.5% in adolescence (range 6.2%–41.3%). The wide variation in prevalence estimates is attributed by the authors (Roberts et al., 1998) to the data collection methods (case ascertainment) and to the diagnostic criteria adopted (case definition). Indeed, the choice of different instruments may account to a certain extent for the variability across studies. Moreover, the introduction of functional impairment as a more stringent diagnostic criterion in the modern nosological systems yielded lower prevalence estimates (Bird et al., 1990; Bird et al., 1996; Roberts et al., 1998).

Psychiatric disorders are more common in boys than in girls in childhood and preadolescence, especially as far as externalising behaviours are concerned (Costello et al., 1996), and the opposite is found during adolescence because of the high rates of internalizing behaviours in females (Gelder et al., 2000).

The relationship between socio-economical level and psychiatric disorders is controversial: most studies found that children with low socio-economical level are at increased risk for psychiatric, especially behavioural disorders, but others did not (Costello et al, 1996; Gelder et al., 2000; Meltzer et al., 2000). Furthermore, socio-economical level may explain the association between geographical area and mental disorders (Rutter, 1981). Costello et al. (1996) found that children living in urban areas are not at higher risk for psychiatric disorders than children living in rural areas if socio-economical level is taken into account.

The relationship between genetic factors and mental disorders

Research data show that genetic factors account for moderate-to-high proportions of variance of several problem behaviours seen relatively early in life; some such behaviours may constitute indicators or predictors of specific mental disorders (Goldsmith et al., 1997). Twin studies indicate clearly and consistently that significant heritability, although of variable size, can be detected for virtually all Child Behavior Checklist (CBCL/4-18; Achenbach, 1991) scales of problem behaviours in middle childhood and early adolescence (Van den Oord et al., 1994; Edelbrock et al., 1995; Schmitz et al., 1995). Despite several, genetic-epidemiological studies using the CBCL (Hudziak et al., 2000), there are only three published molecular genetic investigations using the CBCL scales (Young et al., 2002; Young et al., 2003; Marino et al., 2004).

Dopamine and serotonin receptor and transporter genes (including DRD4 and 5 HTTLPR) have been the focus of recent molecular genetic studies exploring associations of particular polymorphisms with normal traits or psychopathology in adults and children (Ebstein et al., 2000). Specific variants of the dopamine D4 receptor and the serotonin transporter have both been linked to disorders such as ADHD (Swanson et al., 1998; Holmes et al., 2000; Faraone et al., 2001; Manor et al., 2001), Tourette's syndrome (Grice et al., 1996), obsessive compulsive disorder (McDougle et al., 1998), mood disorders and suicidal behaviour (Anguelova et al., 2003). A recent meta-analysis (Munafo et al., 2003) on 5-HTTLPR has shown that the short (s-) allele is probably associated with negative emotions such as interpersonal hostility and depression in adults (Lesch, 2003). However, results for infants and children are not univocal (Jorm et al., 2002; Arbelle et al., 2003; Young et al., 2003; Nobile et al., 2004; Battaglia et al., 2005).

In a prospective longitudinal study of a representative birth-cohort (Dunedin Multidisciplinary Health and Development Study) the 5-HTTLPR polymorphism was found to moderate the influence of stressful life events on depression (Caspi et al., 2003). In the same sample a functional polymorphism in the gene encoding the neurotransmitter-metabolizing enzyme monoamine oxidase A (MAOA) was found to moderate the effect of childhood maltreatment on developing antisocial behaviour (Caspi et al., 2002). However, this longitudinal study did not provide evidence of an association between DRD4 and ADHD or the continuously distributed hyperactivity phenotype and the related personality traits (Mill et al., 2002).

Recently, a combined effect of the DRD4 and the 5-HTTLPR polymorphisms was found to enhance

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avoidant-like behaviour in early childhood (Ebstein et al., 1998; Auerbach et al., 1999; Auerbach et al., 2001; Lakatos et al., 2003). However, the role of these polymorphisms in childhood psychopathology is still controversial. Molecular genetic studies in large epidemiological samples are needed to elucidate the effects of gene-environment and gene-gene interactions on psychopathology.

