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# Collection and storage of psychopathological and neuropsychological data on the risk of development and maintenance of emotional-behavioural disorders using online assessment tools

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# Abstract

Starting from the debate about assessment of psychopathology in children and adolescents, this Ph.D. thesis aims to integrate with empirical data the existing literature about stability of mental disorders from childhood, to adolescence and to adulthood. In the perspective of developmental psychopathology, the early detection of mental health problems involves the hope of being able to prevent or delay their onset. For this reason, it is important to identify specific profiles of stable behavioural-emotional problems, as well as to study their association with neuropsychological markers and possibly personality traits. To do this, it is first necessary to investigate these problems in epidemiological samples, representative of the population of interest. In the same way, it is crucial to follow longitudinally the evolution of the problems during development.

Psychopathological definition of mental disorders during childhood and adolescence is particularly complex, because of a high rate of comorbidity among diagnoses [Caron, C. & Rutter, M., 1991] and continuity both in the same diagnostic category and with the transitions between different categories [Costello, E.J. *et al.,* 2003], indicating high heterogeneity within diagnostic groups. Furthermore, from the *developmental psychopathology* perspective, there is the additional purpose to early detect mental problems [Cicchetti, D. & Toth, S.L., 1995, 1998], mainly in order to improve prevention [Cicchetti, D. & Toth, S.L., 2009], so that also developmental trajectories of diagnoses become important in defining psychological problems in children and adolescents and possibly their causal association [Rutter, M. & Sroufe, A.L., 2000].

Diagnostic assessment of children and adolescents could be conducted from different points of view, using tools oriented to a *categorical/qualitative* approach to psychopathology or to a *dimensional/quantitative* approach. Diagnostic

categories have had and still have great advantages both in adult and in children and adolescents psychopathology [Angold, A. & Costello, E.J., 2009], but these categories are also strongly associated with those empirically derived [Achenbach, T.M., Dumenci, L. & Rescorla, L.A., 2001]. Therefore, in order to obtain a classification as much as possible based on empirical data, the qualitative approach is becoming increasingly integrated with the quantitative one [Bellina, M. *et al.,* 2012], that can be seen as complementary to it [Kasius, M.C. *et al.,* 1997].

Two diagnostic systems strongly oriented to computerized, specifically online, use were presented in the first chapter of this work and they were used in following chapters. The *Development and Well-Being Assessment* is a system designed to obtain psychiatric diagnoses in children and adolescents according to DSM-4-TR and ICD-10 diagnostic criteria [Goodman, R. *et al.,* 2000], thus mainly following a categorical approach. The *Achenbach System of Empirically Based Assessment* [Achenbach, T.M. & Rescorla, L.A., 2001, 2003] includes instruments designed for assessment of psychopathology following a dimensional approach, as the *Child Behaviour Check-List* (CBCL) questionnaires.

Other tools were also used in the studies presented, mainly in relation to the diagnostic assessment systems described: the *Developmental Neuropsychological Assessment* [NEPSY; Korkman, M., Kirk, U. & Kemp, S., 1998, 2007], which is an extensive battery of tests, designed to assess neuropsychological impairments in children and adolescents, and the *Chapman Psychosis Proneness Scales* [Chapman, L.J. & Chapman, J.P., 1987], questionnaires designed to measure personality traits predisposing to the development of psychosis [Chapman, L.J. *et al.,* 1994] or *Bipolar Disorder* [Kwapil, T.R. *et al.,* 2000].

In the second chapter, general data from an epidemiological study were presented. These data were collected about a clinical sample representative of children and adolescents referred to the *Scientific Institute IRCCS "Eugenio Medea"* for behavioural-emotional assessment. The total clinical sample was composed by 1366 children and adolescents, 22.6% of which were females. Participants were between two years and 17 years and four month. Problems that led to the evaluation were mostly behavioural, emotional and attentional, with also a relevant frequency of associated learning difficulties.

Using a cross-sectional methodology, it was showed that internalization problems continuously increment with age both in measure of overall impairment and in its specific components (anxious, depressive and somatic). On the other hand, problems associated with aggressive or delinquent behaviours were related to gender (i.e. with higher scores in males than in females). It was also reported a clear increase in socialization problems with age and an effect of the participants' cognitive level on the presence of attention problems and, partially, of thought difficulties.

In the next chapter, the *Dysregulation Profile* [Biederman, J. *et al.,* 1995] and *Autistic Spectrum Disorder Profile* [Biederman, J. *et al.,* 2010], both calculated from CBCL scores, were examined with respect to neuropsychological characteristics associated with them. The specific behavioural-emotional problems described by these profiles are associated with emotional dysregulation [Althoff, R.R., 2010], and with increased risk of developing psychiatric disorders and behavioural problems [Holtmann, M., Becker, A. *et al.,* 2011]. On the contrary, autistic-like traits are strictly related to internalizing difficulties [Hallett, V., Ronald, A. & Happé, F., 2009; Hallett, V. *et al.,* 2010]. Otherwise, cognitive features related to these profiles have been poorly investigated and it will be important to understand whether cognitive difficulties could be associated with such problems.

Analyses were conducted on sub-samples comprehensively assessed for neuropsychological characteristics. The reported results showed that reduced performances on the NEPSY *Visuomotor Precision* test were associated with emotional dysregulation. On the contrary, imitation abilities were completely preserved in children and adolescents with this dysregulative characteristics, resulting better than those measured in the comparison group. On the other hand, participants with autistic-like problems showed poorer performance in tests assessing memory than comparison group and they did not seem to have other distinctive cognitive characteristics. These results indicates an opportunity of identifying the cognitive markers of behavioural-emotional problems. These cognitive markers could be then taken into consideration as causal factors of those problems.

Longitudinal observations were collected on 218 (16.0% of the discussed clinical sample) children and adolescents between 10 years and 19 years and six month, after 5.5 ± 1.64 years since the first assessment (between 11 months to eight years and six months). These information were used to examine the continuity of dimensional-assessed psychopathology from childhood to adolescence.

The results confirmed the stability of behavioural-emotional problems from childhood to adolescence, despite their observed decrease in frequency. Interestingly, an increased risk of internalized problems have been reported for females, probably partially due to the increase of sample mean age [Hayward, C. & Sanborn, K., 2002]. Furthermore, the CBCL *Social Problems* scale resulted as a statistically significant longitudinal predictor of subsequent problems (i.e. assessed with *Total Problems*, *Internalizing Problems* and *Externalizing Problems* scales), independent from time passed between the two assessments.

In the last chapter, the *Hypomanic Personality Scale* [Eckblad, M. & Chapman, L.J., 1986], the *Magical Ideation Scale* [Eckblad, M. & Chapman, L.J., 1983] and the *Perceptual Aberration Scale* [Chapman, L.J. *et al.,* 1980] were proposed to 141 partecipants of the re-assessed group in order to measure proneness to psychosis and to *Bipolar Disorder* in an at-risk sample. The association between scores on these scales and behavioural-emotional problems was also taken into account. In fact, these questionnaires were designed specifically to assess the risk of future severe psychological problems, so it was important to search for relations with assessment tools through which it was possible to demonstrate the existence of a continuity of psychopathology from childhood to adolescence, and to adulthood. In particular, reported observations showed that the *Hypomanic Personality Scale* was associated with externalization, while the *Perceptual Aberration Scale* was a predictor of internalized problems.

*To the children and adolescents participating in this research*

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# Index

# 1

## Assessment tools

### 1.1  Introduction

The definition itself of mental disorder is always in some way limited, because basically operational and not necessary suitable for all situations in which it is expected to be applied. The same *American Psychiatric Association* (APA) stated that no definition could adequately define clear boundaries for the concept of psychiatric disorder, since different definitions are required in different situations [APA, 2000]. The issue is definitely still unresolved, even in recent proposals and changes in diagnostic systems [Stein, D.J. *et al.,* 2010].

Psychopathological definition of disorders during childhood and adolescence is particularly complex, because of a high rate of comorbidity among diagnosis [Caron, C. & Rutter, M., 1991] and continuity both in the same diagnostic category or with the transitions between different categories [Costello, E.J. *et al.,* 2003], indicating high heterogeneity within diagnostic groups. Also for this reasons, the updating process of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) [1] strongly affects the classification of the disorders currently included among *Disorders Usually First Diagnosed in Infancy, Childhood, or Adolescence*,

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[1] See: '**www.dsm5.org**'.

with the adoption of new disorder groups and the insertion of major changes [Pine, D.S., 2010], especially for *Anxiety Disorders* [Beesdo, K., Knappe, S. & Pine, D.S., 2009]. Furthermore, *developmental psychopathology* has an additional purpose of prevention and early detection of mental problems [Cicchetti, D. & Toth, S.L., 1995, 1998], so that also the causal associations and developmental trajectories become important in defining psychological problems in children and adolescents [Rutter, M. & Sroufe, A.L., 2000].

In the following paragraphs, in the first place two different diagnostic approaches will be presented; they will be then exemplified discussing representative assessment tools. These instruments were chosen primarily because they were specifically oriented to the online collection of diagnostic data (with considerable advantages, see ***Paragraph 1.7***), secondly because they were well known to our research group, that collaborated to their Italian adapatation. The assessment tools chosen are also well represented in child psychiatry literature, especially in epidemiological and longitudinal studies (such as those presented and discussed in the following chapters).

Other tools used in the following work will also be introduced. These are more specific instruments designed to investigate issues linked with the diagnostic aspects in children and adolescents. These tools have also been adapted to Italy by our research group or other associated groups.

## 1.2   Diagnostic interviews

The categorical, or qualitative, diagnostic process in psychiatry involves the use of diagnostic labels according to the rules provided by a diagnostic system. Diagnostic systems most commonly used are the DSM [2] of the APA [3], currently in its fourth revised version [DSM-4-TR; APA, *Task Force on DSM-IV*, 2000], and the of the *International Statistical Classification of Diseases and Related Health Problems* [4]

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[2] See: '**www.psychiatry.org/practice/dsm**'.

[3] See: '**www.psych.org**'.

[4] See: '**apps.who.int/classifications/icd10**'.

of the *World Health Organization* (WHO) [5], in its tenth version [ICD-10; WHO, 1993].

Beyond the differences, both diagnostic systems provide precise criteria for the assignment of a diagnosis and these criteria can be operationalized through the use of clinical interviews, like the *Schedules for Clinical Assessment in Neuropsychiatry* [WHO, 1994]. Furthermore, depending on the desired standardization of the diagnostic process, interviews could be conducted in different formats: with completely open-ended questions (at the discretion of the clinician), with predetermined questions (in which the examinees answer to fixed questions, expressing themselves as they prefer), or with closed-ended questions (fixed questions requiring close-ended answers). In research practice structured or semi-structured interviews are commonly preferred, since they avoid excessive arbitrariness in the diagnostic process.

The qualitative approach to diagnosis essentially follows a top-down methodology, in which the diagnostic categories are defined a priori on the basis of expert judgement [Kasius, M.C. *et al.,* 1997]. These categories were selected to be coherent with those commonly used in clinical practice, although current diagnostic systems are intended to define the disorders as much as possible not theoretically, but in a purely descriptive way. The use of the categorical approach is definitely still desirable, especially to maintain the good level of standardization achieved [Angold, A. & Costello, E.J., 2009]. Precisely in order to obtain a classification as much as possible based on empirical data, the qualitative approach to classification is becoming increasingly integrated with the quantitative one [Bellina, M. *et al.,* 2012], which will be discussed later.

## 1.3   The *Development and Well-Being Assessment*

The *Development and Well-Being Assessment* (DAWBA) is diagnostic tool designed to obtain psychiatric diagnoses in children and adolescents according to DSM-4-TR and ICD-10 rules [Goodman, R. *et al.,* 2000]. The DAWBA comprises structured and semi-structured clinical interviews and questionnaires for both

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[5]  See: '**www.who.int**'.

parents and their children. The system also provides some questionnaires for teachers. The collected information can be evaluated by trained raters to obtain reliable diagnosis. All the components of the diagnostic system are available online [6] and are also suitable to be independently used by the users themselves.

| Diagnostic label | ICD-10 | DSM-4 |
|---|---|---|
| *Emotional Disorders* | | |
| Agoraphobia | × | × |
| Anxiety Disorder, Not Otherwise Specified | × | × |
| Bipolar Disorders | × | × |
| Depressive Disorder, Not Otherwise Specified | × | × |
| Generalised Anxiety Disorder | × | × |
| Major Depression | × | × |
| Obsessive-Compulsive Disorder | × | × |
| Panic Disorder | × | × |
| Post-Traumatic Stress Disorder | × | × |
| Separation Anxiety | × | × |
| Social Phobia | × | × |
| Specific Phobia | × | × |
| *Hyperactivity* | | |
| Attention Deficit and Hyperactivity Disorder, Combined | | × |
| Attention Deficit and Hyperactivity Disorder, Impulsive | | × |
| Attention Deficit Disorder, Inattentive | | × |
| Hyperactivity, Not Otherwise Specified | × | × |
| Hyperkinesia | × | |
| *Conduct or Oppositional Disorders* | | |
| Conduct Disorder | | × |
| Conduct Disorder, Familiar | × | |
| Conduct Disorder, Not-Socialised | × | |
| Conduct Disorder, Socialised | × | |
| Disruptive Behavioural Disorder, Not Otherwise Specified | × | × |
| Oppositional Defiant Disorder | × | × |

**Table 1.1.   Part A.** ICD-10 and DSM-4 diagnoses covered by the *Development and Well-Being Assessme*nt. ×: Diagnosis is present in the specified diagnostic system.

The system is mainly directed to school-age children and adolescents, between five and 17 years. However, there are also versions oriented to preschool children, starting from two years, and adults (although not currently adapted for Italy).

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[6]  See: '**www.dawba.info**'.

The DAWBA system presents three main features: it provides information to diagnostic process employing multiple sources; it organizes the collection of information proceeding from a full structured question format (in the form of questionnaire), to a less structured question  format (structured interview) and adopting open questions only when needed (semi-structured interview); it is intended for computerized use and possibly to for autonomous use; specifically, it appears as an online assessment tool [7]. Currently, in Italy, the DAWBA is the only diagnostic interview completely oriented to online self-assessment.

| Diagnostic label | ICD-10 | DSM-4 |
|---|---|---|
| *Social Disorders* | | |
| Attachment Disorders, Disinhibiting | × | × |
| Attachment Disorders, Inhibiting | | × |
| Attachment Disorders, Other | × | × |
| Attachment Disorders, Reactive | × | |
| Selective Mutism | × | × |
| *Other Disorders* | | |
| Anorexia Nervosa | × | × |
| Asperger Disorder | × | × |
| Autism | × | × |
| Bulimia Nervosa | × | × |
| Eating Disorders, Not Otherwise Specified | × | × |
| Pervasive Developmental Disorders, Not Otherwise Specified | × | × |
| Psychotic Disorders | × | × |
| Substance Use Disorders | × | × |
| Tic Disorders, Chronic | × | × |
| Tic Disorders, Not Otherwise Specified | × | × |
| Tourette Syndrome | × | × |

*Table 1.1.  Part B.* ICD-10 and DSM-4 diagnoses covered by the *Development and Well-Being Assessment*. ×: Diagnosis is present in the specified diagnostic system.

Diagnostic information is collected from up to three sources: parents, children or adolescents themselves, teachers. Self-assessment is intended only between 11 and 17 years, while the assessment generally ranges from five to 17 years. The integration of different sources is essential in the diagnostic process in children especially for the difficulty itself in understanding what is required. Similarly, it is necessary in adolescents, especially since some data are better known to the person

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[7]  See: '**www.dawba.net**'.

itself (in particular those related to emotional experiences, like for anxious and depressive symptoms), whereas other data are more accessible to people who knows that person well than to person itself (derived from behavioural observation, like for aggression or conduct problems). For the same reason, only behavioural-emotional problems that can be observed at school are present in interview for teachers. The goal of the interview is to get a correct and reliable diagnosis, which is also clinically relevant. ***Table 1.1*** (divided in parts, ***A*** and ***B***) reports diagnoses that are actually covered by the DAWBA. Information from different sources should  be combined so to maximize their contribution. As we will see later, computerized tools compounding the DAWBA system, those instruments allow to predict a diagnosis, indicating an associated probability. In particular, six DAWBA *bands* are proposed to estimate the probability to present at least one clinically relevant disorder: *"Very low"*, corresponding to a probability about 0.2%; *"Low"*, about 2%; *"Medium"*, about 20%; and *"High"*, about 75% [Goodman, A. *et al.,* 2011].

The DAWBA starts for every informant administering a questionnaire with general screening purposes. The questionnaire is the *Strength and Difficulties Questionnaire* [SDQ; Goodman, R., 2001] and it is a brief instrument frequently used as stand-alone measure in epidemiological research [Brøndbo, P.H. *et al.,* 2011]. Afterwards, for each diagnostic category examined, symptoms investigated are explained in summary form to respondents, deepening the interview with closed-ended questions only if they claim to recognize the general difficulties indicated. An example of a closed-ended screening question could be: *"Does he ever worry?"*, at the very beginning of the section about *Generalized Anxiety Disorder*, immediately after the explanation of what it means to *"worry about"*. If necessary, following a skip rules system, the interview continues with more detailed closed-ended questions. Thus, open-ended questions may be proposed for clarifications and for the collection of concrete examples of problematic situations, but (according to skips rules) only if respondents recognize that symptoms had recently have an impact in their daily lives. The impact of symptoms is rated with regards to family life, to the academic achievements, to the relations of friendship, and also to the management of recreational activities (like sports or hobbies). An example of open-ended questions could be: *"Please describe in your own words*

*what it is that he worries about"*, proposed after that parents have admitted the presence of symptoms of anxiety with a significant impact on their child's life.

| Section | Parents | Self | Teacher |
|---|---|---|---|
| Strenght and Difficulties Questionnaire. | × | × | |
| Worries about separation from key "attachment figures" (such as parents). | × | × | (×) |
| Specific fears (e.g. spiders, blood, flying). | × | × | (×) |
| Social fears (e.g. speaking or eating in front of other people, meeting new people). | × | × | (×) |
| Panic attacks or fears of crowds, public places, open spaces, etc. | × | × | (×) |
| Stress after a very frightening event. | × | × | |
| Obsessions and compulsions. | × | × | (×) |
| Worrying a lot about many different things. | × | × | (×) |
| Depression. | × | × | (×) |
| Hyperactivity and attention problems. | × | (×) | × |
| Awkward or troublesome behaviour (or Behaviour that sometimes gets you into trouble). | × | × | × |
| Development of language, routines, play, and social ability. | × | | (×) |
| Dieting, bingeing and concern about body shape. | × | × | (×) |
| Tics. | × | (×) | (×) |
| Strange experiences that are surprisingly common. | | × | |
| Other concerns. | × | × | × |
| More about his strengths and good points (or More about your strengths and good points). | × | × | |
| Background (medical, family, educational, etc.) | × | | |

*Table 1.2.* Section of the online version of the *Development and Well-Being Assessment* for school-age form are reported. ×: The section is present in the form for the indicated respondent; (×): The section is only partially present in the form for the indicated respondent.

The sections composing the DAWBA are reported in **Table 1.2**, distinguishing the forms for different respondents. The section named *"More about his strengths and good points"* (or *"your"*, in the auto-assessment) is a peculiar characteristic of

DAWBA: it is a section directed specifically to the evaluation of the positive and protective factors associated with the person under examination. In the same way, the initial questionnaire includes an assessment of the strengths of children and adolescents. The administration of the DAWBA ends with the *Background Section*, a collection of contextual information, especially about potential environmental and familiar risk factors. Also in this section there is a brief open request related to the strengths of the family as well as some close-ended question about social and familiar available supports.