The PrISMA project

The Italian preadolescent mental health project (PrISMA – Progetto Italiano Salute Mentale Adolescenti) is the first Italian study designed to estimate the prevalence of mental disorders in preadolescents (10–14 years old) living in urban areas and to analyse the demographic and biological correlates of emotional and behavioural problems. It is a multi-centre study carried out in collaboration with research institutes, university departments and hospitals in seven Italian towns (Lecco, Milan, Rome, Rimini, Pisa, Cagliari and Conegliano Veneto).

The PrISMA project is a two-phase cross-sectional study that has four aims:

- to estimate and compare the prevalence of common mental disorders in early adolescence across sites and between genders, using both DSM-IV and ICD-10 criteria and taking advantage of the information provided by preadolescents and their parents (primary aim);
- to analyse the association of demographic and social characteristics with mental disorders;
- to analyse the impact of mental disorders on social and school functioning in early adolescence;
- to analyse the association between genetic risk factors and behavioural problems. The analysis will give priority to the association between the DRD4 and 5-HTTLPR polymorphisms and quantitative measures of behavioural problems, as assessed by the CBCL. Then other polymorphisms involved in dopaminergic and serotonergic systems will be examined.

The aim of this paper is to present the design and the methodology of this study.

Sampling

The target population consists of Italian preadolescents aged 10 to 14 years attending secondary school and living in seven urban areas that include two metropolitan areas (Rome and Milan) and five small to medium-size urban areas.

Sampling was conducted separately at each site in order to obtain a representative sample of preadolescents attending local schools. The seven sites were selected on the basis of their willingness to participate in the study.

In each site, a multi-stage stratified sampling design was followed (see Figure 1).

Stage 1 (screening)

Secondary schools at each site were stratified by type (public/private) and district. District was used as a proxy of the social and economic condition of residents. A minimum of four schools were selected from the strata to reflect the public/private ratio and the characteristics of the different urban areas. Schools that refused to participate were replaced, whenever possible, with schools belonging to the same stratum.

One or more classes for each grade level were randomly selected from each school depending on the number of students. An anticipated dropout of 25% of subjects at the screening phase and at the clinical assessment led us to adopt the strategy of oversampling classes. This was done to ensure that the sample size was adequate to permit the prevalence of mental disorder to be compared across sites and between genders.

Students identified by this procedure were eligible for the screening phase. The information provided by participants in the screening was reviewed to determine eligibility for the second phase. Exclusion criteria for the second phase were: certification of handicap, age outside the range 10 to 14 years and illiteracy of parents.

Stage 2 (clinical assessment)

Stage 2 was conducted on probable cases of mental disorders and on a sample of non-probable cases. The cutoff score for probable caseness was determined using the 90th percentile of the frequency distribution of the CBCL Internalizing and Externalizing scales in the sample of Lecco. Two different cutoffs were defined for males and females. The choice of this cutpoint is in line with Achenbach and Rescorla's (2001) procedure. Eligible subjects for the second phase were stratified according to the score on the CBCL internalizing and externalizing scales. All subjects exceeding the cutoff