The DAWBA system is designed to be used either in human-mediated form or in fully computerized one, but it is conceived and set up to be used preferably online. The computer-administered interviews have obvious advantage of cutting down the cost of personnel with specific training in clinical consultation, especially since the tools are designed to not necessary require the interviewers previous clinical experience, but only a relatively brief training. The author also reported that some respondents feel more at ease with questions from a computer because there is no perceived need to present themselves in a positive way.

In computer-administered interviews, even if administered in human-mediated form, there is another important advantage in terms of time saved. First, the respondents answer in electronic form (into simple collection sheets for closed-ended answers and into text boxes for open-ended ones), so that subsequent processing of the data is made easier. This is valid also for interviewer-administered interviews, as the format for submission is the same. Whenever the interviewer wants to add a comment, he can do it directly on the transcription, during the interview, or in the appropriate sections, after its conclusion. Secondly, the administration is carried out at a variable depth through the use of screening questions and of skip rules, as before discussed. For this reason the interview in a community sample could be concluded rapidly: about 50 minutes for parents version; 30 minutes for youth version; less than five minutes for teachers version. It is important to note that skips rules integrate the information derived from the screening close-ended questions with that initially provided by the SDQ, in order to optimize the time needed. Finally, predictions of diagnosis (and its probability) are generated algorithmically, as previously discussed. An experienced and well-

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trained rater can use this information to convert automatically proposed diagnosis in reliable clinical diagnosis, in a relatively small amount of time. A longer and more complex training is required to properly obtain a clinical rating starting from transcriptions; it should be noted, however, that the entire process is fully operationalized in the website of the project.

## 1.4    Empirically-derived psychopathology

The dimensional, or quantitative, approach to psychopathology can be seen as partially complementary to the qualitative one [Kasius, M.C. *et al.,* 1997], proving to be a useful integration for it [Bellina, M. *et al.,* 2012]. It can also be seen as an approach able to overcome the limitations of the use of diagnostic categories [Krueger, R.F. & Piasecki, T.M., 2002]. If on the one side diagnostic categories are proposed, on the other hand the approach is based on a dimensional vision, following a bottom-up methodology. In fact, psychopathological dimensions are derived from empirical observation and they have been recommended also to promote main modifications of current diagnostic systems [Regier, D.A. *et al.,* 2009], in which it was proposed to focus more on a dimensional approach, especially for psychotic disorders [Van Os, J., 2009; Van Os, J. *et al.*, 2009].

In particular, in developmental psychopathology, large samples of children and adolescents were assessed in order to be able to propose data-driven models of symptoms aggregation [Achenbach, T.M. & Edelbrock, C.S., 1984] and to create assessment tools that compare the evaluated persons with the normal population of similar age [Achenbach, T.M. *et al.,* 2008]. If the diagnostic categories commonly used have had and still have great advantages also for children and adolescents psychopathology [Angold, A. & Costello, E.J., 2009], these categories are strongly associated with those empirically derived [Achenbach, T.M. *et al.,* 2001].

In addition to benefits for epidemiology research, in normative population samples the quantitative/dimensional approach to developmental psychopathology is particularly useful in research about longitudinal prediction derived from the presence of behavioural-emotional problems in childhood [Shaw, D.S. *et al.,* 1997; Roza, S.J. *et al.,* 2003]. Furthermore, it simplifies the comparison among different sources of information [Achenbach, T.M., 2011] and allows to identify potential

clinical utility of significant differences among them [Ferdinand, R.F., Van der Ende, J. & Verhulst, F.C., 2007; Israel, P. *et al.,* 2007]. Finally, this approach allows a simple adaptation to different cultural backgrounds, proving thus to be useful in comparing different societies [Verhulst, F.C. *et al.,* 2003; Ivanovaa, M.Y. *et al.,* 2007; Brøndbo, P.H. *et al., 2011].

## 1.5    The *Child Behaviour Check-List*

The *Child Behaviour Check-List* is an empirically-based questionnaire filled out by parents of children and adolescents aged from one year and six months in pre-schooler version (CBCL 1½-5), and from six to 18 years in school-age form (CBCL 6-18). It is the most frequently employed tool of the *Achenbach System of Empirically Based Assessment* (ASEBA) [8], that is an exhaustive evaluation system oriented primarily to childhood and adolescence [Achenbach, T.M. & Rescorla, L.A., 2001], but also available for adulthood [Achenbach, T.M. & Rescorla, L.A., 2003]. ASEBA includes instruments designed for psychopathology assessment following an approach characterised by the recognition of multiple dimensions (e.g. through independent scales), the willingness to integrate multiple sources of information (e.g. parents and teachers), the availability of similar assessments for a wide range of age (from one year and six months to 90 years). Furthermore, the system includes specific software tools for the questionnaires administration, the data collection and organization and for the comparison with the normative sample scores as well. Below, we will refer only to the CBCL, especially to the school-age form, as it is the ASEBA questionnaire used to collect data in the reported studies.

*Table 1.3* presents the list of empirically-derived scales composing the CBCL 6-18. These scales are directly derived from empirical data by means of factor analysis procedures. In particular, eight so called *Syndromic* scales were obtained from the 118 items composing the questionnaire. These scales resulted to be associated with each other so that it was possible to identify two summarizing dimensions, corresponding to two scales. Finally, an overall scale has been maintained, to account for the observed association among all behavioural-

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[8] See: '**www.aseba.org**'.

emotional problems investigated. In the same table, additional six scales are reported, the *DSM-Oriented* scales. These scales were obtained with a top-down approach based on the judgement of experienced clinicians who evaluated nearness between the items of the questionnaire and the diagnostic criteria of the DSM-4, in order to reach a compromise that will improve the consistency between the two systems [Achenbach, T.M. *et al.,* 2001; Achenbach, T.M., Dumenci, L. & Rescorla, L.A., 2003].

| | Scales |
|---|---|
| *Total* scales | *Total Problems* |
| | *Internalizing Problems* |
| | *Externalizing Problems* |
| *Syndromic* scales | *Anxious/Depressed* (in *Internalizing Problems*) |
| | *Withdrawn/Depressed* (in *Internalizing Problems*) |
| | *Somatic Complaints* (in *Internalizing Problems*) |
| | *Social Problems* |
| | *Though Problems* |
| | *Attention Problems* |
| | *Rule-Breaking Behaviour* (in *Externalizing Problems*) |
| | *Aggressive Behaviour* (in *Externalizing Problems*) |
| *DSM-Oriented* scales | *Affective Problems* |
| | *Anxiety Problems* |
| | *Somatic Problems* |
| | *Attention Deficit and Hyperactivity Disorder Problems* |
| | *Oppositional Defiant Problems* |
| | *Conduct Problems* |

**Table 1.3.** Scales derived from the *Child Behaviour Check-List* in school-age form (from six to 18 years).

The CBCL 6-18 was extensively standardized on samples from the normal population in childhood and adolescence. Raw scores on the scales presented below could be standardised in T-scores with excellent psychometric properties. In this regard, the standardised scores can be used to identify individuals with behavioural-emotional problems statistically significant above normal range of variation (labelling as *clinically* significant scores) or high enough to give cause for concern and require further investigation (labelling as *sub-clinical* scores). Specifically, the clinical cut-off identifies as positive the 2% of the normative population: it corresponds to a T-score above 70 for *Syndromic* scales and *DSM-*

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*Oriented* scales and to a T-score above 64 for *Total* scales (more reliable than previous, because their scores are based on a greater number of items). On the contrary, the *sub-clinical* cut-offs select the 7% of the normative sample, so that the 5% of children and adolescents should have a label indicating problems of *sub-clinical* elevation [Achenbach, T.M. & Rescorla, L.A., 2001]. In this case a T-score between 60 and 63 indicates *sub-clinical* problems on *Total* scales, while a T-score between 65 and 69 for other scales.

## 1.5.1    The *Total Problems* scale

This scale score is calculated as the sum of scores of any item of the entire questionnaire. Each item is intended to measure a behavioural-emotional problem shown by the examined child or adolescent in the last six-months period, so that *Total Problems* scale provides a measure of the overall problems experienced by the person under evaluation.

## 1.5.2    The *Internalizing Problems* scale

Through a procedure of factor analysis it was shown that items related to emotional problems were associated to three dimensions, jointly attributable to a single dimension. In particular, a scale has been recognized as composed of anxious/depressive problems as excessive worries and fears or experiences of negative affectivity (*Anxious/Depressed* scale). Another scale was associated with difficulties in social withdrawal, with excessive shyness, sadness and reduction of energy (*Withdrawn/Depressed* scale). Finally, a scale seemed to indicate physical problems with no obvious medical causes, including sleep problems (*Somatic Complaints* scale). The *Internalizing Problems* scale summarise the scores in those three scales.

## 1.5.3    The *Externalizing Problems* scale

Problems related to hetero-directed aggression and to socially undesirable behaviours are summarised by the *Externalizing Problems* scale, which is calculated as the sum of scores of two scales of externalised problems. The first scale indicates the execution of behaviours such as substance abuse, lying or stealing (*Rule-Breaking Behaviour* scale). The other measures the tendency to

physical or verbal aggression, as well as to outbursts of anger or sudden changes in mood (*Aggressive Behaviour* scale).

### 1.5.4    Other syndromic scales and items

Other three dimensions have been recognized empirically, being independent of one another. The *Social Problems* scale is composed by behavioural problems associated with situations of social interaction with peers (e.g., jealousy, lack of popularity, clumsiness). Especially unusual behaviour or thoughts are associated in a score in the *Though Problems* scale, including obsessions, compulsions, hallucinations, or self-harming behaviours. Finally, a set of problems of attention and concentration are also found to be associated (*Attention Problems* scale).

In addition, 17 items of the questionnaire were not associated to any scale or dimension, but they have been maintained, since they contribute effectively to the score on the *Total Problems* scale.

### 1.5.5    The *DSM-Oriented* scales

As previously mentioned, the items of the questionnaire were evaluated in order to determine their adherence to the criteria of the DSM-4 for: *Dysthymic Disorder* and *Major Depression Disorder* (*Affective Problems* scale); *General Anxiety Disorder*, *Panic Disorder*, *Specific Phobias*, and *Social Phobias* (*Anxiety Problems* scale); *Somatization Disorder* and *Somatoform Disorders* (*Somatic Problems* scale); *Attention Deficit and Hyperactivity Disorder* both *Hyperactive-Impulsive* and *Inattentive* types (*Attention Deficit and Hyperactivity Disorder Problems* scale); *Oppositional Defiant Disorder* (*Oppositional Defiant Problems* scale); *Conduct Disorder* (*Conduct Problems* scale).

The *Avoidant Personality Disorder* and the *Obsessive-Compulsive Disorder* were also taken into consideration, but their diagnostic criteria were too poorly represented in questionnaire for the creation of ad-hoc scales.

### 1.5.6    Software tools

The ASEBA is a widely employed system both in clinic assessment and in research activities. As mentioned above, it is a complex system as well, composed of questionnaires and structured interviews for preschool children, school-age

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children and adolescents, adults and elderly, too. Every instrument is available in different forms: for self-assessment and for evaluation by other people. In the case of children and adolescents assessments are possible both by parents and by teachers, while forms for evaluation by their partner are provided for adults. Some software were made available to facilitate the use of such a system, also to make possible the management of normative data of many different societies. This software can be used with substantially all the ASEBA tools, but it will be described here referring specifically to the CBCL.

The *Assessment Data Manager* (ADM) software [9] is oriented to the correction and scoring according to the normative data of all the forms in the system. In clinical practice, it is a tool mainly intended to provide the profiles of behavioural-emotional problems of examined children or adolescents (with 38 different cultural adaptations, organised in three normative groups of societies), however it also contains normative data for adults and for elderly (although only in accordance with standard normative values, not to Italian ones). In research activities, however, the main purpose of the software is the maintenance of information about a possibly large number of individuals. Actually, the software also contains a catalogue with the list of all children, adolescents and adults about whom information was collected. Within this catalogue, new forms can be entered and entered forms can be edited, verified, and scored. It is important to note that the software allows you to manage multiple sources of information for the same person (e.g. the judgements of one or two parents, along with those of the teachers and possibly of the person itself), as well as information collected from the same source at different times (e.g. at the beginning and at the end of the school year). In this way, multiple sources of information may be easily compared with each other within the ADM itself, or the data can be exported for analysis with other statistical tools.

Other tools have been specially designed for the administration of questionnaires and of other instruments of the assessment system. In particular, the

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[9] See: '**www.aseba.org/adm.html**'.

*WebForms Direct* software [10] is oriented to the administration of all questionnaires included in the system and it is specifically intended for online completion by respondents. It can be used both in the presence of the clinician on a stand-alone computer, or in a completely self-managed version (by sending a link that the respondent can use to begin the rating form online). *WebForms Direct* also permits the scoring of compiled forms and it provides scored and raw data are available for analysis. The *Web-link* is a similar software [11], it is oriented to completion and scoring of online questionnaires of the system. Furthermore, it makes immediate the transmission of data to ADM, for their later handling.

## 1.6   Other assessment tools

For the sake of completeness, other tools used in the following work will be presented in the next paragraphs. Specifically, a neuropsychological battery for children and adolescents and three questionnaires designed to assess the risk of developing psychiatric disorders.

Results obtained from these tools application could be presented and associated with the results obtained through diagnostic procedures that have been previously discussed. Especially with evaluations based on an empirical approach.

### 1.6.1    The *Developmental Neuropsychological Assessment*

The *Developmental Neuropsychological Assessment* [NEPSY; Korkman *et al.,* 1998] is an extensive battery of tests, designed to assess neuropsychological impairments in children and adolescents. It is mainly oriented to assess people with acquired or neurodevelopmental disorders and it has normative data obtained on a sample representative of the normal population, having demonstrated acceptable reliability and validity. This battery is based on Lurian's theoretical assumptions, therefore it is an instrument composed of complex tests that aim to have good ecological validity.

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[10]  See: '**www.aseba.org//webdirect.html**'.

[11]  See: '**www.aseba.org/weblink.html**'.

The full version of the battery also includes specific tests for preschool children, but subsequently tests will be used for the school-age range. ***Table  1.4*** reports the four cognitive domains that compose the Italian version of the battery for children and adolescents between five and 16 years, the table also reports tests composing each of these domains. As shown, the evaluation is extended to diversified cognitive functions: *Attention and Executive Functions* (with three tests), *Visuospatial Functions* (with two tests), *Sensorimotor Functions* (with three tests), and *Memory and Learning* (with three tests).

| Cognitive domains | Test |
|---|---|
| *Attention and Executive Functions* | *Auditory Attention* |
| | *Tower* |
| | *Visual Attention* |
| *Visuospatial Functions* | *Arrows* |
| | *Design Copying* |
| *Sensorimotor Functions* | *Fingertip Tapping* |
| | *Imitation of Hand Positions* |
| | *Visuomotor Precision* |
| *Memory and Learning* | *Memory for Faces* |
| | *Memory for Names* |
| | *Narrative Memory* |

***Table  1.4.*** Cognitive domains of the *Developmental Neuropsychological Assessment* and tests that compose them.

The *Second Version* of the battery [Korkman, Marit, Kirk, U. & Kemp, S., 2007] has been recently adapted for Italy [Urgesi, C., Campanella, F. & Fabbro, F., 2011]. This version extended the previous adding two new cognitive domains and reaching a total of 33 tests. In particular, the *Language* domain was already present in the first version of battery (with three tests), but not in its Italian adaptation. Instead, the *Social Perception* domain has been entirely added so that it is present only in the new version.

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### 1.6.2    The *Chapman Psychosis Proneness* scales

The *Chapman Psychosis Proneness* scales [Chapman, L.J. & Chapman, J.P., 1987] are questionnaires designed to measure personality traits predisposing to the development of psychosis or *Bipolar disorder*. Three of these scales are in an advanced state of adaptation for Italy by our group, also on community samples of children and adolescents.

The *Hypomanic Personality* scale is a 48-item true/false questionnaire investigating the presence of hypomanic symptoms [Eckblad, M. & Chapman, L.J., 1986]. It was originally conceived to be employed with young adults and the symptoms outlined are not intended to have clinically significant impact on daily life. It was shown that high scores on this scale predict both hypomanic episodes and mood disorders with a 14 years follow-up research [Kwapil, T.R. *et al.,* 2000].

The *Magical Ideation* scale consists of 30 items measuring ways of thinking involving non-realistic cause-effect relations [Eckblad, M. & Chapman, L.J., 1983]. Also this scale has been used on young adults to estimate the risk of emergence of thought disorders.

Finally, the *Perceptual Aberration* scale is a 35-item questionnaire making an inventory of unusual perceptual experiences [Chapman, L.J., Chapman, J.P. & Raulin, M.L., 1978; Chapman, L.J., Edell, W.S. & Chapman, J.P., 1980]. Together with the previous scale, it has shown to predict the onset of psychotic disorders. In fact, people with high scores on *Magical Ideation* and *Perceptual Aberration* scales showed longitudinally greater vulnerability to them [Chapman, L.J. *et al.,* 1994].

## 1.7   Conclusion

In the previous paragraphs, we have introduced tools oriented to diagnostic evaluation of children and adolescents. The main focus has been directed to systems oriented to psychopathological diagnosis, either representative of a *qualitative/categorical* approach or of a *quantitative/dimensional* approach.

Then, other tools have been shown, which will then be put in relation to diagnostic evaluation. In particular, a battery for neuropsychological assessment and three questionnaires related to the risk for psychiatric disorders.

The diagnostici instruments described are strongly oriented to computerized, specifically online, use. This seems to be an increasingly advantageous characteristic.

In the case of the presented clinical interview, the DAWBA, we have discussed also a specific mode to assign diagnostic labels through a well-defined clinical rating process. The clinical rating process is made possible by the adopted online data collection, in fact, it can be adopted in an identical way for interviews conducted by clinical or for self-administered ones. There are indications of acceptable consistency with the standard procedures in community samples [Brøndbo, P.H. *et al.,* 2012]. In the same way, compuer-based diagnosis could result less expensive than consensus diagnosis, maintaining a medium-to-high reliability for specific disorders [Krebs, G. *et al.,* 2012]. Moreover, this special diagnostic procedure also allows reliability evaluations hardly available for other clinical interviews [Aebi, M. *et al.,* 2012].

It has also been proposed that these processes could be usefully implemented in clinical practice [Ford, T. *et al.,* 2012] and the most effective way to obtain this could be to initially use online-based procedures as a complement to standard practice. However, it is currently still crucial to consider how clinicians evaluate this type of diagnostics opportunity [Martin, A.M. *et al.,* 2011]. In some special cases, the self-administered form of the interview could be preferable to improve reliability, as in the case of person with *Autistic Spectrum Conditions* [Barrow, W. & Hannah, E.F., 2012].

Furthermore, the DAWBA includes a computerized data storage for diagnostic information. This feature increases the possibility to manage diagnostic data following an interactive procedure [Axford, N., Hobbs, T. & Jodrell, D., 2012], so to have advantages in the management of public health services, particularly those for children and adolescents [Axford, N. *et al.,* 2009]. In any case, the introduction of new forms of information management in public services is a complex issue, requiring a step-by-step procedure before obtaining a stable routine [Batty, M.J. *et al.,* 2012]. However, the use of computerized procedures for the assessment of psychological well-being of large samples of children and adolescents could be desirable also with the aim of normal population monitoring [Hobbs, T., 2010],

although currently with low expectations and partial unsatisfactory results [Hobbs, T., Axford, N. & Jodrell, D., 2010].