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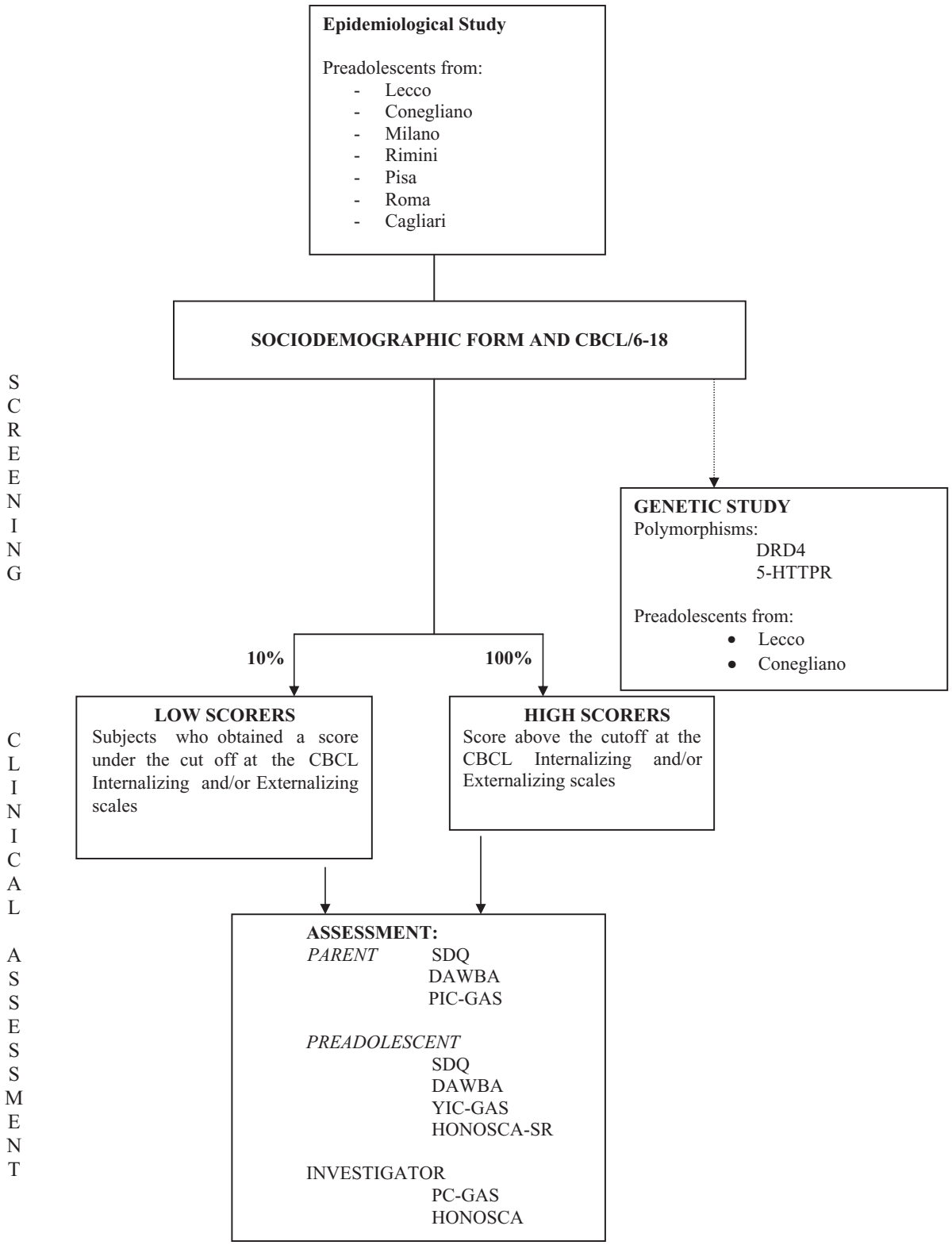

Figure 1. The study design.

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scores of CBCL internalizing and/or externalizing scales and a 10% random sample of those who did not exceed the cutoff scores were selected for the second phase.

The distribution of the sample by site and type of school as well as the percentage of dropouts at each stage are provided in Table 1.

Instruments

Stage 1: screening

Socio-demographic form

Socio-demographic variables were collected using an *ad hoc* form to be filled out by parents. This form includes demographic data (child's gender and age, number of brothers/sisters, parents' marital status, place of residence), variables related to child education and need of services (school and grade attended, repeated year at school, presence of a remedial teacher, recourse to mental health services); variables related to the family socio-economic status (mother's and father's educational level, employment and income).

Parents also had to specify if they were biological or adoptive parents. For families coming from foreign countries only, the nationality and the number of the years of residence in Italy was collected.

The socio-economic status (SES) was evaluated using two indicators: the parents' employment and family yearly income. In the first case, it was coded according to information provided by parents, on the basis of the Hollingshead (1975) nine-point scale for parental occupation. A score (from 1 to 9) was assigned to each job; the higher of two scores was used when both parents were employed. In the second case, the income levels were defined according to criteria defined by the Italian law for tax declaration (IRPEF, Gazzetta Ufficiale, 2001).