Similar considerations can be made more easily for tools used in empirical-based/dimensional approach. Auto-administered questionnaires are obviously suitable to be employed online and no doubt they take benefit from the computerized operations in scoring the results data and storage,in particular for their employement in research projects [Russell, C.W. *et al.,* 2010]; although the equivalence of the different forms in epidemiological research it is not fully demonstrated, therefore it is strongly recommended to better investigate the differences [Heiervang, E. & Goodman, R., 2011]. But, especially for large samples, the advantages seem however undeniable [Goodman, R. & Scott, S., 1999].

The time when the internet potentialities will be employed in therapeutic practice seems very close. Some examples are already represented in the literature about *Mood Disorders* [Berger, T. *et al.,* 2011] as well as *Anxiety Disorders* [Hedman, E. *et al.,* 2011] intervention. The results are encouraging, especially if compared to other auto-administration procedures or group interventions. Specific or general proposals began to be suggested [Ritterband, L.M. *et al.,* 2009]. However, a complete and shared operational definition for internet-supported intervention are still needed before it is possible to extend the use of these [Barak, A., Klein, B. & Proudfoot, J.G., 2009]. Moreover, there are experiences of use of online tools for the purpose of screening and prevention [12]. Interestingly, a similar project, mainly oriented towards clinicians, is also present in Italy and promoted by the *Scientific Institute IRCCS "Eugenio Media"* [13].

Considering what stated in previous paragraphs, a crucial step is the development of valid and reliable diagnostic procedures that take advantage of the use of internet. Furthermore, it is essential that these instruments are able to satisfy requirements of both categorical and dimensional approaches, so as to promote either the clinical and research practices. The works presented here are oriented in

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[12] See: '**www.youthinmind.info**'.

[13] See: '**www.webcounseling.it**'.

this direction and can be seen in the perspective of developmental psychopathology: the search for risk and protective factors associated with continuity in psychopathology from childhood to adolescence and adulthood.

# 2

## Clinical sample

### 2.1  Introduction

The *Association "La Nostra Famiglia"* [14] is a non-profit organization of social utility, whose purpose is to promote and safeguard health care, education and services for people with special needs, in particular children and adolescents. There are 35 centres in Italy and abroad, representing a unique national network for the diagnosis, treatment and rehabilitation of developmental disorders. The *Scientific Institute IRCCS "Eugenio Medea"* [15] is a research section the association founded in 1985 to develop clinical research, particularly in the field of child neuropsychiatry.

In recent years, the institute has promoted research projects specifically oriented to diagnostic assessment and longitudinal observation of children and adolescents with behavioural-emotional problems. They have been conducted in order to study risk and protection factors associated with onset and evolution of psychiatric disorders, from childhood to adolescence and adult age. More specifically, the project *"Gene-Environment Interaction and Neurodevelopmental Markers in Pre-*

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[14] See: '**www.lanostrafamiglia.it**'.

[15] See: '**www.lanostrafamiglia.it/irccs.php**'.

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*Psychosis: An Integrated Multidisciplinary Study"* (GENESIS) was conducted under the supervision of *Dr.* Paolo Brambilla, and it is currently carried on as *"Caratterizzazione di bambini ed adolescenti con profilo comportamentale di deficit di autoregolazione (Dysregulation Profile – DP)"* (CABALA), under the supervision of *Dr.* Maria Nobile. These projects have been actually implemented in four centres of the institute in the North of Italy: Bosisio Parini (Lecco), Conegliano (Treviso), Pasian di Prato (Udine), and San Vito al Tagliamento (Pordenone) and they are proceeding in the same places.

The behavioral assessment of a large epidemiological sample of children and adolescents will be presented below. The sample was collected as a basis for longitudinal studies, such as that presented in the ***Chapter 4***, as well as to study the association between behavioural-emotional problems and neuropsychological characteristics, as in ***Chapter 3***. Moreover, from this sample, the projects introduced will allow innovative research, based on the integration of behavioral data with results of neuroimaging techniques and genetics investigation.

The data reported in the present chapter have their own interest linked to their representativeness of the situation of Italian neuropsychiatric Services. Further, the results obtained about psychopathology with a cross-sectional methodology have allowed us to evaluate the consistency of the sample collected with the expectations from the literature.

## 2.2  Participants

The initial phase of the indicated research projects was primarily observational, having at first epidemiological purposes. In this phase social, demographic, and psychopathological data were collected during clinical assessment at selected centres.

Children and adolescents referred to these centres for behavioural-emotional problems were included in the study if they received a diagnosis of: *Behavioural and Emotional Disorders With Onset Usually Occurring in Childhood and Adolescence* (ICD-10 codes: F90-F98), *Neurotic, Stress-Related and Somatoform Disorders* (F40-F48), *Schizophrenia, Schizotypal and Delusional Disorders* (F20-F29), *Mood/Affective Disorders* (F30-F39), or *Personality Disorders* (F60-F69).

The first diagnostic category (F90-F98) was the most represented in the sample, and it included: *Hyperkinetic Disorders* (F90), *Conduct Disorders* (F91), *Mixed Conduct-Emotions Disorders* (F92), *Emotional Disorders* (F93), *Tic Disorders* (F95), and *Other Behavioural and Emotional Disorders* (F98). On the contrary, participants were subsequently excluded from clinical sample if they presented one or more diagnoses of *Mental Retardation* (F70-F79), *Pervasive Developmental Disorders* (F84), or severe *Receptive Language Disorder* (F80.2). Exclusion criteria included also the presence of neurological syndromes (e.g. epilepsy), severe sensory impairments (e.g. severe hypoacusia or hypovision), and both congenital and acquired lesions of central nervous system (included traumatic brain injuries with neuropsychological outcomes). As a precaution, participants were excluded also if they presented a measure of cognitive level below the norm (i.e., standardized points ≤ 70), although they were not diagnosed with mental retardation label. Diagnoses were assigned according to ICD-10 classification criteria by means of consensus meeting among clinicians (child or adult psychiatrists, child psychologists).

In order to be part of the clinical sample, participants needed to be evaluated also by a parent (usually the mother, in the 92.2% of the cases) with the *Child Behaviour Check-List* in at least one of school-age (CBCL 6-18, 86.5%, CBCL 4-18, 2.5%) or preschool (CBCL 1½-5, 11.0%) forms. It is important to note that only parents were employed as informant in this work, mainly because differences between informants are clearly established [Achenbach, T.M., 2011]. This choice has been made in order to better manage the collected data, even if it implies the loss of losing clinically relevant information [Ferdinand, R.F., Van der Ende, J. & Verhulst, F.C., 2006] in particular in respect to internalization problems [Shin, Y.M. *et al.,* 2008].

The whole procedure has been approved by the *Ethics Committee* of the *Scientific Institute IRCCS "Eugenio Medea"*.

## 2.3  Statistical analyses

Categorical variables were described with frequencies or percentages, using $\chi^2$-*test* to control the homogeneity of distribution in groups of interest (since none of the

expected frequencies were under five). Normative *clinical* or *sub-clinical* cut-offs for T-scores on CBCL scales were used to calculate the number of significant behavioural-emotional problems in the sample.

Continuous variables were summarized reporting means, standard deviations and ranges of variation. The assumption of homoscedasticity was checked by *Levene's test*, using non-parametric analyses to confirm parametric results in case of statistically significant violations. Thus, direct between-group differences were analysed with *t-test* or with *Mann-Whitney test* if only two groups were confronted. On the other hand, *univariate analysis of variance* or *Kruskal-Wallis analysis by ranks* were used to compare three or more groups. *One-way* and *two-ways analyses of covariance* were also used to take into account confounding effects of cognitive level. Post-hoc comparisons were conducted using *Tukey's honest significant difference test*.

A conventional significance level was adopted throughout the analyses ($\alpha = 0.05$). In multiple independent comparisons the statistical significance was corrected with *Bonferroni's method*, setting the same level for all the dependent variables analysed so that overall significance level remain the desired (corresponding $\alpha$ was reported on the basis of the number of independent comparisons performed).

*Pairwise deletion* was adopted to manage missing data. Then, the data were shown as available.

Presented statistical analyses were performed using *R, version 2.15.0* [*Development Core Team*, 2012].

## 2.4    Socio-demographic and main cognitive characteristics of the clinical sample

The total clinical sample was composed by 1366 children and adolescents, 22.6% of which were females. Participants were between two years and 17 years and four month old. For descriptive purposes, the whole sample was divided in different age-groups. Since the majority of the participants (73.3%) were between six and 12 years, the sample was subdivided in: *preschoolers* (younger than five

years and 11 months), children in *grades  1-2* (from six years to seven years and 11 months), *grades  3-4* (from eight years to nine years and 11 months), *grades  5-6* (from 10 years to 11 years and 11 months), and *adolescents* (from 12 years to 17 years and 11 months). Gender seemed to homogeneously distribute in these age-groups ($\chi^2_4$ = 2.99, p = 0.560).

*Table 2.1* reports general demographic characteristics of the sample (in **Part A**). It also shows data about cognitive level of participants (in **Part B**), indicating the number of available evaluations. In particular, standardized scores are reported for *Total Intelligent Quotient* (T-IQ; i.e., *WISC-R*, 59.4%; *WISC-3*, 18.4%, *WPPSI*, 10.3%; *WAIS-R*, 0.3%; *Stanford-Binet Scale of Intelligence* in *L-M Form*, 1.3%; *Griffiths Mental Development Scales*, 0.8%; *Raven's Progressive Matrices*, 0.5%; *Leiter International Performance Scale* in *Revised Form*, 0.2%; *Culture Fair Intelligent Test* in one case) and for *Verbal* (V-IQ) or *Performance* (P-IQ) ones if a *Wechsler Intelligence Scale* was administered. For 118 participants (8.6%) there were no data about cognitive level available. There were not gender-related statistical significant differences in T-IQ ($t_{1232}$ = 0.78, p = 0.434), nor in V-IQ ($t_{1200}$ = 1.58, p = 0.114) or P-IQ ($t_{1198}$ = 0.72, p = 0.475) ones. Unexpectedly, a between-group statistical significant difference was observed in T-IQ for age-groups ($F_{4,1229}$ = 3.76, p = 0.005), in particular with children in *grades 1-2* showing a higher score than *preschoolers*, children in *grades  3-4*, and *adolescents* (respectively: p = 0.044, p = 0.028, p = 0.022; Tukey's post-hoc test). The same tendency was observed for the V-IQ ($F_{4,1197}$ = 5.08, p < 0.001) and for the P-IQ ($F_{4,1195}$ = 5.25, p < 0.001). At post-hoc analyses, *grades 1-2* group showed a higher V-IQ than *grades  5-6* group (p = 0.049) and *adolescents* (p = 0.002), and a higher performance score than children in *grades  3-4*; instead, *preschoolers* had a lower performance score than children in *grade  1-2* (p = 0.001) and *adolescents* (p = 0.040). These differences suggested to take into account IQ in the following between-group analyses.

Children and adolescents were conducted under observation by autonomous choice of their family in the 33.8% of the cases, on advice of the school in the 33.3% of them and with the involvement of the general practitioner or the paediatrician in the 25.6% of  the cases. In the 7.4% of the the assessment was

conducted after indication by others, including the Social Services in the 1.2% of the cases. Percentages refer to participants of which we had this information, that is the 66.6% of the whole clinical sample.

| (A) | n (females %) | Age | (min; Max) |
|---|---|---|---|
| *Preschoolers* | 151 (21.2%) | 4.7 ± 0,80 | (2:0; 5:11) |
| *Grades 1-2* | 378 (19.8%) | 7.1 ± 0,55 | (6:0; 7:11) |
| *Grades 3-4* | 380 (24.5%) | 8.9 ± 0,59 | (8:0; 9:11) |
| *Grades 5-6* | 252 (23.8%) | 10.9 ± 0,57 | (10:0; 11:11) |
| *Adolescents* | 205 (23.9%) | 13.2 ± 1,17 | (12:0; 17:4) |
| *All* | 1366 (22.6%) | 8.9 ± 2,62 | (2:0; 17:4) |

**Table 2.1.    Part A.** Demographic main characteristics of the whole clinical sample. Range of variation of age is reported in years and months (years:months). Max: Maximum observed value; min: Minimum observed value; n: number of observations.

| (B) | Total IQ Mean ± SD (n) | (min; Max) | V-IQ Mean ± SD (n) | P-IQ Mean ± SD (n) |
|---|---|---|---|---|
| *Preschoolers* | 100.9 ± 13.75 (130) | (71; 133) | 101.2 ± 14.64 (105) | 99.9 ± 14.74 (109) |
| *Grades 1-2* | 105.1 ± 14.45 (354) | (73; 151) | 103.4 ± 13.71 (352) | 106.2 ± 15.50 (349) |
| *Grades 3-4* | 101.8 ± 14.04 (340) | (72; 139) | 101.0 ± 14.96 (338) | 102.3 ± 14.32 (335) |
| *Grades 5-6* | 102.2 ± 15.60 (228) | (72; 151) | 99.6 ± 15.87 (226) | 104.5 ± 15.41 (228) |
| *Adolescents* | 101.1 ± 15.28 (182) | (71; 145) | 97.7 ± 15.72 (181) | 105.0 ± 15.56 (179) |
| *All* | 102.6 ± 14.68 (1234) | (71; 151) | 100.9 ± 14.98 (1202) | 104.1 ± 15.21 (1200) |

**Table 2.1.    Part B.** Cognitive characteristics of the whole clinical sample. IQ: *Intelligence Quotient*; Max: Maximum observed value; min: Minimum observed value; n: Number of observations; P-: *Performance*; SD: Standard Deviation; V-: *Verbal*.

*Parents education*

| Mean ± SD | Attained qualification | Mothers | Fathers |
|---|---|---|---|
| Mothers' year: | *Nothing* | 0.1% | 0.1% |
| 11.0 ± 3.16 | *Primary School* | 2.3% | 4.9% |
| Fathers' years: | *Junior High School* | 42.8% | 46.0% |
| 10.5 ± 3.23 | *General Educational Development exams* | 6.6% | 9.7% |
| | *High School graduate* | 39.8% | 31.6% |
| | *Bachelor Degree* | 1.9% | 0.4% |
| | *Master Degree* | 6.6% | 7.4% |

*Siblings*

| Mean ± SD | Number of children | (%) |
|---|---|---|
| Number: | *Only child* | 27.1% |
| 1.0 ± 0.78 | *One sibling* | 55.3% |
| Order of geniture: | *Two siblings* | 14.1% |
| 1.5 ± 0.69 | *Three-to-seven siblings* | 3.5% |

***Table 2.2.*** Parents education and number of siblings. Years of education are reported for mothers and fathers, together with attained qualification. SD: Standard Deviation.

The reasons that had motivated the clinical evaluation were available for the 70.0% of the participants. In particular, more common problems reported were: behavioural (31.4% of the cases), emotional (15.5%), and attentional (14.9%). The 14.1% of the participants had scholastic difficulties and the 13.4% linguistic ones. In the 10.6% of the cases other problems were also reported, among which: difficulty in psychomotor development (2.3%), enuresis or encopresis (1.4%), sleep problems (0.7%), socio-economical problems (0.7%) or difficulties in feeding (0.7%).

Data about parents' education, number of siblings and order of geniture are shown in ***Table 2.2***, without distinction for age or gender, since there were not statistically significant gender-related differences, and age-related differences were expected.

In order to include potential risk or protective factors, data about families characteristics and composition were collected, too. General information were available about the 98.8% of the involved families and the 73.9% of the parents of

the participants. It is interesting to note that the 22.3% of the participants lived in a non-standard familiar situation, intending for *"standard"* a household in which two biological parents live together with their children, and for *"non-standard"* situation with the presence of a single biological parent (mono-parental families or stepfamilies). Moreover, the 2.9% of the participants were adopted. No statistical significance gender-related differences were observed for frequencies of non-standard families ($\chi^2_1 = 0.23$, p = 0.635) or adoptions ($\chi^2_1 = 0.03$, p = 0.861). Similarly, there weren't statistical significant differences in age between adopted and not-adopted participants ($t_{1348} = 0.87$, p = 0.386) or between children living in a standard and in a non-standard family (U = 83941.0, p = 0.269).

Data were also collected about obstetric complications (both prenatal or perinatal), percentages of these complications are reported ***Table 2.3***. Frequencies of children and adolescents who have had obstetric complications seemed to be homogeneous in respect to gender ($\chi^2_1 = 0.09$, p = 0.766) and age-groups ($\chi^2_4 = 9.46$, p = 0.051).

Finally, since four centres were involved in the main epidemiological projects (as described in the first paragraph of the chapter), differences among the samples collected in these centres were taken into consideration. Since the data collection process was standardized among centres (e.g. in terms of available diagnoses and admission to clinical evaluation), only data about socio-demographic and cognitive level were compared below. Samples of different sizes were from the four involved centres: 630 (46,1%) participants were from Pasian di Prato (UD), 326 (23.9%) from Bosisio Parini (LC), 296 (21.7%) from San Vito al Tagliamento (PN) and 114 (8,4%) from Conegliano (TV). Gender seemed to distribute homogeneously in centres ($\chi^2_3 = 7.19$, p = 0.066) and, similarly, no statistical significant differences were observed in parents' years of education (mothers: $F_{3,1154} = 1.97$, p = 0.116; fathers: $F_{3,1138} = 1.18$, p = 0.317), frequencies of non-standard families ($\chi^2_3 = 5.63$, p = 0.131), or adoptions ($\chi^2_3 = 1.82$, p = 0.611). On the contrary there was a statistical significant between-group difference in participants' age ($F_{3,1362} = 26.10$, p < 0.001), in particular: LC showed older participants than PN and UD (both with p < 0.001) and TV showed older participants than PN and UD (respectively: p = 0.047 and p = 0.011), too. Furthermore, in the LC sample all

participants were in school-age. Interestingly, UD showed more participants who have had obstetric complications (45.1% of the sample; $\chi^2_3 = 28.06$, $p < 0.001$). Statistical significant differences were observed for T-IQ ($H_{3\,with\,1234} = 51.40$, $p < 0.001$; Levene's $F_{3,1230} = 2.70$, $p = 0.044$), as well as for V-IQ ($F_{3,1198} = 28.01$, $p < 0.001$) and P-IQ ($F_{3,1196} = 4.83$, $p = 0.002$). All differences were statistically significant on T-IQ (non-parametrically) and on V-IQ, with: PN > UD > LC > TV. On P-IQ measure, PN resulted significantly higher than LC and TV (respectively: $p = 0.041$ and $p = 0.003$), but not UD ($p = 0.073$).

| Obstetric complication | Percentage |
|---|---|
| *Caesarean section, or complicated or emergency birth.* | 17.9% |
| *Threatened miscarriage.* | 9.3% |
| *Incubator or intensive care.* | 4.5% |
| *Short gestation (< 37 weeks).* | 3.9% |
| *Use of forceps or other tools.* | 3.9% |
| *Long gestation (> 42 weeks).* | 3.0% |
| *Preeclampsy, gestosis.* | 2.7% |
| *Umbelical cord prolapse, breackage, or twisting.* | 2.6% |
| *Twin birth.* | 1.9% |
| *Podalic or abnormal version.* | 1.7% |
| *Long (> 24 hours), difficult, or precipitous labor.* | 1.3% |
| *Low birthweight (< 2 kg).* | 1.3% |
| Total (at least one complication). | 37.6% |
| Single complication. | 25.2% |
| Multiple complications (from two to five). | 12.4% |
| Two complications. | 9.1% |
| Three complications. | 2.7% |
| Four complications. | 0.6% |
| Five complications. | 0.1% |

*Table 2.3.* Percentages of children or adolescents in the clinical sample who have had pre- or perinatal complications are reported. Percentages of participants with single or multiple obstetric complications are reported, too.

| Scale | Mean ± SD | (min; Max) | N | S | C |
|---|---|---|---|---|---|
| *Total Problems* | 61.9 ± 8.97 | (29; 91) | 37.4% | 17.4% | 45.2% |
| *Internalizing Problems* | 61.3 ± 9.25 | (33; 87) | 39.3% | 16.7% | 43.9% |
| *Externalizing Problems* | 59.1 ± 9.39 | (32; 88) | 50.4% | 17.5% | 32.2% |
| *Anxious/Depressed* | 62.1 ± 8.79 | (50; 90) | 61.3% | 19.7% | 19.0% |
| *Withdrawn/Depressed* | 61.2 ± 9.05 | (50; 94) | 65.7% | 16.7% | 17.7% |
| *Somatic Complaints* | 57.3 ± 6.97 | (50; 90) | 84.8% | 7.8% | 7.4% |
| *Social Problems* | 61.3 ± 7.50 | (50; 90) | 65.7% | 20.0% | 14.3% |
| *Thought Problems* | 59.0 ± 8.09 | (50; 88) | 75.9% | 9.1% | 14.9% |
| *Attention Problems* | 64.4 ± 9.44 | (50; 100) | 52.8% | 22.7% | 24.5% |
| *Rule-Breaking Behaviour* | 57.9 ± 6.99 | (50; 81) | 83.1% | 7.6% | 9.3% |
| *Aggressive Behaviour* | 60.7 ± 8.74 | (50; 100) | 68.4% | 18.1% | 13.5% |

**Table 2.4.   Part A.** Scores from *Child Behaviour Check-List* questionnaire for school-age are reported (*Total* and *Syndromic* scales), together with number and percentage of participants above *clinical* or *sub-clinical* cut-off for each scale. C: *Clinical*; Max: Maximum observed value; min: Minimum observed value; N: *Normal*; S: *Sub-clinical*; SD: Standard Deviation.

| Scale | Mean ± SD | (min; Max) | N | S | C |
|---|---|---|---|---|---|
| *Affective Problems* | 61.9 ± 8.28 | (50; 92) | 61.0% | 17.1% | 21.9% |
| *Anxiety Problems* | 62.9 ± 7.99 | (50; 94) | 49.2% | 23.9% | 26.8% |
| *Somatic Problems* | 56.4 ± 6.75 | (50; 83) | 85.4% | 9.0% | 5.5% |
| *Attention Deficit and Hyperactivity Problems* | 62.5 ± 8.35 | (50; 80) | 58.6% | 20.6% | 20.8% |
| *Oppositional Defiant Problems* | 59.2 ± 7.67 | (50; 80) | 74.4% | 11.6% | 14.0% |
| *Conduct Problems* | 58.6 ± 7.72 | (50; 90) | 74.4% | 15.4% | 10.1% |

**Table 2.4.   Part B.** Scores from *Child Behaviour Check-List* questionnaire for school-age are reported (*DSM-Oriented* scales), together with number and percentage of participants above *clinical* or *sub-clinical* cut-off for each scale. For the legend, see **Table 2.4.   Part A**.

## 2.5  Dimensional psychopathology in the clinical sample

**Table 2.4** (divided in parts, **A** and **B**) reports standardized scores obtained by participants in the empirical-derived (*Total* and *Syndromic*) and in the *DSM-*

*Oriented* scales of the CBCL. It also shows frequencies of children and adolescents positioned above the *sub-clinical* or *clinical* cut-off in every scale. Data reported in the table describe the whole sample, regardless of the age at the evaluation and, consequently, of the form of the questionnaire compiled (preschool or school-age forms). Thus, some of the scales shown are present only in the school-age forms (i.e., *Social Problems*, *Thought Problems*, *Rule-Breaking Behaviour*, *Somatic Problems* and *Conduct Problems* scales). Scales present only in the preschool form (i.e., *Emotional Reactive*, *Sleep Problems*, and *Pervasive Developmental Problems* scales) were not reported or further discussed, since the low frequency of their employement. It is also important to note that a score above the *clinical* cut-off identifies as positive the 2% of the normative population, whereas the *sub-clinical* one the 7%, so that the 5% of children and adolescents should have a label indicating problems of *sub-clinical* entity [Achenbach, T.M. & Rescorla, L.A., 2001].

The age-groups presented above were used in order to evaluate gender and age effects on dimensional psychopathology assessed with CBCL. To better understand these effects, cognitive level (i.e. T-IQ) was used as covariate to control the statistically significant results found, since age-related statistical significance difference was observed (as reported above). Furthermore, only empirical-derived scales were considered.

First, it is important to control significant differences between preschool and school-age forms of CBCL, since both were administered. Children and adolescents evaluated with school-age forms showed higher scores on all the examined scales. Differences were statistically significant for most of the examined scales: *Total Problems* ($U = 836952.5$, $p < 0.001$), *Internalizing Problems* ($t_{1348} = 2.75$, $p = 0.006$), *Externalizing Problems* ($t_{1347} = 3.04$, $p = 0.002$), *Anxious/Depressed* ($t_{1348} = 3.56$, $p < 0.001$), *Attention Problems* ($t_{1348} = 5.99$, $p < 0.001$), and *Aggressive Behaviour* ($U = 830641.0$, $p < 0.001$). On the contrary, no statistically significant differences were observed only for *Withdrawn/Depressed* ($U = 812751.5$, $p < 0.559$) and *Somatic Complaints* ($t_{1347} = 1.88$, $p = 0.060$) scales.
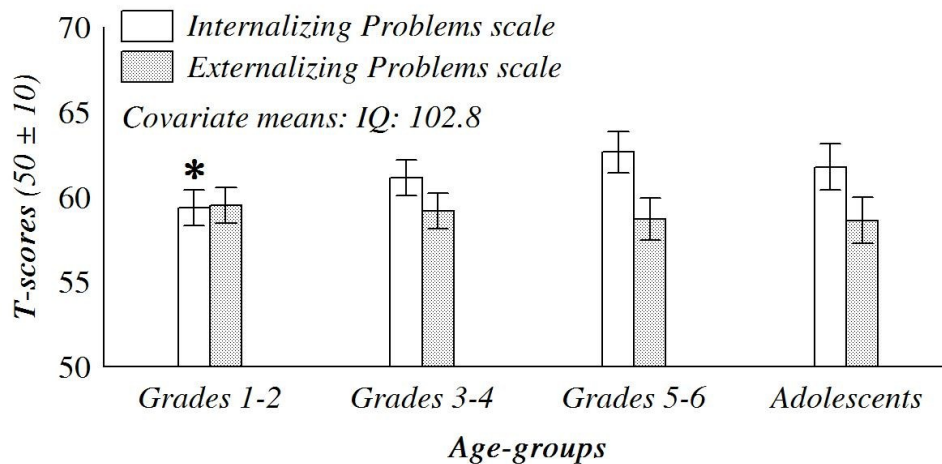
**Figure 2.1.** Age-relate differences in *Internalizing* and *Externalizig* problems scales of *Child Behaviour Check-List*. Two-way analyses of covariance showed effect of age-group for *Internalizing*, but not *Externalizig*, problems scale. IQ: *Intelligence Quotient*; SD: Standard Deviation. *: Statistically significant with p < 0.05 (Tukey honest significant difference post-hoc test).

Taking into account the reported data, the following analyses primarily focused on older children and on adolescents (i.e., from six to 17 years and 11 months), in order to use only the school-age forms of the CBCL. Data about preschoolers were reported only for gender-related statistically significant effects.

### 2.5.1     *Total* scales

Three independent comparisons were considered to correct significance level for multiple tests ($\alpha$ = 0.017, to maintain a 95% overall confidence interval).

There weren't statistically significant differences between genders (p = 0.723) or age-groups (p = 0.346) on the *Total Problem* scale, whereas scores in *Internalizing Problems* scale showed a statistically significant effect of age-group ($F_{3,1090}$ = 6.22, p < 0.001) and these in *Externalizing Problems* scale that of gender ($F_{1,1200}$ = 6.57, p < 0.011), both after covariation for cognitive level. Since Levene's test indicate a violation in homoscedasticity assumption for *Internalizing Problems* scale by gender ($F_{1,1204}$ = 4.67, p = 0,031), between-gender effect was controlled with a non-parametric test, resulting non-significant (U = 121746.0, p = 0,296). In particular, children in *grades 1-2* showed lower internalization

scores than other groups, reaching a statistically significant difference in respect to children in *grade 5-6* (Tukey's post-hoc test: p < 0.001) and *adolescents* (p = 0.028). Moreover, parents reported higher externalization scores for males than for females, independently of age.

*Figure 2.1* reports scores on these two scales by age-groups.

### 2.5.2   *Syndromic* scales

For those scales, eight independent comparisons were considered (establishing statistical significance for p < 0.006).

The three scales related to internalization showed a trend of scores mainly linked to age-groups. *Anxious/Depressed* scale score incremented with age ($F_{3,1091}$ = 5.29, p = 0.001), reaching statistical significance in comparison among children in *grades 1-2* with those in *grades 5-6* (p = 0.003) and with *adolescents* (p = 0.005). The group effect was confirmed non-parametrically ($H_{3with1207}$ = 19.57, p < 0.001), given the results of the Levene's test ($F_{3,1203}$ = 2.75, p = 0.042). Scores on *Withdrawn/Depressed* scale were higher in males than in females ($F_{1,1091}$ = 13.77, p < 0.001) and they showed an age-group effect ($F_{3,1091}$ = 5.31, p = 0.001). In particular, children in *grades 5-6* had highest scores (VS *grades 1-2*, p < 0.001; VS *grades 3-4*, p = 0.006; VS *adolescents*, p = 0.025). This effect is detectable also in non-parametric analysis ($H_{3with1207}$ = 15.33, p = 0.002; Levene's $F_{3,1203}$ = 3.25, p = 0.021). Increment in scores with age was also observed for *Somatic Complaints* scale ($F_{3,1091}$ = 5.31, p = 0.001), with non-parametrical confirmation ($H_{3with1206}$ = 18.60, p < 0.001; Levene's $F_{3,1202}$ = 3.75, p = 0.011), too. Children in *grades 1-2* had lowest problems (VS *grades 3-4*, p = 0.048; VS *grades 5-6*, p = 0.006; VS *adolescents*, p = 0.001). This scale showed higher scores in females than in males, but only closed to statistical significance (U = 116516.0, p = 0.038; Levene's $F_{1,1204}$ = 11.04, p = 0.001).

Non-statistically significant between-groups effect was present for *Rule-Breaking Behaviour* and for *Aggressive Behaviour* scales, but only a trend to higher scores in males than in females (respectively: $F_{1,1091}$ = 5.68, p = 0.017; $F_{1,1090}$ = 4.48, p = 0.035).

The score of *Social Problems* scale incremented with age ($F_{3,1091} = 6.54$, $p < 0.001$), in particular in *adolescents* (with higher scores than children, statistically significant in comparison to those in *grades 1-2*, $p < 0.001$, and in *grades 3-4*, $p = 0.007$). This was true also controlling homoscedasticity ($H_{3 \, with \, 1207} = 15.40$, $p = 0.002$; Levene's $F_{3,1203} = 3.18$, $p = 0.023$). Instead, gender had not statistically significant effect ($U = 160141.5$, $p = 0.348$; Levene's $F_{1,1205} = 13.86$, $p < 0.001$).

In *Thought Problems* scale there was not effect of age-groups ($F_{3,1091} = 1.24$, $p = 0.293$), but, without correction for cognitive level, females showed a trend to higher scores than males ($F_{1,1202} = 6.72$, $p < 0.010$) not present otherwise ($F_{1,1091} = 3.74$, $p = 0.054$). This tendency was confirmed non-parametrically ($U = 115519.0$, $p = 0.018$; Levene's $F_{1,1205} = 4.12$, $p = 0.043$), although not reaching statistical significance.

Interestingly, cognitive level also had a statistically significant effect in *Attention Problems* scale ($F_{1,1091} = 15.97$, $p < 0.001$), without between-group effects, in parametric ($F_{1,1091} = 1.67$, $p < 0.173$) and also non-parametric ($U = 160524.0$, $p = 0.389$; Levene's $F_{1,1205} = 10.13$, $p = 0.002$) analyses. Finally, in *Attention Problems* scale, *preschoolers* showed a between-gender difference close to statistical significance after correction for cognitive level ($F_{1,120} = 4.63$, $p = 0.033$). However, the difference was definitely not statistically significant otherwise ($t_{141} = 1.97$, $p = 0.051$).

## 2.6  Conclusion

*Developmental psychopathology* aimed to define the influence of biological, psychological and social-environmental factors on normal and abnormal development during the whole life course [Cicchetti, D. & Toth, S.L., 1998]. Achieving this goal might be crucial to improve efficacious strategies for prevention and early intervention [Costello, E.J., Egger, H. & Angold, A., 2005]; strategies that take in consideration risk and protection factors associated with the onset of mental diseases  and potentially of great social interest [Petrou, S. *et al.,* 2010].

In this chapter, we have presented general data from an epidemiological study. These data were collected to define a clinical sample representative of children and adolescents referred to four different centres of an Italian neuropsychiatric service for behavioural-emotional assessment, primarily for difficulties experienced by the families themselves. The problems that led to the evaluation were mostly behavioural, emotional and attentional,  with a relevant frequency of associated learning difficulties. A sample of acceptable numerosity was collected from this population.

Demographic and social data were reported together with potential risk factors, showing a sample characterized by wide age differences and a stable prevalence of males in all age-groups. The sample was substantially homogeneous by age and gender for familiar characteristics. Similarly, there was no evidence of heterogeneity in history of pre- or perinatal diseases. On the contrary, cognitive level was distributed in a differentiated manner in age-groups, revealing as a potential confounding factor to be taken into account. It is also important to note that children and adolescents from different centres significantly differed in some critical aspects: age at the evaluation, cognitive level and frequencies of reported obstetric complications. The observed differences among centres should be thoroughly investigated, but this was beyond the aims of our work. However, these differences represent a limitation to the generalizability of the results, since it was reported an association between age and cognitive level (as mentioned above) and it is not possible to exclude differences in the selection of participants, due to uncontrolled geographical factors.

The importance of family relations has a known impact on the well-being of children [Teubert, D. & Pinquart, M., 2010] and in developing behavioural-emotional problems [Gunther, N. *et al.,* 2003] in preschoolers [Halpern, L.F., 2004] and school-age children [Jouriles, E.N. *et al.,* 1991]. In a similar way, parents' educational level was reported to be a risk factor for mood disorders [Shin, Y.M. *et al.,* 2008] and development and maintenance of general psychosocial problems [Bot, M., De Leeuw den Bouter, B.J.E. & Adriaanse, M.C., 2011]. It is also important to note that association between risk factors seems to be particularly relevant in prevention and in prognostic processes [Najman, J.M. *et al.,* 2005].

Data about dimensional psychopathological characteristics of the sample were also reported and analysed on the basis of age and gender. First, frequencies of problems in CBCL were used to define psychopathological features of the sample, considering the known diagnostic reliability of the instrument [Achenbach, T.M. *et al.,* 2001]. Reported frequency of problems was obviously higher than those observed in normal population studies [Frigerio, A. *et al.,* 2009], since the presented sample was composed by clinically referred children and adolescents.

Using a cross-sectional methodology, it was shown that internalization problems continuously increment with age both in measure of overall impairment and in its specific components (anxious, depressive and somatic). This result was quite homogeneous, though specific observed developmental trajectories were different. On the other hand, problems associated with aggressive or delinquent behaviours didn't prove to be associated with age of the participants, but with gender. In this case, however, there has been an effect only for the summarized measure, possibly because of the relatively low presence of major externalized problems in the sample. In addition, it was reported a clear increase in socialization problems with age. Finally, the cognitive level of the participants seemed to directly affect the presence of attention problems and, partly, of thought difficulties.

The data reported above are significant to weigh the results of the studies presented in the following chapters, which will be based on sub-samples taken from the one presented here. In this regard, it should be emphasized again that the presented sample was composed by children and adolescents who were being evaluated by for behavioural-emotional problems. Thus, the characteristics presented were consistent with expectations and somewhat similar to those observed in epidemiological studies on normal population, but the scample showed obviously also special characteristics, linked to be constituted by participants referred to child psychiatric services.

It is important to note that presented data described the psychopathology in the sample from the dimensional point of view and it would be relevant to integrate this with categorical diagnostic approach [Kasius, M.C. *et al.,* 1997]. However, relevant information about association of behavioural-emotional problems with gender and age were presented. Demographic aspects showed to have important

effects on psychopathology during childhood and adolescence [Visser, J.H. *et al.,* 2003], in particular for anxious and depressive symptomatology [Hayward, C. & Sanborn, K., 2002].

From the point of view of the developmental psychopathology, behavioural-emotional problems showed to be stable from childhood to adolescence [Pihlakoski, L. *et al.,* 2006] to adulthood [Visser, J.H. *et al.,* 1999]. In this perspective, to better understand continuity in psychopathology [Bayer, J.K.J.K. *et al.,* 2008] and its effects on psychological and psychiatric problems in adulthood [Baiano, M. *et al.,* 2009], it was informative the use of validate and dimensional-oriented assessment tools together with clinical judgement [Ferdinand, R.F. *et al.,* 2004] and direct observation by specialists [Ferdinand, R.F. *et al.,* 2003].

# 3

## Profiles of behavioural-emotional problems

### 3.1 Introduction

The *Child Behaviour Check-List* (CBCL) is a widely used assessment tool for children and adolescents [Achenbach, T.M. & Rescorla, L.A., 2001]. It is characterized by a quantitative and dimensional view of psychopathology [Kasius, M.C. *et al.,* 1997] and it has been adopted in different cultural contexts as a reliable instrument [Ivanovaa, M.Y. *et al.,* 2007]. In Italy it has been also used to conduct epidemiological research in normal population [Frigerio, A. *et al.,* 2009].

Several methods have been proposed for the employment of the scores in the items of the questionnaire, for example complementing traditional scores obtained with an empirical bottom-up approach with differently obtained scores, derived by expert judgement [Achenbach, T.M. *et al.,* 2001].

A different approach was described and adopted below. It consists in using available scores recombining them in order to obtain new measures, identifying specific profiles of problems. In particular, two profiles derived from CBCL were considered: *Dysregulation Profile* and *Autistic Spectrum Disorder Profile*. Both have proved to be reliable methods to assess respectively emotional dysregulation and autistic-like problems in children and adolescents.

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In the following paragraphs, neuropsychological characteristics associated with these profiles were examined in order to recognise cognitive components possibly associated with specific behavioural difficulties.

## 3.2    The *Dysregulation Profile* at the *Child Behaviour Check-List*

A specific profile derived from CBCL was originally proposed as a method to screen children and adolescents with manifestations of Bipolar disorder [Biederman, J. *et al.,* 1995] or at elevated risk to develop an early or very-early onset form of it [Biederman, J. *et al.,* 2009]. However, this profile was not observed to be specifically associated to juvenile mania manifestation, but it was considered as a marker of self-regulation processes associated with developmental risk, specifically of difficulties in emotional regulation [Holtmann, M., Buchmann, A.F. *et al.,* 2011].

The emotional regulation is promoted by all the processes that can monitor, evaluate, and possibly modify the emotional reactions of an individual [Keenan, K., 2000]. Difficulties in those regulatory processes seemed to be related to psychiatric disorders like *Major Depression*, *Schizophrenic Disorder*, *Bipolar Disorder*, and *Disruptive Behavioural Disorders* [Moses, E.B. & Barlow, D.H., 2006]. In children and adolescents, a poor emotional regulation may result in children developing a *Severe Mood Dysregulation* [Leibenluft, E., 2012] with increased emotional lability and thus frequent periods of mood instability characterized by hyperarousal, irritability, aggression, and distractibility.