Child Behaviour Checklist/6-18 (CBCL)

The CBCL/6-18 (Achenbach and Rescorla, 2001) is a questionnaire to be filled out by parents. It is designed to assess the type and degree of social competence and behavioural problems in children and adolescents aged 6 to 18 years. The first part of the scale includes 20 items exploring children's and adolescents' social competence, such as their degree of participation in sports, home and school activities, games and relationship with peers, siblings and parents. The second part of the CBCL is focused on the children's and adolescents' behavioural and emotional problems; it consists of 118 items rated 0 = not true, 1 = somewhat/sometimes true, 2 = very true or often true.

The CBCL/6-18 includes eight cross-informant syndrome scales derived from a principal component analysis:

1. anxious/depressed;
2. withdrawn/depressed;
3. somatic complaints;
4. social problems;
5. thought problems;
6. attention problems;
7. rule-breaking behaviour;
8. aggressive behaviour.

Other scores include the broad-band internalizing and externalizing scores, encompassing syndromes 1, 2, 3 and 7, 8, respectively and a total problem score.

Validity and reliability studies have shown that the CBCL is a useful and effective instrument for assessing emotional and behavioural problems in children (Achenbach and Rescorla, 2001). Therefore, it is widely employed as a screening measure in two-phase epidemiological studies aiming to investigate the prevalence of mental disorders (Jensen et al., 1995; Costello et al., 1996; Verhulst et al., 1997). The Italian version of the CBCL/6-18 was obtained using an independent back-translation authorized and approved by T. Achenbach. Although no normative data on the CBCL/6-18 are available to date for the Italian population, the psychometric properties of a former CBCL version (Achenbach, 1991) were investigated in a recent study (Frigerio et al., 2004) showing that this instrument has good validity and reliability in the Italian population.

Stage 2: clinical assessment

The clinical assessment was conducted using the Strengths and Difficulties Questionnaire (SDQ), the Development and Well Being Assessment (DAWBA), the Health of Nation Outcome Scale for Children and Adolescents (HoNOSCA) and the Children Global Assessment Scale (C-GAS).

Strengths and Difficulties Questionnaire (SDQ)

The SDQ (Goodman et al., 2000b) is a brief behavioural screening questionnaire designed for subjects between 3 and 16 years of age. In the present study

DOI: 10.1002/mpr

Table 1. Description of the sample

	SITE							
	Lecco	**Rimini**	**Cagliari**	**Roma**	**Milano**	**Pisa**	**Conegliano**	**Total sample**
Target population	1154	3047	4201	66856	25395	1834	1299	103786
Type of school								
private	3	2	5	89	43	1	1	144
public	2	6	12	147	66	8	3	244
Number of schools sampled	4	4	6	9	9	4	4	40
Number of subjects screened	665	549	898	1436	979	543	557	5627
Percentage dropout *	33.2	35.2	63.7	31.1	41.9	27.8	22.8	38.9
Number not eligible for interview	10	12	36	49	0	3	5	115
Number randomized to phase 2	115	101	112	277	156	93	118	972
Percentage refusals **	23.5	15.8	45.5	31	51.3	71	10.2	34.7
Number interviewed	88	85	61	191	76	27	106	634

*Forms not returned, not filled out, or not delivered.
**Subjects who refused to be interviewed.

the two versions for parents and preadolescents were administered. These include 25 items organized into five scales: 'emotional symptoms', 'conduct problems', 'hyperactivity/inattention', 'peer relationship problems' and 'prosocial behaviour'. Items are rated on a three-point scale (0 = 'not true', 1 = 'somewhat true' or 2 'certainly true').

The SDQ, designed to identify probable cases, can improve the detection of child mental health problems (Goodman et al., 2000c).