The sum of standardised T-scores of the *Anxious/Depressed*, *Attention Problems* and *Aggressive Behaviour* scales of the CBCL was proposed as a measure of emotional dysregulation in children and adolescents [Jucksch, V. *et al.,* 2011], so that a profile with extreme scores in all these scales was named *Dysregulation Profile* [CBCL-DP; Althoff, R.R., 2010]. In children and adolescents, the CBCL-DP was proposed as risk factor of developing multiple and severe psychopathological conditions and of showing behavioural problems [Meyer, S.E. *et al.,* 2009], as well as to experiment poor academic performances and work adaptation [Spencer, T.J. *et al.,* 2011]. Children with CBCL-DP resulted at risk for drug abuse, suicidal ideation and suicidality [Holtmann, M., Becker, A. *et al.,*

2011], and also for *Anxiety*, *Mood* and *Disruptive Behavioural* disorders [McGough, J.J. *et al.,* 2008; Halperin, J.M. *et al.,* 2011] and for *Personality Disorders* of *Cluster B* [Ayer, L.A. *et al.*, 2009]. Furthermore, this index frequently marks severe symptomatology in population-based observations [Althoff, R.R., 2010] and additional difficulties in clinical samples, in particular in comorbidity with *Attention Deficit and Hyperactivity Disorder* [Biederman, J. *et al.,* 2009; Spencer, T.J. *et al.,* 2011] but also in association with anxiety, aggressive behaviour and feeding problems [McLaughlin, K.A. *et al.*, 2011].

Below, the distribution of this profile will be described in the whole available clinical sample of children and adolescents with behavioural-emotional problems. Then, since the neuropsychological profile of children and adolescents with CBCL-DP was not previously studied, data will be shown for a sample extensively assessed for neuropsychological characteristics. The aim was the comparison between children and adolescents with CBCL-DP and without that profile, in order to detect differences in specific cognitive tasks.

## 3.3    The *Autism Spectrum Disorder Profile* at the *Child Behaviour Check-List*

The *Autism Spectrum Disorders* (ASDs) include *Autistic Disorder*, *Asperger Disorder* and *Pervasive Developmental Disorder Not Otherwise Specified*. These disturbances are characterized by impairments in behaviour, social interactions and communication [APA, *Task Force on DSM-IV*, 2000]. Their prevalence has increased in recent years [Newschaffer, C.J., Falb, M.D. & Gurney, J.G., 2005]. This seems to be due to widening of diagnostic criteria [Baron-Cohen, S. *et al.,* 2009] as well as to decrease of the age of the first diagnosis [Schieve, L.A. *et al.,* 2012]. Thus, many children not previously diagnosed fall now in the broadened spectrum, also called *Autism Spectrum Condition* [Baron-Cohen, S. *et al.,* 2009]. Furthermore, the ASDs have often been conceptualized as extremes of a continuum, since autistic-like traits can be commonly observed in general school-age population [Posserud, M.-B., Lundervold, A.J. & Gillberg, C., 2006], showing to be continuously distributed [Constantino, J.N., Hudziak, J.J. & Todd, R.D., 2003]. Moreover, these traits resulted to be highly stable from nine to 13 years

[Robinson, E.B. *et al.,* 2011]. Studies focused on twins showed genetic susceptibility for ASD and for sub-threshold autistic-like traits [Constantino, J.N. *et al.,* 2006], probably with genetic links between them [Lundström, S. *et al.,* 2012].

It is interesting to note that ASDs are frequently associated with comorbid psychiatric disorders in children [Simonoff, E. *et al.,* 2008], especially with *Anxiety/Phobic Disorders*, *Disruptive Behavioural Disorders* and *Attention Deficit and Hyperactivity Disorder*. Furthermore, parents reported high frequent and severe behavioural-emotional problems such as obsessions, compulsions, social and specific phobias in preschool [Gadow, K.D. *et al.,* 2004] and school-age children [Gadow, K.D. *et al.,* 2005; Lecavalier, L., 2006]. Similarly, autistic-like traits were frequent  in adults and children with *Obsessive-Compulsive Disorder* [Bejerot, S., Nylander, L. & Lindström, E., 2001; Ivarsson, T. & Melin, K., 2008], and in children and adolescents with *Anxiety* or *Mood Disorders* [Van Steensel, F.J.A., Bogel, S.M. & Wood, J.J., 2012]. In the same way, both children and adults with autistic-like traits showed an increased frequency of psychiatric diagnoses [Lundström, S. *et al.,* 2011], internalizing problems [Hallett, V. *et al.,* 2009, 2010] and inattention and impulsivity [Reiersen, A.M. *et al.,* 2008]. Furthermore, a mutual bi-directional association between autistic-like traits and internalizing problems was demonstrated: children and adolescents with autistic-like traits showed longitudinally an increase of internalizing traits and those with internalizing traits showed an increase of autistic-like traits [Hallett, V. *et al.,* 2010].

Autistic-like traits seem to be particularly associated with specific CBCL scales: *Withdrawn/Depressed*, *Social Problems* and *Thought Problems* scales, so that a composite score could be obtained as the sum of standardised T-scores of these scales and a profile compatible with the presence of an ASD could be individuated from that score (CBCL-ASDP). The CBCL-ASDP was proposed for use in school-aged children and adolescents with a cognitive level within the normal range, resulting a reliable method for distinguishing between children and adolescents with ASDs from comparison group with different psychiatric problems [Biederman, J. *et al.,* 2010].

In following paragraphs, the CBCL-ASDP was adopted as an index of autistic-like traits. As for CBCL-DP, the CBCL-ASDP will be described in the whole clinical sample and neuropsychological performances of children and adolescents with it will be compared to those of a group without the profile. The aim is to search for cognitive markers of autistic-like problems in children and adolescents with behavioural-emotional problems.

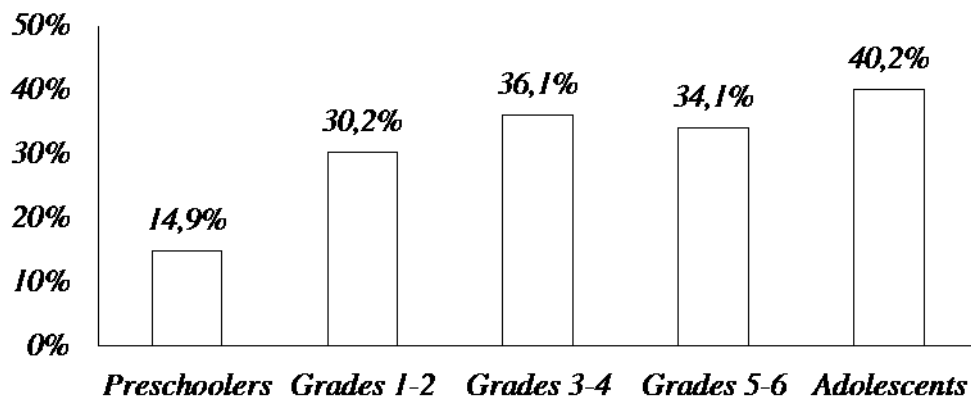|  | Mean ± SD | (min; Max) |
|---|---|---|
| Age | 9.4 ± 2.41 | (3:6; 16:6) |
| Total IQ | 101.6 ± 14.00 | (71; 145) |
| Verbal IQ | 99.4 ± 14.31 | (63; 147) |
| Performance IQ | 103.7 ± 14.71 | (58; 138) |
|  | n (%) |  |
| Gender | 97 females (22.0%) |  |
| Total number | 441 (32.4%) |  |
| *Preschoolers* | 22 (14.9%) |  |
| *Children in grade 1-2* | 114 (30.2%) |  |
| *Children in grade 3-4* | 137 (36.1%) |  |
| *Children in grade 5-6* | 86 (34.1%) |  |
| *Adolescents* | 82 (40.2%) |  |

**Table 3.1.** Characteristics of children and adolescents with CBCL-DP (*Dysregulation Score >* 195). Range of variation of age is reported in years and months (years:months). IQ: Intelligence Quotient; Max: Maximum observed value; min: Minimum observed value; n: Number of observations; SD: Standard Deviation.

## 3.4   The CBCL-DP in the clinical sample

Considering the whole clinical sample, data were available for 1360 participants (307 female, 22.6%) between two years and 17 years and 11 months. Six participants were excluded because of missing data in *Aggressive Behaviour Scale* (used to calculate the profile) [16].

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[16] Parts of **Section 3.4** and **Section 3.5** were modified by the paper in preparation by Negri, G.A.L., Nobile, M., Garzitto, M., Isola, M., Gregoraci, G.,

*Figure 3.1.* Age-relate differences in frequencies of children or adolescents with CBCL-DP. Percentages by age-group are shown.

As described above, the *Dysregulation Score* was calculated as the sum of T-scores of *Anxious/Depressed*, *Attention Problems* and *Aggressive Behaviour* scales (Biederman, J. *et al.,* 1995) and CBCL-DP was considered present if that sum was greater than 195, as this cut-off was proved to be the most efficient in order to detect major psychopathology [Diler, R.S. *et al.,* 2009]. **Table 3.1** reports the main characteristics of children and adolescents with CBCL-DP (data were shown as available).

Children and adolescents with CBCL-DP resulted older than those without it (U = 332262.5, p < 0.001). To describe distribution of CBCL-DP in different ages, age-groups were individuated: *preschoolers* (younger than five years and 11 months), children in *grades 1-2* (from six years to seven years and 11 months), *grades 3-4* (from eight years to nine years and 11 months), *grades 5-6* (from 10 years to 11 years and 11 months), and *adolescents* (from 12 years to 17 years and 11 months). The distribution of CBCL-DP appeared to be inhomogeneous by these age-groups ($\chi^2_4$ = 30.00, p < 0.001); as shown in **Figure 3.1** the profile was less frequently present in *preschoolers* (14.9% of the children), and it was quite similar in other age-groups, although increasing with age (from the 30.2% to the 40.2%).

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Bellina, M., Moretti, A., Fornasari, L., Bonivento, C., Piccin, S., Lestani, A., Fabbro, F., Soaresd, J.C., Molteni, M., & Brambilla, P.; *Cognitive Features of Children and Adolescents at Risk for Mental Disorders.*

Besides, no differences were observed in frequencies of children and adolescents with CBCL-DP between males and females ($\chi^2_1 = 0.13$, p = 0.724). Finally, participants with CBCL-DP were compared with those without it for cognitive level. They resulted having lower scores in *Total*, *Verbal* and *Performance* cognitive level (T-IQ, V-IQ, and P-IQ, respectively), but differences were statistically significant only for V-IQ ($t_{1194} = 2.40$, p = 0.017).

## 3.5    Neuropsychological characteristics associated with CBCL-DP

The whole *Developmental Neuropsychological Assessment* battery (NEPSY) was administered to a sub-sample of 102 children and adolescents with CBCL-DP.

| | n | Gender n (females) | Age Mean ± SD | (min; Max) | IQ Mean ± SD | (min; Max) |
|---|---|---|---|---|---|---|
| CBCL-DP | 102 | 23 | 9.4 ± 1.85 | (5:8; 14:7) | 103.0 ± 14.20 | (76; 141) |
| No CBCL-DP | 128 | 23 | 9.1 ± 1.89 | (5:9; 15:10) | 101.3 ± 14.19 | (73; 139) |

*Table 3.2.* Age, gender and cognitive level of a group of children and adolescents with CBCL-DP and a comparison group without CBCL-DP. Range of variation of age is reported in years and months (years:months). IQ: *Intelligence Quotient*; Max: Maximum observed value; min: Minimum observed value; n: Number of observations; SD: Standard Deviation.

As reported above, statistically significant differences were observed between groups with or without the CBCL-DP both in age and in cognitive level in the whole clinical sample, so a comparison sub-sample of 128 children and adolescents was selected and assessed. Anyway, data were also collected for total intelligence quotient, gender and age at evaluation for each subject. Data are presented by groups in *Table 3.2*.

The procedure was approved by the *Scientific Institutional Review Board* of *Scientific Institute IRCCS "Eugenio Medea"*.

### 3.5.1    Statistical analyses

Means and standard deviations, possibly with range of variation, were used to describe continuous variables, while frequencies and percentages were adopted for categorical variables. For descriptive purposes, a performance in a test of the NEPSY was considered as poor if it was under the 10th percentile of normative data (i.e., test scaled score $<$ 6).

In preliminary analyses, normal distribution of continuous variables was tested using the *Shapiro-Wilk test* and parametric analyses were performed only for normally distributed variables. In particular, the scores of cognitive level and differences in age at evaluation were compared between groups using *t–test* or *Mann-Whitney test*, as appropriated. On the other hand, gender proportions were compared by *$\chi^2$-test* (since all the observed and expected frequencies were higher than five). In these analyses a standard value of α was used to establish statistical significance (p $<$ 0.05).

Neuropsychological scores were tested as predictors of the presence of emotional dysregulation. *Univariate logistic regression analysis* was used to estimate the association between the neuropsychological tests and presence of dysregulation, as indicated by the presence of the CBCL-DP. The dichotomic dependent variable was coded assigning *"1"* to participants in the group with CBCL-DP and *"0"* for those in group without it. Then, a *multivariate stepwise analysis* was performed including all variables significant at p $\leq$ 0.15 [Hosmer, D.W., Jovanovic, B. & Lemeshow, S., 1989]. A *backward procedure* was adopted, setting a significance level of 0.05 for removing variables from the model.

All analyses were performed using *SPSS for Windows, version 15.0* [SPSS Inc., 2006].

### 3.5.2    Results

The two selected groups were comparable for age at evaluation (U = 5769.5, p = 0.130), gender ($\chi^2_1$ = 0.74, p = 0.388) and cognitive level ($t_{228}$ = 0.86, p = 0.390).

*Table 3.3* reports the results of univariate regression. It could be noted that only two tests survived the threshold (p $\leq$ 0.15). They both resulted statistically

significant in the multivariate stepwise logistic regression. In particular, scores on *Imitation of Hand Positions* test were positive associated with the presence of dysregulation (OR 95% c.i.  = 0.99-1.20, p = 0.07), while scores on *Visuomotor Precision* test were negatively associated to it (OR 95% c.i.  = 0.83-0.99, p = 0.03).

| Domain | Test | OR | 95% c.i. | p |
|---|---|---|---|---|
| *Attention and* | *Tower* | 1.01 | 0.92-1.12 | 0.77 |
| *Executive* | *Auditory Attention* | 1.06 | 0.93-1.21 | 0.35 |
| *Functions* | *Visual Attention* | 0.99 | 0.90-1.08 | 0.76 |
| *Visuospatial* | *Design Copying* | 0.97 | 0.89-1.06 | 0.50 |
| *Functions* | *Arrows* | 0.94 | 0.86-1.03 | 0.18 |
| *Sensorimotor* | *Fingertip Tapping* | 0.96 | 0.87-1.05 | 0.38 |
| *Functions* | *Imitation of Hand Positions* | 1.09 | 0.99-1.20 | 0.07* |
| | *Visuomotor Precision* | 0.90 | 0.83-0.99 | 0.03* |
| *Memory and* | *Memory for Faces* | 0.99 | 0.91-1.08 | 0.78 |
| *Learning* | *Memory for Names* | 0.95 | 0.87-1.04 | 0.30 |
| | *Narrative Memory* | 1.06 | 0.97-1.16 | 0.18 |

*Table 3.3.* Results of the univariate logistic regression conducted on neuropsychological tests of the *Developmental Neuropsychological Assessment* battery. c.i.: Confidence interval, OR: Odd ratio. *: Significant results.

*Figure 3.2* shows between-group differences in performances on all the NEPSY tests, reporting standardised scores. Interestingly, participants showed relatively few poor performances on NEPSY tests, exceeding the 10% only in the *Sensorimotor Functions* domain: Fingertip Tapping (15.2%), *Imitation of Hand Positions* (13.9%), and Visuomotor Precision (13.0%). Group with CBCL-DP showed more poor performances than group without it on all NEPSY tests, with the exception of: *Imitation of Hand Positions* (respectively, 9.8% VS 17.2%), *Narrative Memory* (5.9% VS 9.4%), and *Tower* (with no poor performances in CBCL-DP group and one in the other). Finally, between-group differences were not statistically significant for scores on NEPSY domain: *Attention and Executive Functions* ($t_{228}$ = 0.15,  p = 0.882), *Sensorimotor Functions* ($t_{228}$ = 0.86,

p = 0.389), *Visuospatial Functions* ($t_{228}$ = 0.88, p = 0.378), and *Memory and Learning* ($t_{228}$ = 0.21, p = 0.834).
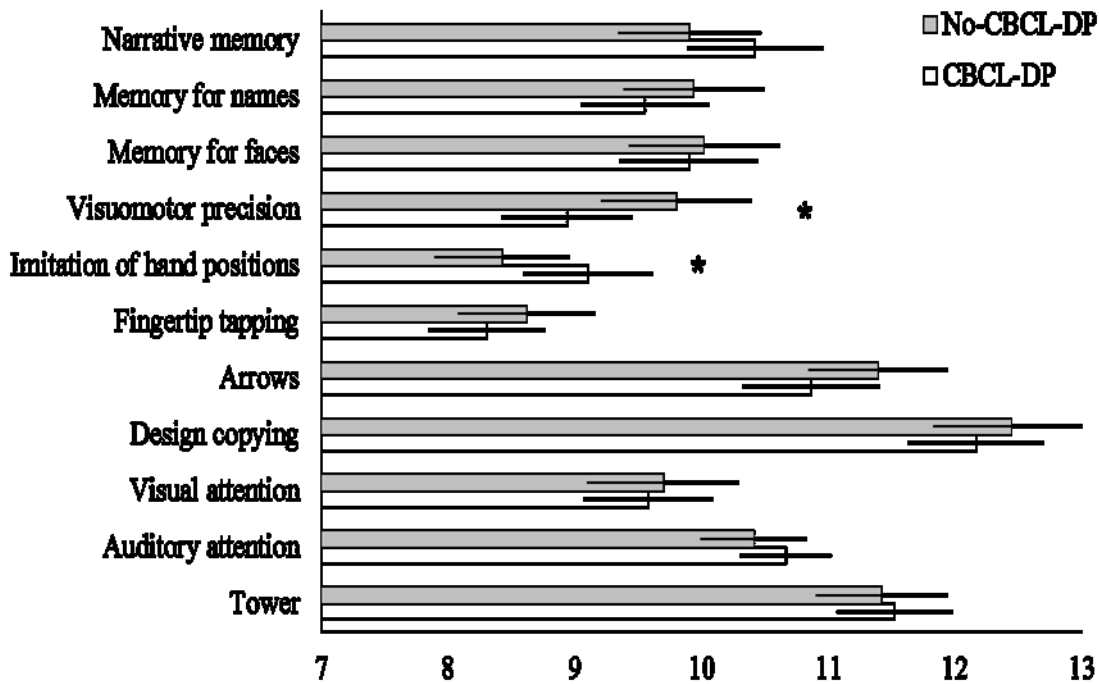


***Figure 3.2.*** Performances of group with CBCL-DP and without it in neuropsychological tests of the *Developmental Neuropsychological Assessment* battery. Scores were standardised with mean = 10 and standard deviation = 3. Horizontal bars denote 95% confidence interval of the mean. *: Significant results in multivariate stepwise logistic regression.

## 3.6  The CBCL-ASDP in the clinical sample

The *Autistic Spectrum Disorder Score* was available for 1207 children and adolescents of the clinical sample (of which 273 females, 22.6%). The scales used to calculate the profile are available only in school-age forms of the CBCL, so participants were between six years and 17 years and four months [17].

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[17] Parts of **Section 3.6** and **Section 3.7** were modified by the paper in preparation by Garzitto, M., Nobile, M., Fornasari, L., Moretti, A., Lestani, A., Molteni, M., Fabbro, F., and Brambilla, P.; *Reduced Mnesic Skills in Children and Adolescents With Behavioural-Emotional Problems and Autistic-Like Traits*.

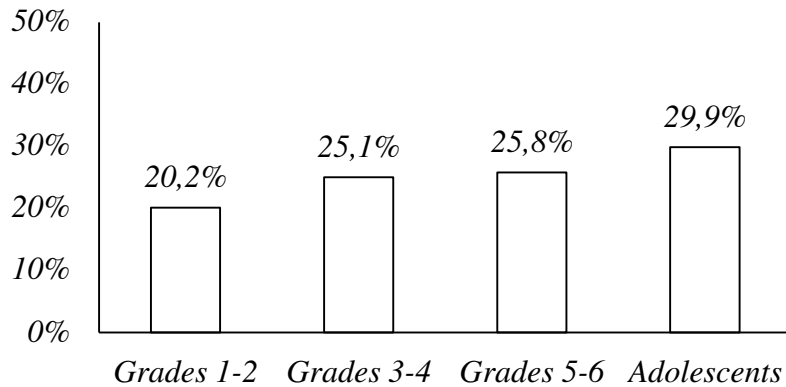|  | Mean ± SD | (min; Max) |
|---|---|---|
| Age | 9.7 ± 2.24 | (6:0; 16:6) |
| Total IQ | 103.2 ± 14.68 | (71; 145) |
| Verbal IQ | 101.1 ± 14.65 | (63; 145) |
| Performance IQ | 104.6 ± 15.34 | (58; 147) |
|  | n (%) |  |
| Gender | 65 females (22.0%) |  |
| Total number | 296 (24.5%) |  |
| *Children in grade 1-2* | 75 (20.2%) |  |
| *Children in grade 3-4* | 95 (25.1%) |  |
| *Children in grade 5-6* | 65 (25.8%) |  |
| *Adolescents* | 61 (29.9%) |  |

**Table 3.4.** Characteristics of children and adolescents with CBCL-ASDP (*Autistic spectrum disorder score* > 194). Range of variation of age is reported in years and months (years:months). Max: Maximum observed value; min: Minimum observed value; n: number of observations; SD: Standard Deviation.

**Table 3.4** reports characteristics of 296 participants with the CBCL-ASDP. They were identified since they had a *Autistic Spectrum Disorder Score* score over 194. The CBCL-ASD score was calculated as the sum of T-scores of *Withdrawn/Depressed*, *Social Problems* and *Thought Problems* scales.

It was interesting to note that participants with CBCL-ASDP were older than participants without it ($t_{1205} = 2.27$, p = 0.023). However, as shown also in **Figure 3.3**, the distribution of CBCL-ASDP by age-groups could be considered homogeneous ($\chi^2_3 = 7.29$, p = 0.063).

Similarly, no gender-related differences were statistically significant ($\chi^2_1 = 0.97$, p = 0.755), nor differences were observed in the *Total* ($t_{1095} = 0.47$, p = 0.637), *Verbal* ($t_{1088} = 0.31$, p = 0.757), or *Performance* ($t_{1082} = 0.17$, p = 0.863) cognitive level between the groups with or without CBCL-ASDP.

***Figure 3.3.*** Age-relate differences in frequencies of children or adolescents with CBCL-ASDP. Percentages by age-group are shown.

## 3.7  Neuropsychological characteristics associated with CBCL-ASDP

From the whole sample of 1207 children and adolescents with a CBCL-ASD score (both with a without a CBCL-ASDP), 297 participants were selected and their neuropsychological features were assessed with the NEPSY battery. One of them was maintained in the final sample although she had only total scores on the four domains (without component test scores) and she was excluded from some analyses. Other two remained in the sample without scores on tests of *Sensorimotor Functions* Domain (i.e., *Fingertip Tapping*, *Imitating of Hand Positions*, *Visuomotor Precision*), but they entered into the general analyses performed. Finally, six participants were excluded because they showed standardised scores below the normative cut-off on sub-scales of the *Wechsler Intelligence scale*. In particular, two participants were excluded because they showed a low V-IQ (67 and 69) and four because of a low P-IQ (58, 62, 66, and 69). The examined sample consisted of 291 children and adolescents (of which 58 females, 19.9%), between six years and seven months and 14 years and four months, without cognitive deficits.

The procedure was approved by the *Scientific Institutional Review Board* of *Scientific Institute IRCCS "Eugenio Medea"*.

### 3.7.1     Statistical analyses

Statistical analyses were performed using *SPSS for Windows, version 15.0* [SPSS Inc., 2006].

Normative *clinical* or *sub-clinical* cut-off for T-scores on CBCL were used to show frequencies of significant behavioural-emotional problems in the sample. A performance in a test of the NEPSY under the $10^{th}$ percentile of normative data (i.e., test scaled score < 6) was considered as poor, as well as a domain score positioned two or more Standard Deviations under the normative sample mean (i.e., standard score $\leq$ 70).

Groups were distinguished using the CBCL-ASD score with the cut-off of 195 proposed by Biederman and colleagues [Biederman, J. *et al.,* 2010] to identify children or adolescents with a CBCL-ASDP.

Categorical variables were described with frequencies and percentages, using *Fisher's exact test* to control homogeneity of distribution in groups (since some expected frequencies were under five, and there were no differences with the results of a $\chi^2$-*test* for remaining ones).

Continuous variables were summarized reporting means, standard deviations and ranges of variation. Assumption of homoskedasticity was checked by *Levene's test*, using parametric analyses only if there were no statistically significant violations. Direct between-group differences were analysed with *t-test. One-way univariate analyses of covariance* were performed to evaluate between-group differences, using gender, age at evaluation and verbal cognitive level as covariates. Significance level and *effect sizes* ($\eta^2$) were presented for statistically significant group-factor effects.

A conventional significance level was adopted throughout the analyses ($\alpha$ = 0.05). In multiple independent comparisons the significance level was corrected with *Bonferroni's method* (p < 0.0127, for four independent comparisons; p < 0.0170, for three independent comparisons).

*Pairwise deletion* was adopted to manage missing data.

### 3.7.2    Results

The CBCL-ASD score was calculated for the selected participants. According to this result, 72 participants present a CBCL-ASDP (score ≥ 195), unlike the others 219 without it.
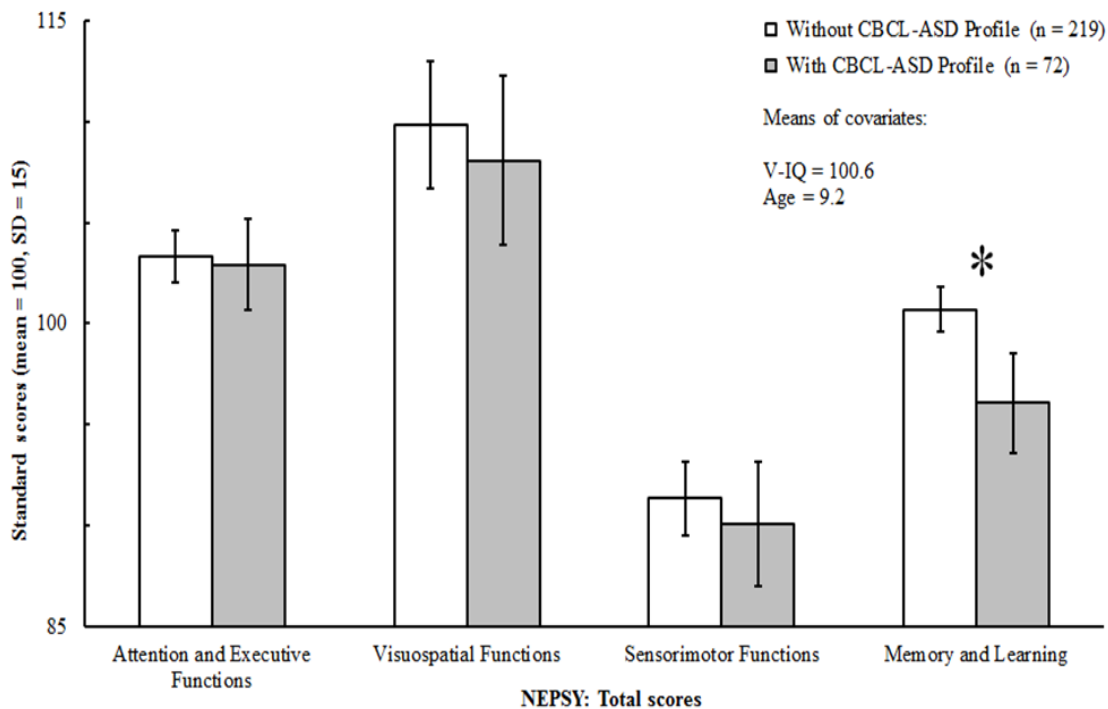


***Figure 3.4.*** Results from one-way between-groups analyses of covariance performed on total scores in the four *Developmental Neuropsychological Assessment* domains. The mean values of covariates are reported, too. ASD: *Autism Spectrum Disorder*; CBCL: *Child Behaviour Check-List*; n: Number of available observations; NEPSY: *Developmental Neuropsychological Assessment*; SD: Standard Deviation; V-IQ: *Verbal Intelligence Quotient*. *: $p < 0.05$, after correction for four multiple comparisons.

The results indicate that there were no statistically significant differences between groups in gender distribution (females: 16.7% VS 21.0%; $p = 0.498$, Fisher's exact test), average age at evaluation (9.3 ± 1.92 VS 9.1 ± 1.80; $t_{289} = 0.76$, $p = 0.446$), T-IQ (103.9 ± 13.80 VS 100.8 ± 14.73; $t_{289} = 1.58$, $p = 0.116$), and P-IQ (103.3 ± 15.26 VS 102.2 ± 15.22; $t_{289} = 0.53$, $p = 0.596$). On the other hand, the group with CBCL-ASDP had a higher V-IQ (103.6 ± 13.49

VS 99.6 $\pm$ 15.06; $t_{289}$ = 2.00, p = 0.047) than the group without it. For this reason, *Verbal* score was used as covariate in the following analyses.

| | No ASDP | (n = 219) | ASDP | (n = 72) | | |
|---|---|---|---|---|---|---|
| | Mean $\pm$ SD | (min; Max) | Mean $\pm$ SD | (min;Max) | Statistics | p |
| Gender | Females = 46 | (21.0%) | Females = 12 | (16.7%) | [1] | 0.498 |
| Age [2] | 9.1 $\pm$ 1.8 | (6:8; 14:3) | 9.3 $\pm$ 1.92 | (6:7; 14:0) | $t_{289}$ = 0.76 | 0.446 |
| FS-IQ | 100.8 $\pm$ 14.73 | (75; 151) | 103.9 $\pm$ 13.8 | (76; 139) | $t_{289}$ = 1.58 | 0.116 |
| V-IQ | 99.6 $\pm$ 15.06 | (73; 151) | 103.6 $\pm$ 13.49 | (71; 145) | $t_{289}$ = 2.00 | 0.047* |
| P-IQ | 102.2 $\pm$ 15.22 | (72; 148) | 103.3 $\pm$ 15.26 | (71; 138) | $t_{289}$ = 0.53 | 0.596 |
| ASD | 173.8 $\pm$ 12.07 | (150; 194) | 209.7 $\pm$ 10.84 | (195; 243) | - | - |
| A&EF [3] | 103.1 $\pm$ 12.78 | (63; 150) | 103.6 $\pm$ 13.63 | (74;131) | $F_{1,286}$ = 0.02 | 0.904 |
| VF [3] | 109.6 $\pm$ 13.86 | (68; 136) | 109.0 $\pm$ 14.42 | (73; 136) | $F_{1,286}$ = 0.67 | 0.413 |
| SF [3] | 91.1 $\pm$ 14.90 | (57; 124) | 90.8 $\pm$ 15.32 | (57; 136) | $F_{1,286}$ = 0.33 | 0.567 |
| M&L [3] | 100.5 $\pm$ 14.06 | (59; 138) | 96.7 $\pm$ 13.55 | (63; 129) | $F_{1,286}$ = 6.34 | 0.012* |

*Table 3.5.* Description of groups with and without the CBCL-ASDP: The main characteristics and scores on the four *Developmental Neuropsychological Assessment* domains and results from between-group statistical analyses are reported. A&EF: *Attention and Executive Functions* domain; ASD: *Autistic Spectrum Disorder Score*; FS-: *Full-scale*; IQ: *Intellingence Quotient*; Max: Maximum observed value; M&L: *Memory and Learning*; min: Minimum observed value; n: Number of available observations; NEPSY: *Developmental Neuropsychological Assessment*; P-: *Performance*; SD: Standard Deviation; SF: *Sensorimotor Functions*; V-: *Verbal*; VF: *Visuospatial Functions*. [1]: Result of two-tailed Fisher's exact test is reported; [2]: Minimum and maximum values are expressed in years and months (y:m); [3]: Group-related results of analyses of covariance are reported. *: p < 0.05, possibly after correction for four multiple comparisons.

The group-factor results of the four analyses of covariance performed on the NEPSY domains total scores are showed in **Figure 3.4**, together with covariate means. Participants with CBCL-ASDP showed lower performance than the group without it on the *Memory and Learning* domain (96.7 $\pm$ 13.55 VS 100.5 $\pm$ 14.06;

$F_{1,286} = 6.34$, p = 0.012, $\eta^2 = 0.02$). No statistically significant group effects were observed for the other three domains: *Attention and Executive Functions* ($F_{1,286} = 0.02$, p = 0.904), *Sensorimotor Functions* ($F_{1,286} = 0.33$, p = 0.567), and *Visuospatial Functions* ($F_{1,286} = 0.67$, p = 0.313). Group descriptive data and results from between-group comparisons are reported in ***Table 3.5***.

V-IQ covariate had statistically significant effects on all domains (*Attention and Executive Functions*: $F_{1,286} = 11.63$, p < 0.001; *Sensorimotor Functions*: $F_{1,286} = 12.41$, p < 0.001; *Visuospatial Functions*: $F_{1,286} = 11.22$, p < 0.001; *Memory and Learning*: $F_{1,286} = 14.61$, p < 0.001). On the other hand, no age- or gender-related statistically significant effects were observed.

|  | No ASDP | ASDP | Total |
|---|---|---|---|
| *Attention and Executive Functions* | 1 (0.5%) | - | 1 (0.3%) |
| *Visuospatial Functions* | 4 (1.8%) | - | 4 (1.4%) |
| *Sensorimotor Functions* | 22 (10.0%) | 5 (6.9%) | 27 (9.3%) |
| *Memory and Learning* | 3 (1.4%) | 2 (2.8%) | 5 (1.7%) |
| *Arrows* | 6 (2.8%) | 3 (4.2%) | 9 (3.1%) |
| *Auditory Attention* | 3 (1.4%) | 4 (5.6%) | 7 (2.4%) |
| *Design Copying* | 5 (2.3%) | 3 (4.2%) | 8 (2.8%) |
| *Fingertip Tapping* | 38 (17.5%) | 8 (11.3%) | 46 (16.0%) |
| *Imitation Hand Positions* | 30 (13.8%) | 9 (12.7%) | 39 (13.5%) |
| *Memory for Faces* | 13 (6.0%) | 5 (6.9%) | 18 (6.2%) |
| *Memory for Names* | 13 (6.0%) | 7 (9.7%) | 20 (6.9%) |
| *Narrative Memory* | 20 (9.2%) | 5 (6.9%) | 25 (8.6%) |
| *Tower* | 1 (0.5%) | - | 1 (0.3%) |
| *Visual Attention* | 19 (8.7%) | 8 (11.1%) | 27 (9.3%) |
| *Visuomotor Precision* | 29 (13.3%) | 13 (18.1%) | 42 (14.5%) |

***Table 3.6.*** Frequencies and percentages of participants with and without the CBCL-ASDP, showing poor performances on the NEPSY (i.e., under the 10th percentile of normative data for test scores, and under two standard deviation from the normative mean for domain scores). n: Number of available observations.

Three similar analyses of covariance were performed on scores of those tests that form the *Memory and Learning* domain. No group-factor effect survives to correction for multiple comparisons: *Memory for Faces* (9.4 ± 2.80 VS 10.1 ± 3.08; $F_{1,285} = 3.43$, p = 0.065), *Memory for Names* (9.1 ± 2.79 VS 9.8 ± 2.89; $F_{1,285} = 4.58$, p = 0.033), and *Narrative Memory* (9.8 ± 2.80 VS

$10.1 \pm 3.04$; $F_{1,285} = 1.42$, $p = 0.235$). Statistically significant V-IQ effects are observed on *Memory for Names* ($F_{1,285} = 9.82$, $p = 0.002$) and *Narrative Memory* tests ($F_{1,285} = 14.63$, $p < 0.001$), while age at evaluation and gender have no statistically significant effects.

For descriptive purposes, frequencies and percentages of participants with poor performances on the NEPSY are reported in **Table 3.6**. No statistically significant difference is observed on between-group comparisons ($p > 0.05$ with Fisher's exact tests).

## 3.8  Conclusion

The reported results do not show severe neuropsychological difficulties on the NEPSY tests and total domain scores in participants with behavioural-emotional problems and normal intellectual functioning (**Table 3.6**), but it was reported that specific neuropsychological patterns could characterise children and adolescents with definite profiles of difficulties also in comparison with other participants with similar behavioural-emotional problems but without the same profile.

In particular, children and adolescents with probable emotional dysregulation (as suggested by the presence of a CBCL-DP) were compared to a clinical group of children with similar origin and diagnoses, age at evaluation, gender, and cognitive level. Performances in two tests of motility resulted predictive of the presence of emotional dysregulation: higher scores in *Imitating of Hand Positions* test were associated to an increased probability to present a CBCL-DP, as well as a low score in the *Visuomotor Precision* test.

It can be expected to observe an association between CBCL-DP and alterations of specific brain structures, possibly limbic and medial frontal, since children with severe emotional dysregulation showed increased activation of anterior cingulate and medial frontal cortex in response to negative feedbacks [Rich, B.A. *et al.,* 2011]. This is coherent with reported difficulties in the *Visuomotor Precision* test, also because motor impairments showed to be associated with *Anxiety* [Grisham, J.R. *et al.,* 2009] and *Mood Disorders* [Sasayama, D. *et al.,* 2012]. Besides, it is interesting to point out that an imitation ability resulted to be preserved in evaluated children and adolescents with CBCL-DP. This could indicate that

emotional regulation was partially independent by the mirror neuron system represented, in particular in parietal cortical regions [Iacoboni, M. & Mazziotta, J.C., 2007].

In a different way, children and adolescents with a CBCL-ASDP showed a reduced score on the NEPSY *Memory and Learning* domain if compared with a group with behavioural-emotional problems, but without that profile. In this case, neuropsychological performances were conditioned by intellectual functioning, in particular verbal, and age at the evaluation, but the mnesic difficulties survived also if controlled for this variables. It is important to note that children and adolescents with ASDs, but without intellectual disabilities, usually showed poor performances on neuropsychological tasks, partially independently by their intellectual functioning level [Hooper, S.R. *et al.,* 2006]. Autistic-like traits were also reported to be possibly associated with difficulties in *Executive Functions* [Warren, Z.E. *et al.,* 2012], although this association is not clear [Maes, J.H.R. *et al.,* 2012]. These traits could also be associated to linguistic difficulties [Dworzynski, K. *et al.,* 2007] and problem-solving strategies [Fugard, A.J.B., Stewart, M.E. & Stenning, K., 2011].