Studies conducted in Europe and in Bangladesh provided evidence of acceptable internal consistency and test-retest reliability for the parent, teacher and self-report versions (Smedje et al., 1999; Goodman et al., 2000c; Klasen et al., 2000; Koskelainen et al., 2000; Mullick and Goodman, 2001; Muris et al., 2003). These studies suggested that the instrument has high predictive validity in identifying clinical cases (Kendall's tau b between 0.49 and 0.73; $p < 0.001$) (Goodman et al., 2000b). Further, the preadolescent and parent versions of the SDQ showed a good concurrent validity (Koskelainen et al., 2000; Muris et al., 2003).

The Development and Well Being Assessment (DAWBA)

The DAWBA (Goodman et al., 2000a) is an interview that allows current psychiatric diagnoses to be made, according to DSM IV and ICD 10 criteria. In the present study, we used the parent and adolescent versions of the instrument, which consist of a structured part including 11 sections and a semi-structured part including two sections.

The 11 sections comprising the first part explore the following psychopathological areas: separation anxiety, simple phobia, social phobia, panic disorder with/without agoraphobia, post-traumatic stress disorder, obsessive-compulsive disorder, generalized anxiety, major depression, attention deficit and hyperactivity, behavioural disorder and less common disorders. Each section starts with a probe question to determine the presence/absence of the problem of interest. If the problem is present, the interviewer proceeds with further questions exploring the severity of symptoms in the area, as well as their duration, onset and impact on social, family and school functioning. The semi-structured part of the interview explores in deeper detail the problems identified in the first part and the strengths of the preadolescent in order to obtain a verbatim account of any reported problems.

The DAWBA can be administered by lay interviewers but the diagnoses should be allocated by experts in child psychiatry, specifically trained in the clinical rating of the interview. In the present study, five clinicians from Lecco reviewed all the interviews conducted at the seven sites and assigned the diagnoses. When the diagnoses were uncertain or no sufficient information was provided in the semi-structured part of the interview, a consensus diagnosis was obtained during staff meetings. If difficult-to-diagnose cases still remained, they were resolved with the help of R. Goodman.

The validity of the English version of the DAWBA was established in a number of studies showing:

- marked differences in the prevalence of the disorders between community and clinical samples (odds ratio between 13 and 102) (Goodman et al., 2000a)
- good agreement between the clinical diagnosis and the DAWBA diagnosis in clinical samples (Goodman et al., 2000a), and
- significant differences on independent measures – used as external validators – between children with and without mental disorders in community samples (Goodman et al., 2000a).

Furthermore, DAWBA showed satisfactory inter-rater reliability with Cohen's kappas of around 0.7 (Goodman et al., 1996).

Health of Nation Outcome Scale for Children and Adolescents (HoNOSCA)

The Health of Nation Outcome Scale for Children and Adolescents (HoNOSCA, Gowers et al., 1999a; Gowers et al., 1999b) is a scale to assess functioning in children and adolescents between 5 and 17 years of age. It explores three areas of functioning: social relationships, family and school, with reference to the two weeks before the index assessment. We used two versions of the instrument, one interview based and one self-report (HoNOSCA-SR) to be filled out in the presence of the investigator.

The version for the clinician consists of 13 scales that concur in determining the total score. These scales are:

- disruptive behaviour;
- aggressive and antisocial behaviour;

DOI: 10.1002/mpr

- hyperactivity;
- attention and concentration deficits;
- intentional self-injury;
- alcohol and substance abuse;
- language and school problems;
- physical problems or problems associated with disability;
- hallucinations, delusions and misperceptions;
- non-organic somatic symptoms;
- emotional disorders;
- problems with peer relations;
- poor self-care and independence;
- family and social problems;
- low school attendance.

Each of these dimensions is rated on a five-point scale from 0 (no problem) to 4 (severe problem).

The second section consists of two scales exploring the insight of parents about the problem and the use of services.

The self-report version (HoNOSCA-SR) includes 13 questions, rated on a five-point scale ('not at all', 'insignificantly', 'mild but definitely', 'moderately', 'severely'), that probe the same areas investigated in the first part of the HoNOSCA.