Hovever, there were no indications of specific difficulties with mnesic abilities of children with autistic-like traits. Nevertheless, future investigations should clarify whether the reduced mnesic skills observed are consistently associated with autistic-like traits or more directly linked with the behavioural-emotional problems that defined the CBCL-ASDP. Possibly, the CBCL-ASDP represent a marker of reduced social competencies and should have an impact on social adaptation. It will be important to understand whether early cognitive difficulties, as the non-specific menesic problems reported, could be associated longitudinally to a different outcome as problems in socialization, since autistic-like traits are significantly associated with following anxious and depressive problems [Hallett, V. *et al.,* 2009, 2010, 2012].

**4**

<span style="color:gray">Longitudinal re-assessment</span>

## 4.1 Introduction

In the *developmental psychopathology* perspective, the psychopathological continuity should be investigated longitudinally and explained as far as possible individuating causal links between disorders [Rutter, M. & Sroufe, A.L., 2000]. Mental disorders in adulthood are often in continuity with those arisen in adolescence and those links remained significant, although less strong [Dingle, K. *et al.,* 2010], even considering the disorders of childhood with more than a decade long follow-up [Hofstra, M.B., Der Ende, J. & Verhulst, F.C., 2000]. This continuity is evident for specific disorders, such as *Mood Disorders* [Van Lang, N.D.J., Ferdinand, R.F. & Verhulst, F.C., 2007]. Furthermore, the continuity was confirmed also between childhood and adolescence [Pihlakoski, L. *et al.,* 2006] and during adolescence itself [Nestadt, G. *et al.,* 2010]. However, there are examples of less defined situations, in which the access to the diagnostic services has probably an important role [Baiano, M. *et al.,* 2009]. Furthermore, the definition of mental disorder that will be adopted in the next version of the *Diagnostic and Statistical Manual of Mental Disorders* of the *American Psychiatric Association* [18] will not

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[18] See: **'www.dsm5.org'**.

include the presence of risk of clinical consequences to better distinguish the risk factors from diseases itself [Stein, D.J. *et al.*, 2010]. In this re-definition process a greater relevance will be given to the prognostic value of the diagnosis, hence, for example, the choice to include the *Attenuated Psychosis Syndrome* among the *Other Psychotic Disorders*, rather than adopting a new category [De Koning, M.B. *et al.*, 2009; Moran, M., 2009] primarily based on future risk (i.e. *Psychosis Risk Syndrome*).

Clearly, the developmental psychopathology must also take account of social [Shaw, D.S. *et al.,* 1997], behavioural [Chaiton, M.O. *et al.,* 2009] and genetic factors  [Weissman, M.M. *et al.,* 2005] that may increase or the risk of such a continuity. At the same time, it should try to find possible interventions or protective factors associated to reduce such risk [Cheng, S. *et al.,* 2007].

The *Child Behaviour Check-List* (CBCL) is an assessment tool especially suitable for longitudinal studies in childhood and adolescence [Visser, J.H. *et al.,* 2003]. In the next paragraphs, some data longitudinally collected with CBCL for school-age (CBCL 6-18) will be reported: data relating to the dimensional-assessed psychopathology continuity from childhood to adolescence .

## 4.2  Participants

Children and adolescents from the whole clinical sample previously described were re-contacted to propose a new assessment with purposes of research. It was interesting to longitudinally observe the evolution of the disorders which had motivated contact with neuropsychiatric services at the first assessment.

For 570 children and adolescents (corresponding to the 41.7% of the whole sample, described in ***Chapter 2***), there is information about the results of contacting them back. These data were collected at the local centers of Conegliano, Pasian di Prato, and San Vito al Tagliamento. The 24.4% of those contacted agreed to proposed re-evaluation, while the 64.4% of them did not accept. The remaining families were untraceable (8.3%). Preliminary analyses were conducted to evaluate the effect of rejection and rejection-rate on collected data. Children and young people who have not joined the re-evaluation were found to have a statistically significant reduction of cognitive level with respect to the others (101.9 VS 106.0;

$t_{457}$ = 2.56, p = 0.011), specifically of the score of the performance intelligence quotient (102.7 VS 107.1; $t_{450}$ = 2.65, p = 0.008). This finding was important for the following analysis, but it will have to be taken into account especially in evaluating the generalizability of the longitudinal results obtained.

## 4.3    Statistical analyses

Normative *clinical* or *sub-clinical* cut-off for T-scores on CBCL were used to show frequencies of significant behavioural-emotional problems in the sample. In particular, for *Total* scales (i.e. *Total Problems*, *Internalizing Problems*, and *Externalizing Problems* scales) a T-score above 60 (*sub-clinical* cut-off) was considered to indicate the presence of a behavioural-emotional problem.

Categorical variables were described with frequencies and percentages, using $\chi^2$-*test* to control homogeneity of distribution in groups (since all the expected frequencies were over five). In some analyses, two groups were distinguished, based on the time that had passed between the two assesments of participant. Specifically, these group were separated using the median of the sample (five years and 10 months), so to obtain two groups of equal numerosity: one re-evaluated after a maximum of five years and 11 months, the other after more than six years from the first assessment.

Continuous variables were summarized reporting means, standard deviations and ranges of variation. Assumption of homoskedasticity was checked by *Levene's test*, using parametric analyses only if there weren't statistically significant violations. Whithin group differences were tested using *t-test for repeated measures*. Direct between-group differences were analysed with *t-test* if comparison was between two groups, while *one-way univariate analysis of variance* was performed to evaluate differences among three or more groups. *Mann-Whitney test* was used in place of t-test as non-parametric alternative. In evaluation of predictive significance of selected covariates, *multivariate logistic regression* was performed using *backward stepwise method* with *likelihood ratio* selection of variables. *Pearson's correlations* were also calculated and reported only if comfirmed as statistically significant by non-parametric *Spearman's rank correlations*.

Data were analysed when available for preliminary presentation of groups. On the contrary, *listwise deletion* was adopted to manage missing data in multivariate logistic regressions.

A conventional significance level was adopted throughout the analyses ($\alpha = 0.05$). In stepwise backward method, a probability of 0.05 was chosen to entry variables in the model, while a probability of 0.10 was used to remove them.

Statistical analyses were performed using *SPSS for Windows, version 15.0* [SPSS Inc., 2006].

| N = 218 (23.4% of females) | Mean ± SD | (min; Max) |
|---|---|---|
| Age at the first assessment | 9.6 ± 2.52 | (4:2; 15:7) |
| Age at the second assessment | 15.2 ± 2.34 | (10:0; 19:6) |
| Time between first and second assessment | 5.5 ± 1.64 | (0:11; 8:6) |
| *Total* IQ at the first assessment * | 104.3 ± 15.09 | (73; 145) |
| *Verbal* IQ at the first assessment * | 101.2 ± 15.25 | (58; 144) |
| *Performance* IQ at the first assessment * | 106.7 ± 14.78 | (71; 148) |
| Estimated IQ at the second assessment * | 103.9 ± 12.71 | (72; 135) |

*Table 4.1.* Demographic and cognitive main characteristics of the longitudinally re-evaluate sample. Range of variation of age is reported in years and months (years:months). IQ: *Intellectual Quotient*; Max: Maximum observed value; min: Minimum observed value; N: Number of observations; SD: Standard Deviation. *: Number of observation is reduced due to missing data.

## 4.4    Main characteristics of the re-assessed sample

The longitudinally evaluated sample was composed by 218 children and adolescents, 23.4% of which were females. Participants were between 10 years and 19 years and six month (with a mean age of 15.2 ± 2.24 years). Their first assessment took place 5.5 ± 1.64 years ago on average, when they were between four years and two months and 15 years and seven month (with an average age of 9.7 ± 2.52 years). Approximately half of the sample was re-evaluated within six years after the first assessment (*1-to-5 years* group: 113 participants, 51.8%;), while the other half after more than six years later (*6-to-8 years* group: 105 participant, 58.2%; 30.5% of females). The *1-to-5 years* group was composed of fewer females than the *6-to-8 years* one (16.8% VS 30.5%; $\chi_1 = 5.67$, p = 0.017)

and the average age at the recent assessment was obviously lower (14.8 ± 2.36 VS 15.5 ± 2.05; U = 4919.0, p = 0.029), while age at the previous assessment was higher (10.6 ± 2.39 VS 8.6 ± 2.21; $t_{216}$ = 6.60, p < 0.001).

Demographic and cognitive data of the sample at the first and second evalutation are reported in *Table 4.1*. It was be note that no statistically significant difference was present between the assessed *Total Intelligent Quotient* (IQ) at the first assessment and the estimated IQ at the second (respectively: 105.0 ± 15.32 VS 103.7 ± 12.9; $t_{175}$ = 1.33, p = 0.185), Furthermore, correlation between cognitive levels was moderate and statistically significant (r = +0.588, p < 0.001).

| Scale | Normal n (%) | Sub-clinical n (%) | Clinical n (%) |
|---|---|---|---|
| *Total Problems* | 140 (59.8%) | 47 (20.1%) | 47 (20.1%) |
| *Internalizing Problems* | 144 (61.5%) | 32 (13.7%) | 58 (24.8%) |
| *Externalizing Problems* | 179 (76.5%) | 34 (14.5%) | 21 (9.0%) |
| *Anxious/Depressed* | 178 (76.1%) | 31 (13.2%) | 25 (10.7%) |
| *Withdrawn/Depressed* | 183 (78.2%) | 27 (11.5%) | 24 (10.3%) |
| *Somatic Complaints* | 201 (85.9%) | 14 (6.0%) | 19 (8.1%) |
| *Social Problems* | 183 (78.2%) | 30 (12.8%) | 21 (9.0%) |
| *Thought Problems* | 206 (88.0%) | 17 (7.3%) | 11 (4.7%) |
| *Attention Problems* | 174 (74.4%) | 35 (15.0%) | 25 (10.7%) |
| *Rule-Breaking Behaviour* | 215 (91.9%) | 15 (6.4%) | 4 (1.7%) |
| *Aggressive Behaviour* | 212 (90.6%) | 11 (4.7%) | 11 (4.7%) |

**Table 4.2.** Number and percentage of participants longitudinally re-evaluated above *clinical* or *sub-clinical* cut-off for each *Total* or *Syndromic* scale of *Child Behaviour Check-List* questionnaire is reported. n: Number of observations.

## 4.5   Dimensional psychopathology in the re-assessed sample

*Table 4.2* reports frequencies and percentages of behavioural-emotional problems reported by parents of the participants in the empirical-derived (*Total* and *Syndromic*) scales of the CBCL 6-18. It shows children and adolescents falling above the *sub-clinical* or *clinical* cut-off in every scale. It could be note that the

score at the *Total Problems* scale reports the maximum frequency of problems (40.2%, summing *sub-clinical* and *clinical* elevations), while externalized difficulties are less represented in the sample (as it was in the whole clinical sample from which the current was extracted). **Figure 4.1** shows the same data, it is interesting to note that expected frequency of problems is of the 2% of normal population for *clinical* threshold and of the 7% for the *sub-clinical* one. The sample re-evaluated showed a substantially greater number of problems than expected in all the examined scales.
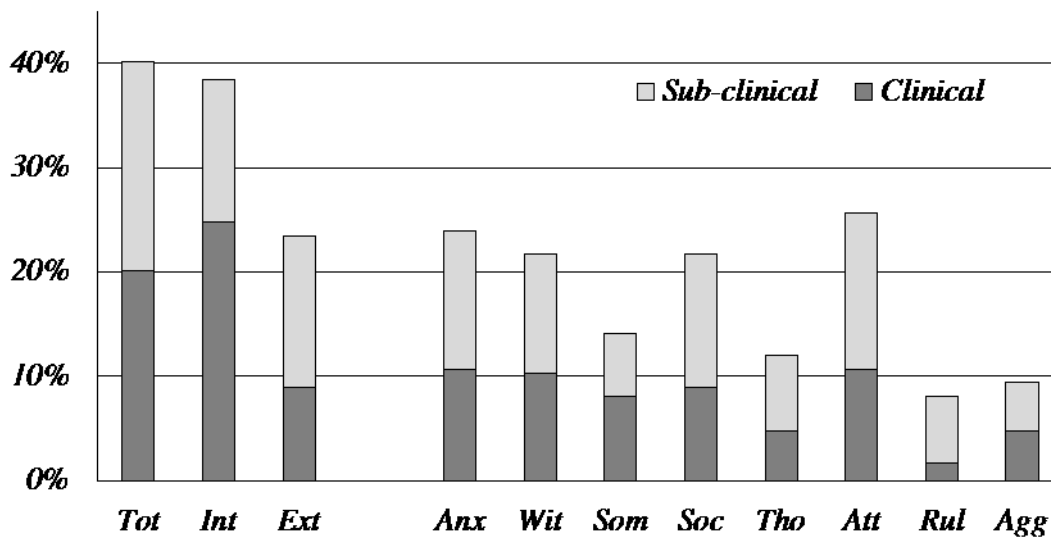


**Figure 4.1.** Percentages of participants longitudinally re-evaluated above *clinical* or *sub-clinical* cut-off for each *Total* or *Syndromic* scale of *Child Behaviour Check-List* questionnaire are reported. Agg: *Aggressive Behaviour* scale; Anx: *Anxious/Depressed* scale; Att: *Attention Problems* scale; Ext: *Externalizing Problems* scale; Int: *Internalizing Problems* scale; Rul: *Rule-Breaking Behaviour* scale; Soc: *Social Problems* scale; Som: *Somatic complaints* scale; Tho: *Thought Problems* scale; Tot: *Total Problems* scale; Wit: *Withdrawn/Depressed* scale.

As shown, the *Total* scales showed problems more frequently than *Syndromic* scales, especially on the *Total Problems* and on the *Internalizing Problems* scale. Therefore, the following analyses focused on the three *Total* scales. Furthermore, *clinical* and *sub-clinical* problems were considered together to identify children and adolescents with behavioural-emotional problems.

First, there were no statistically significant differences in the number of gender-related problems. This is true in *Total Problems* scale ($\chi^2_1 = 1.24$, p = 0.266), as

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for internalized ($\chi^2_1$ = 3.09, p = 0.079) or externalized ($\chi^2_1$ = 1.13, p = 0.287) problems. Similarly, even if females showed more elevated scores on the *Total* and *Internalizing* problems scales, the was not observed statistically significant difference ($t_{216}$ = 0.97, p = 0.334; U = 3726.5, p = 0.177), as well as for externalized problems: more elevated in males but still not statistically significant ($t_{216}$ = 0.14, p = 0.890).

Age at the previous assessment was not corralate with *Total* scales scores, as well as no statistically significant correlation was present with the actual age. The time between the first and the second assessment showed a trend towards a weak negative correlation with the score of externalization (r = –0.15, p = 0.029), but it was not comfirmed with not-parametric method ($r_s$ = –0.12, p = 0.080). As confirmation of these results, the *1-to-5* and the *6-to-8* years groups did not differ in respect of total ($t_{216}$ = 1.28, p = 0.201), internalized ($t_{216}$ = 0.91, p = 0.367), nor externalized ($t_{216}$ = 1.74, p = 0.083) scores.

## 4.6   Longitudinal previsions

As discussed in **Chapter 2**, pre-school children assessed with the CBCL 1½-5 showed lower scores than the participants evaluated with the school-age forms of the CBCL. For this reason, the analyses presented below were conducted only on the participants who were assessed with a CBCL school-age form at the first assessment. Consequently, 15 children were excluded: 14 from the *6-to-8 years* group and one from the *1-to-5 years* group.

**Table 4.3** reports scores from CBCL questionnaire at the first and at the second assessment for *Total* and *Syndromic* scales. Within-group t-test results are reported, too. It is interesting to note that, there has been a substantial statistically significant improvement on all the scales. This improvement is modest in some scales (e.g. *Somatic Complaints* or *Rule-Breaking Behaviour* scales), but it is about half a standard deviation on other scales (e.g. *Total Problems* scale).

**Figure 4.2** shows the correlation between the *Total Problems* scale score at the first assessment and at the second one. There was a clear reduction of the scores, as reported in **Table 4.4**. However, the two scores were moderate positive correlate (r = +0.53, p < 0.001). It is also important to note that, as reported in the figure,

the correlation is weaker for the *6-to-8 years* group (r = +0.46) than for the *1-to-5 years* one (r = +0.58). This was a expected because of the longer time passed, but the two correlation did not differ in a statistically significant way (p = 0.126). This can be considered an indication of continuity of behavioural-emotional problems assessed and of stability of the chosen measure.

| Scale | 1st assessment Mean ± SD | 2nd assessment Mean ± SD | Pre-post Difference | t-test P |
|---|---|---|---|---|
| *Total problems* | 62.0 ± 8.20 | 56.3 ± 9.41 | 5.7 | < 0.001* |
| *Internalizing Problems* | 61.2 ± 9.45 | 57.3 ± 9.54 | 3.9 | < 0.001* |
| *Externalizing Problems* | 58.1 ± 9.11 | 53.1 ± 9.48 | 5.0 | < 0.001* |
| *Anxious/Depressed* | 62.1 ± 8.54 | 58.7 ± 8.34 | 3.3 | < 0.001* |
| *Withdrawn/Depressed* | 61.0 ± 9.50 | 58.6 ± 8.07 | 2.4 | < 0.001* |
| *Somatic Complaints* | 58.2 ± 7.45 | 56.8 ± 7.15 | 1.5 | = 0.006* |
| *Social Problems* | 60.9 ± 7.21 | 57.7 ± 7.91 | 3.1 | < 0.001* |
| *Thought Problems* | 59.2 ± 7.93 | 55.8 ± 6.69 | 3.5 | < 0.001* |
| *Attention Problems* | 64.7 ± 9.11 | 60.5 ± 9.08 | 4.2 | < 0.001* |
| *Rule-Breaking Behaviour* | 56.7 ± 6.57 | 55.1 ± 6.17 | 1.6 | = 0.001* |
| *Aggressive Behaviour* | 59.8 ± 7.97 | 56.0 ± 7.15 | 3.8 | < 0.001* |

**Table 4.3.** Scores from *Child Behaviour Check-List* questionnaire at the first and at the second assessment are reported, *Total* and *Syndromic* scales are considered. Within-group t-test results are reported, too. n: Number of available observation; SD: Standard Deviation. *: Statistically significant difference (p < 0.05).

A series of logistic regression analysis were conducted in order to find among information collected at the first assessment predictors of the problems present in current one. Scores on *Total* scales of CBCL were used to identify children and adolescents with behavioural-emotional problems, as their score were above *sub-clinical* cut-offs.

Gender (as categorical variable, with females coded as *"1"* and males as *"0"*), age at the first evaluation, *Total* IQ measured at the first evaluation and

membership in *1-to-5 years* (coded as *"1"*) or *6-to-8 years* (coded as *"0"*) group were entered in the analyses presented below. In first set of analyses, also *Total* scales scores assigned by parents at the first assessment were entered (significant results are reported in **Table 4.4**). On the other hand, **Table 4.5** shows other analyses, in which *Syndromic* scales scores at the first evaluation were used.

### 4.6.1    Predictors of problems in the *Total Problems* scale

The model obtained with *Total* scales as predictors was completed in six steps, with the correct classification of the 71.3% of the participants. Specifically, it classified correctly the 79.8% of children and adolescents without problems in the *Total Problems* scale and 59.5% of those who have problems. The cognitive level and the *Total Problems* scale score were manteined in the final model as predictors, but only the last resulted a statistically significant predictor of problems of interest.