The HoNOSCA provides an index of clinical severity with good face validity, sensitivity to change and high inter-rater reliability (Gowers et al., 2000). It correlates highly with the C-GAS but, according to the author, it has a higher sensitivity to change (Gowers et al., 2000).

The validity and the reliability of the HoNOSCA-SR were investigated in a small clinical sample of patients who had mainly a diagnosis of eating disorders (Gowers et al., 2002). This preliminary study showed evidence of good test-retest reliability (r = 0.81), adequate concurrent validity as evidenced by the correlation between HoNOSCA-SR and SDQ (r = 0.66) but poor agreement between clinician and patient ratings (r = 0.27).

Children Global Assessment Scale (C-GAS)

The Children Global Assessment Scale (C-GAS) is an instrument to assess the lowest level of functioning achieved in the previous 3 to 6 months. It was developed by Schaffer et al. (1983) as an adaptation, for children between 4 and 16 years, of the Global Assessment Scale (Endicott et al., 1976). In the present study we used the three non-clinical versions of the scale (Bird et al., 1996): the Parent Interview C-GAS (PICGAS), filled out by the rater after the interview with the parent, the Youth Interview C-GAS (YICGAS), filled out by the rater after the interview with the preadolescent and the Parent C-GAS, filled out by the parent (PCGAS).

Scores range between 1 (severely impaired functioning) and 100 (excellent functioning). The English and Spanish non-clinical version of the C-GAS showed good construct, discriminant and concurrent validity (Bird et al., 1996); the rating of the lay interviewer based on the parent reports (PICGAS) was better correlated with ratings provided by clinicians than those based on youth report (YICGAS) and parent report (PCGAS).

Clinically significant functional impairment was defined by a score of 70 (Shaffer et al., 1983; Bird et al., 1990).

Genetic assessment

DNA collection and DNA extraction

Buccal epithelial cells were collected by vigorously agitating 10 ml of 4% sucrose in the mouth for 20 s. Samples were collected in screw-cap urine collection containers and kept at +4°C.

In the laboratory, samples were transferred to 50 ml tubes and centrifuged for 10 minutes at 4,000 rpm. Pellets were resuspended in 1 ml of 10 mM NaCl/10 mM EDTA and transferred to 1.5 ml microcentrifuge tubes. Samples were centrifuged for 15 s at full speed and the supernatant was discarded. If necessary, pellets were stored at −80°C.

Genomic DNA was extracted with DNAzol genomic DNA isolation reagent (MRC, Cincinnati, OH). In detail, each pellet was resuspended in 0.5 ml of DNAzol supplemented with 5 µl of Polyacryl Carrier (MRC) and stored for 10 minutes at room temperature (RT). The homogenate was sedimented for 10 minutes at 10,000 g at RT and the supernatant was transferred to a new 1.5 ml tube. DNA was precipitated by addition of 250 µl of 100% ethanol and stored at RT for 3 minutes, then sedimented by centrifugation at 5,000 g for 5 minutes at RT. The precipitate was washed twice with 1 ml of 75% ethanol, drained thoroughly and dissolved in 150 µl of 8 mM NaOH. When the pellet had fully dissolved, pH was adjusted to 7.5 by the addition of 24 µl of 100 mM HEPES and the DNA was stored at +4°C.

DOI: 10.1002/mpr

One μl of DNA was used for each amplification reaction.

Genotyping

Primers and methods for determining the DRD4/48bp-repeat and 5-HTTLPR polymorphisms have been described by Macciardi et al., (1994) and Lesch et al., (1996).

Procedure

The PrISMA project was approved and funded by the Italian Ministry of Health. The study protocol was also approved by the ethics committee of each site. According to Italian law (DL 30 July 1999, n. 281 and 282), the informed consent was not required for the epidemiological part of the study because the primary aim of the study is to assess the health condition of the population. A written informed consent was instead required for participation in the genetic study, as approved by the ethics committee.

Screening phase

The study aim and protocol were presented to the local officers of the Provveditorato alla Pubblica Istruzione and to the chiefs of the selected schools. First contacts with the chiefs of the schools were made by phone. On that occasion the chiefs accepted the submission of the project to the council of the institute and, in case of approval, a meeting was arranged with teachers and the representatives of parents to illustrate the study procedures. One or 2 weeks after the meeting, the research staff visited the school and distributed an envelope containing the study material to the students of the classes selected for participation. Each envelope and the materials in the envelope were identified by a research code. The study materials included: the demographic form, the CBCL/6-18, the study protocol and the consent form for the genetic study (only for Lecco and Conegliano). The envelopes were collected about 10 days after. Genetic samples were collected a few days after, as soon as parents' written informed consent was available.

Clinical assessment

The research staff contacted the families of the students participating in the study by telephone in order to arrange an appointment for the interview. The interviews were conducted in the school building and in a way that did not interfere with the schedule of the lessons. Students were interviewed during school time, while there was more flexibility for the appointments with parents. Clinical assessment was conducted in the same way with students and parents, using the instruments in the following order:

1. Strengths and Difficulties Questionnaire (SDQ)
2. Development and Well-Being Assessment (DAWBA)
3. HoNOSCA–SR (preadolescents)
4. PCGAS (parents).

The interviewer filled out the YICGAS after interviewing the student, the HoNOSCA and the PICGAS after interviewing both.

Parents who made written requests received a report with the scores on the different instruments as a feedback of the assessments.

Staff training

The five clinicians from Lecco were trained to the clinical rating of the DAWBA as follows. First they practised on 60 English cases described in the training manual (available at the following DAWBA Web site: www/dawba.com/manual/m3.html) and on a clinical sample of 54 children attending the Neurorehabilitation Unit of Bosisio Parini, Lecco. Subsequently, R. Goodman held intensive training sessions in which all problems that came out during the practice were reviewed and subjects from Lecco were assessed. Afterwards, diagnoses for the interviews of subjects recruited at other centres were made by the trainees and for a random sample of 100 interviewed subjects by an independent Italian speaking child psychiatrist. The inter-rater agreement, calculated on this subsample of 100 participants was 0.71 (Cohen's kappa), a value overlapping with that obtained for the original English version (Goodman et al., 1996). A final review of the diagnoses was made by Goodman, as specified above.

Training in the study procedures and in the administration of the study instruments was conducted at the unit at Lecco. The staff from the participating sites (including 13 psychologists and 12 residents in child and adolescent psychiatry) attended a one-day training course. The training consisted of the co-rating of videotapes and role-playing sessions. At the end of the day, a questionnaire was administered to all participants to verify the learned competences.

DOI: 10.1002/mpr

Data management and control

The Coordinating Centre of Lecco served as data monitoring and training centre. A data entry program was specifically developed in Access to prevent trivial errors such as entering data out of range or double identification codes. Labels with identification codes for each site were automatically generated on the basis of the list of students provided by the participating schools. These identification codes did not include any personal information.

Data were entered at each site using the Access application and then sent to the Coordinating Centre at Lecco for formal data quality assessment. This consisted of a protocol for reviewing missing data and checking for inconsistencies. Feedback was given to the sites in order to retrieve missing data and to resolve logical inconsistencies. During data collection, reports were generated periodically and sent to the sites to help them monitor the progress of recruitment.

Analysis plan

The analyses focused on estimating the prevalence of common mental disorders in early adolescence, analysing the association of demographic and social characteristics with mental disorders, analysing the impact of mental disorders on the relational and school functioning of early adolescents and analysing the association between genetic variables and mental disorders.

Data analysis will be conducted at the Coordinating Centre of Lecco on the pooled sample and separately for each site.

Sampling weights will be obtained using logistic regression on first-phase subjects, with response (yes/no) as the dependent variable and the CBCL internalizing and externalizing scores, gender and site as the independent variables. The individual weight is the reciprocal of the resulting probability so that, among responders, subjects with lower response probability have a higher weight that those with a high response probability (Dunn et al., 1999; Bisoffi et al., 2000).

Logistic regression models will be used to analyse the association of demographic and social characteristics with mental disorders.

Multiple linear regression models will be used to analyse the impact of mental disorders on the different measures of functioning.

The analysis of the association between genotypes and problem behaviours will be conducted as follows. The internalizing, the externalizing and the attention scales will be used alternately as dependent variables in analyses of variance (ANOVA), with the genotypes and their interaction as independent variables. Following significant ANOVAs, *post hoc* pairwise comparisons between genotypes will be conducted at the Bonferroni-corrected alpha level of 0.016 (= 0.05/3).

Analyses of covariance will be then carried out to determine whether and to what extent the association between the genotypes and the scales of interest depends on the effect of gender and age.

All the statistical analyses will be conducted by using SPSS, version 12.0, its module Sample Power for power analysis, and STATA, Version 8, which includes a family of procedures for survey data (Hamilton, 2004).

Power analysis for the epidemiological study

The sample size for each site was determined to estimate the prevalence of mental disorders in the population of that site. We were interested in a discrepancy between the prevalence in the population and our estimate of ±4 at 95% confidence level. The sample size was defined as $600 = (196/4)^2\ (0.5)(0.5)$, with no assumption about the prevalence in the population. We were also interested in finding at least 18 cases per site. Should the true prevalence rate in the population be as low as 6.2% (Shaffer et al., 1996), with 600 subjects screened and an anticipated drop-out rate of 25% we expected to identify between 18 and 40 cases per site.

Power analysis for the genetic study

Two sites agreed to participate in the genetic study (Lecco and Conegliano). Assuming that the dropout rate is about 60%, we estimated that the final sample would consist of about 450 subjects. The genotype distribution of 5-HTTLPR and DRD4 was obtained by using data available in the literature (Cusin et al., 2002; Serretti et al., 2002). DRD4 genotypes were grouped according to presence or absence of 7-repeat allele.

The power analysis for 5-HTTLPR is for one-way fixed effects ANOVAs with three levels. The effect size (f) was assumed to be medium = 0.25 and alpha = 0.05. The computation of the power is based on an equal number of subjects per level, so we used the lowest cell frequency (72) as a conservative estimate. With a sample of 450 subjects we can expect significant differences on the scale scores across genotypes at a power of 91% for 5-HTTLPR.

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The power analysis for DRD4 is for a t-test to compare the mean scores on the internalizing and externalizing scales of the CBCL between the two genotypes. Assuming that 30% of subjects have the 7-repeat allele and 70% have no risk allele, the study will have power of 90.3% to yield statistically significant results. This computation assumes that the mean difference is 2, and the common within group standard deviation is 6.

The power analysis was conducted using Sample Power, Release 1.20 (1997).

Conclusions

The PrISMA study addresses two important methodological challenges for the epidemiological research on childrens' and adolescents' mental disorders. First, the use of a diagnostic interview – which successfully combines the characteristic of respondent-based and investigator-based measures and allows diagnoses to be made according to the two major classification systems (DSM IV and ICD 10) using information provided both by parents and children – has been preferred in order to have a more reliable case ascertainment. Second, it includes an investigation of genetic factors probably associated with emotional and behavioural problems in childhood and adolescence in an epidemiological sample. Some intrinsic methodological limitations of the present study should be kept in mind. First, the sample is not representative of the Italian population of preadolescents as the sites were selected on the basis of their willingness to participate in the study. Second, the age of the sample is restricted to a relatively narrow range, which does not allow the identification of developmental thresholds for risk of mental disorders. Third, the choice of the 90th percentile as the cutoff point of the CBCL for identifying possible cases may yield a large number of false negatives, which are only partially captured by the 10% sampling of low scorers for the second stage. Indeed, this problem is mitigated by the fact that the definition of high scorers was based on exceeding the 90th percentile of the distribution of the externalizing and/or the internalizing scales score and was determined separately for males and females. Fourth, the investigation on genetic factors has been limited to two sites (Lecco and Conegliano) due to organizational and budget constraints. However, this ensured a higher homogeneity in the collection and management of genetic samples.

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