The analysis with all the *Syndromic* scales produced a model in nine steps (with 70.4% of correct classification, but up to 42.7% of missing). In this case, cognitive level resulted a statistically significant predictor (negative associated with problems), together with the *Somatic Complaints*, *Social Problems*, and *Aggressive Behaviour* scales.

### 4.6.2    Predictors of problems in the *Intenalizing Problems* scale

The model with *Total* scales as predictor was obtained in six steps, with the 68.0% of correct classifications (82.5% for those without and 42.2% for those with problems). Interestingly, gender resulted to be associated with the presence of internalized problems (with more risk for females). Score on *Internalizing Problems* scale was also a statistically significant predictor.

Looking at the *Syndromic* scales analyses, the model was completed in nine steps (72.6% of correct classifications, 85.1% and with 50.8%). Both *Anxious/Depressed* and *Social Problems* scales resuted statistically significant longitudinal predictors.

### 4.6.3    Predictors of problems in the *Externalizing Problems* scale

There were relatively few children and adolescents with externalized difficuities, so the final model classified correctly the 93.9% of those without and the 36.2% of

those with problems (78.7% overall). The *Externalizing Problems* scale resulted a predictor, but also the *Total Problems* scale and the age at the first evalutation (participants who came later to the attention of services resulted to have an increased risk).

The other model had similar performances (91.7% and 42.6% of correct classification of participants without or with problems, respectively). The *Aggressive Behaviour* scales was the stronger predictor of externalized problems, with *Social Problems* scale, too. Interestingly, children and adolescents with higher scores at the *Withdrawn/Depressed* scale had less probabilities to show behavioural problems.

## 4.7  Conclusion

In the previous paraghraps, data of a new observation of children and adolescents previously referred to neuropsychiatric services were reported. Results about psychopathological continuity were also shown. Finally, some data collected between 11 months and eight years and six months after the first assessment have proved that they can predict behavioural-emotional problems actually reported by parents.

The results reported are consistent and expected, given the available literature on developmental psychopathology. The stability from childhood to adolescence of behaviour-emotional problems is confirmed by these observations, but in addition there have been some interesting points.

First, a striking effect wasn't found of the time between the two assessments. Even distinguishing between two groups evaluated in clearly different times, they were rather homogeneous. The amount of time from the first assessment was not associated to the current problems frequency, which was unexpected, also considering that almost all the participants had completed clinical interventions.

Secondly, against the expectations, an increased risk of internalizing problems have been reported for the female gender without the expected increase in risk for males. This was probably due to the increase of the mean age of sample [Hayward, C. & Sanborn, K., 2002], but it was not completely explained, since there were relatively

more females in the *6-to-8 years* group for which the psychopathological continuity is lower (although at a non-statistically significant level).
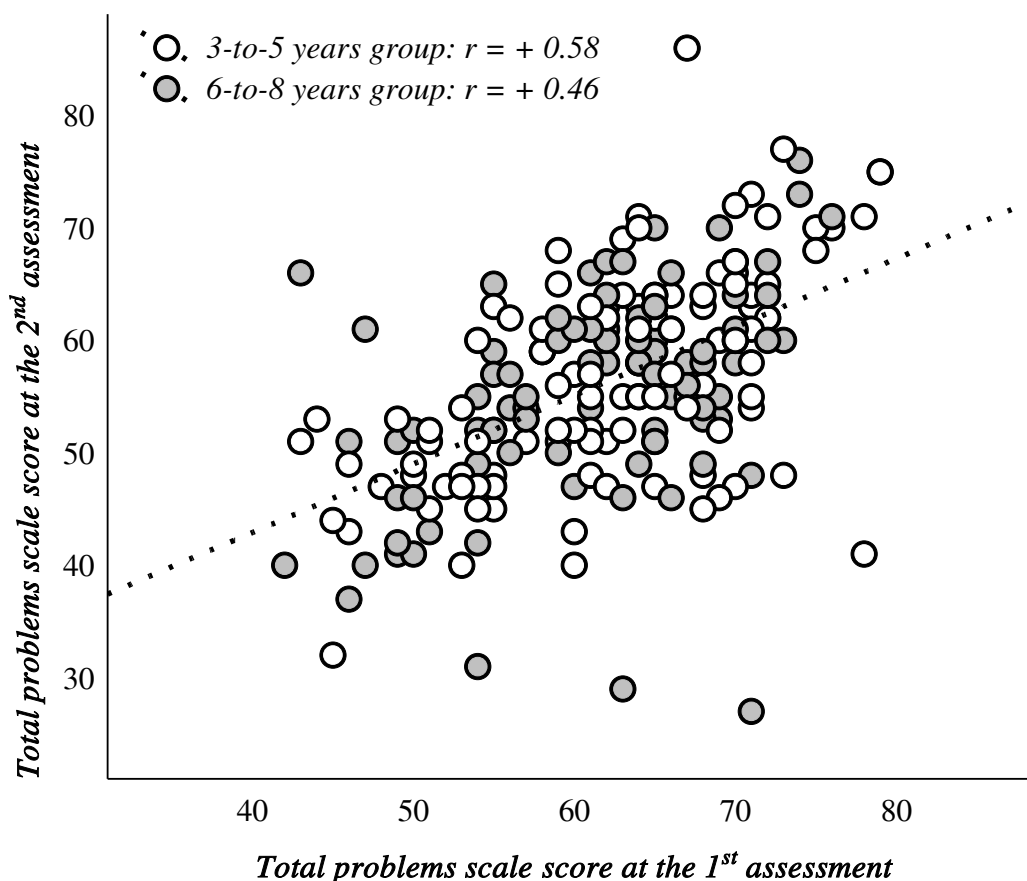


**Figure 4.2.** Scatterplot of correlation between scores on *Total Problems* scale of the *Child Behaviour Check-List* obtained at the first assessment and at the second one. Participants assessed after more than six years later are emphasized. Separated correlation are reported for this group and the other, while the dashed line shows the longitudinal correlation for the entire sample. *1-to-5 years* group: Group re-assessed between 11 months and five years and 11 months from the first assessment; *6-to-8 years* group: Group re-assessed between six years and eight years and six months from the first assessment.

Finally, it was really interesting that the *Social Problems* scale resulted a statistically significant predictor of all types of problems examined. Especially, this is surprising because the scale was not included in the calculation of either the *Internalizing Problems* nor the *Externalizing Problems* scales, but predicts problems on both. On the one hand, it is a scale that evaluates problems of adaptation to social environments that may of course have different origins. On the

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other hand, items that compose this scale are quite heterogeneous (from the language problems to the clumsiness, to jealousy) and they thus may be considered non-specific markers of difficulties. However, this point needs further analysis.

| Predictors 1st assessment | Problems, 2nd assessment | | | | | |
|---|---|---|---|---|---|---|
| | Total | | Internalizing | | Externalizing | |
| | OR (95% c.i.) | p | OR (95% c.i.) | p | OR (95% c.i.) | P |
| *Gender (Female = 1)* | - | | 2.05 (0.911; 4.61) | 0.08 | - | |
| *Age* | - | | - | | 1.16 (0.97; 1.38) | 0.09 |
| *Total IQ* | 0.98 (0.95; 1.00) | 0.04 | - | | - | |
| *Total Problems* | 1.16 (1.10; 1.22) | < 0.01 | - | | 1.09 (1.01; 1.19) | 0.03 |
| *Internalizing Problems* | - | | 1.12 (1.07; 1.17) | < 0.01 | - | |
| *Externalizing Problems* | - | | - | | 1.10 (1.03; 1.19) | 0.01 |

***Table 4.4.*** Results of the univariate logistic regressions conducted on predictors longitudinally associated with *sub-clinical* or *clinical* problems at the *Total* scales of the *Child Behaviour Check-List*. Odd ratio are reported with their 95% confidence intervals and corresponding significance level only for predictors maintained in the final model after multivariate logistic analyses with stepwise backward method. Also time since the first assessment were evaluated as predictors (as categorical variable), but it is not shown because it was not maintained in any final model. c.i.: Confidence interval; IQ: *Intelligent Quotient*; OR: Odd ratio.

| | Problems, 2nd assessment | | | | | |
|---|---|---|---|---|---|---|
| *Predictors* | Total | | Internalizing | | Externalizing | |
| *1st assessment* | OR | p | OR | p | OR | p |
| *Age* | - | | - | | 1.18 | 0.08 |
| *Total IQ* | 0.97 | 0.02 | 0.98 | 0.07 | - | |
| *Anxious/ Depressed* | - | | 1.06 | 0.02 | - | |
| *Withdrawn/ Depressed* | - | | - | | 0.95 | 0.04 |
| *Somatic Complaints* | 1.07 | 0.02 | 1.04 | 0.10 | - | |
| *Social Problems* | 1.11 | < 0.01 | 1.08 | 0.01 | 1.09 | 0.02 |
| *Thought Problems* | - | | - | | - | |
| *Attention Problems* | - | | - | | - | |
| *Rule-Breaking Behaviour* | - | | - | | - | |
| *Aggressive Behaviour* | 1.07 | 0.01 | - | | 1.18 | < 0.01 |

***Table 4.5.*** Results of the univariate logistic regressions conducted on predictors longitudinally associated with *sub-clinical* or *clinical* problems at the *Total* scales of the *Child Behaviour Check-List*. Odd ratio are reported with corresponding significance level only for predictors maintained in the final model after multivariate logistic analyses with stepwise backward method. Also gender and time since the first assessment were evaluated as predictors, but they are not shown because they were not maintained in any final model. c.i.: Confidence interval; IQ: *Intelligent Quotient*; OR: Odd ratio.

# 5

## Proneness to psychosis and mood disorders

### 5.1  Introduction

Individuals with *Psychotic Disorders* and those considered at *High Risk* of developing these disorders usually show similarities and similar abnormalities [Phillips, L.K. & Seidman, L.J., 2008]. In the case of *Schizophrenic Disorder*, people are considered at-risk if they have a familiar history of the disease, if they shows schizotypal characteristics or prodromal symptoms could be detected. The so-called *Ultra High Risk* approach [Yung, A.R. *et al.,* 2006] has emerged as a method of investigation, and it consists in identifying the presence of attenuated positive symptoms, signs of apparent functional decline, symptoms that cause infrequent adaptive problems [Yung, A.R. *et al.,* 2003; Yung, A.R., McGorry, P.D. *et al.,* 2004; Yung, A.R., Phillips, L.J *et al.,* 2004]. Seeking help is often increased by such symptoms. Many researches on people at high risk have been implemented, mainly with a longitudinal methodology: the *New York High-Risk Project* [Erlenmeyer-Kimling, L. *et al.,* 1991], the *Copenhagen Project* [Cannon, T.D. & Mednick, S.A., 2007], the *Israeli High-Risk Study* [Mirsky, A.F., 1995]. The *UCLA High-Risk Project* was partially similar but more oriented to behaviours observable during adolescence than to adulthood [Goldstein, M.J., 1987]. However,

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these studies have always had to overcome really significant methodological difficulties [Erlenmeyer-Kimling, L. & Cornblatt, B., 1987].

Another perspective is to identify people at risk for developing psychosis or other major psychiatric disorders for the presence of under-threshold traits. This view is in line with the dimensional vision, in which tendencies toward psychiatric disorders are considered distributed in normal population. This perspective is shared by researches on profiles derived from the *Minnesota Multiphasic Personality Inventory* [Peterson, D.R., 1954; Gilberstadt, H. & Duker, J., 1960; Fine, H.K., 1973; Steronko, R.J. & Woods, D.J., 1978] but also the proposal of questionnaires for personality as the *Eysenck Psychoticism Scale* [Eysenck, S.B.G., Eysenck, H.J. & Barrett, P., 1985; Eysenck, H.J., 1992] or of specific rating scales for the risk, as the *Schizophrenism Scale* [Nielsen, T.C. & Petersen, K.E., 1976]. The *Chapman Psychosis Proneness Scales* are to be seen in this research perspective [Chapman, L.J. *et al.,* 1978, 1980; Eckblad, M. & Chapman, L.J., 1983, 1986; Chapman, L.J. & Chapman, J.P., 1987].

These two perspectives can be partially merged through the use of a longitudinal methodology on populations at risk and the measure of personality traits associated with the risk itself.

Longitudinal epidemiological studies designed to observe the progress of psychopathology in the context of normal development may also be important for prevention [Carter, A.S., Briggs-Gowan, M.J. & Davis, N.O., 2004], although it is not clear the actual possibility of preventing the onset of major psychiatric disorders. However, it appear possible to try to postpone the onset of disorders, alerting the medical or psychological services and promoting social support [Yung, A.R. *et al.,* 2007]. Even the possibility of early psychopharmacological intervention seems to lead to better effects of the treatments [Perkinns, D.O. *et al.,* 2005]. The aim of prevention remains the reduction of the disorders incidence and morbidity, through the promotion of protective factors and the reduction of the effects of those of risk. Among the protective factors, many proposals have been made about what is possible to promote: ability to deal with stress and with conflicts, problem-solving skills, adaptability, sociability, proper self-esteem, early cognitive stimulation, management of emotions, support to the parental function,

promotion of appropriate attachment styles [Luthar, S. & Cicchetti, D., 2000; Cicchetti, D. & Toth, S.L., 2009].

## 5.2  Participants

Children and adolescents from the whole clinical sample previously described (**Chapter 2**) were re-contacted to propose a new assessment with purposes of research. Among these, three of the *Chapman Psychosis Proneness Scales* were administered to 141 participants. In particular, children and adolescents were assessed with the *Hypomanic Personality Scale*, the *Magical Ideation Scale* and the *Perceptual Aberration Scale*. Four participants (2.8%) have completed only two scales of the three proposed.

All the participants were also assessed with the school-age form of the *Child Behaviour Check-List* (CBCL).

## 5.3  Statistical analyses

Normative *clinical* and *sub-clinical* cut-off for T-scores on CBCL were used to identify significant behavioural-emotional problems in the sample.

Continuous variables were summarized reporting means, standard deviations and ranges of variation. Assumption of homoscedasticity was checked by *Levene's test*, using parametric analyses only if there were no statistically significant violations. Direct between-group differences were analysed with *t-test* and *Mann-Whitney test* were used in place of t-test as non-parametric alternative. In evaluation of predictive significance of selected covariates, *multivariate logistic regressions* were performed using *backward stepwise method* with *likelihood ratio selection* of variables. *Pearson's correlations* were also calculated and reported only if confirmed as statistically significant by non-parametric *Spearman's rank correlations*.

*Pairwise deletion* was adopted to manage missing data, also in multivariate logistic regressions.

A conventional significance level was adopted throughout the analyses (α = 0.05). In stepwise backward method, a probability of 0.05 was chosen for entry variables in the model, while a probability of 0.10 was used for their removal.

Statistical analyses were performed using *SPSS for Windows, version 15.0* [SPSS Inc., 2006].

| Scales | | n | Mean ± SD | (min; Max) |
|---|---|---|---|---|
| *Hypomanic Personality* | (48 item) | 141 | 18.4 ± 7.76 | (3; 37) |
| *Magical Ideation* | (30 item) | 137 | 6.7 ± 4.54 | (0; 24) |
| *Perceptual Aberration* | (35 item) | 140 | 4.08 ± 4.41 | (0; 24) |

**Table 5.1.** *Hypomanic Personality*, *Magical Ideation*, and *Perceptual Aberration* scales in the whole examined sample. Max: Maximum observed value; min: Minimum observed value; n: Number of observations; SD: Standard Deviation.

## 5.4  Results

The sample was composed by 141 children and adolescents, 24.8% of which were females. Participants were between 10 years and four months and 19 years and five months (with a mean age of 15.2 ± 2.15 years). Their first assessment took place 5.6 ± 1.66 years ago on average. The estimated intelligent quotient of the participants was between 75 and 135 (105.1 ± 12.60).

**Table 5.1** reports scores at the used *Chapman Psychosis Proneness Scales* of the whole sample.

No gender-related differences were observed for the *Hypomanic Personality* ($t_{139}$ = 0.31, p = 0.761), the *Magical Ideation* (U = 1752.0, p = 0.870), nor the *Perceptual Aberration* ($t_{138}$ = −1.08, p = 0.284) scales. Furthermore, none of the three scales was found to correlate with age at the evaluation or with the estimated cognitive level (obtained as the mean of performances in two tests of *Wechsler Intelligence Scales*: *Vocabulary* and *Block Design*).

Three logistic regression analysis were conducted in order assess whether the selected *Chapman Scales* could be predictors of behavioural-emotional problems reported in *Total Problems*, *Internalizing Problems* and *Externalizing Problems* scales of the CBCL. **Table 5.2** shows statistically significant results. It should be

noted that, gender, age at the evaluation and estimate cognitive level were also entered in the analyses, but they were not found significant predictors.

The three models had really a modest capacity to correctly categorize individuals with problems: 31.9% for children and adolescents with total problems, 17.4% for those with internalized difficulties, and 8.7% for those with externalized ones.

The *Magical Ideation Scale* wasn't maintained in any final model, while other scales were retained in all models. Specifically, the *Hypomanic Personality Scale* demonstrated to be a statistically significant predictor of externalized problems, while the *Perceptual Aberration Scale* was associated to both total and internalized problems.

| | Problems | | | | | |
|---|---|---|---|---|---|---|
| | Total | | Internalizing | | Externalizing | |
| *Chapman Scales* | OR (95% c.i.) | p | OR (95% c.i.) | p | OR (95% c.i.) | p |
| *Hypomanic Personality* | 1.05 (1.00; 1.11) | 0.06 | 0.95 (0.91; 1.00) | 0.07 | 1.11 (1.04; 1.21) | < 0.01 |
| *Magical Ideation* | - | | - | | - | |
| *Perceptual Aberration* | 1.11 (1.02; 1.22) | 0.02 | 1.11 (1.01; 1.21) | 0.03 | 1.10 (1.00; 1.21) | 0.06 |

**Table 5.2.** Results of the univariate logistic regressions conducted on the three used *Chapman Psychosis Proneness Scales* as predictors for *sub-clinical* or *clinical* problems at the *Total* scales of the *Child Behaviour Check-List*. Odd ratio are reported with their 95% confidence intervals and corresponding significance level only for predictors maintained in the final model after multivariate logistic analyses with stepwise backward method. Gender, age at the evaluation and estimate cognitive level were also entered in the model, but they are not shown because not maintained in any final model. c.i.: Confidence interval; OR: Odd ratio.

## 5.5  Conclusion

Three scales for the assessment of proneness to psychosis and to *Bipolar Disorder* showed to be associated with behavioural-emotional problems in a selected sample of children and adolescents. It should be pointed that the

administered scales were originally designed for young adults. Normative data for Italy are not available, as well as for children and adolescents. Currently, these data are in an advanced state of adaptation on Italian community samples. For this reason, it was actually impossible to distinguish between participants classifiable as *at-risk* and participants *not-at-risk*. However, the observed associations with behavioural-emotional problems were weak, but statistically significant for two of these scales.

In particular, the *Hypomanic Personality Scale* appeared to be associated with externalization, while the *Perceptual Aberration Scale* was a predictor of internalized disorders.

The results could be expected, given the characteristics of the instruments adopted, but this association was not observed in children or adolescents, although indirectly there were indications of association between etero-assessed anxious/depressive tendencies and behavioural problems [Schmidt, N.B. *et al.,* 2007]. Moreover, the frequency of sub-threshold psychotic symptoms in children and adolescents is significant [Kelleher, I. *et al.,* 2012], so that it is important to understand how these conditions are associated with behavioural-emotional problems.

These questionnaires were designed specifically to assess the risk of future severe psychological problems, so it is important to consider their relation with assessment tools through which it was possible to demonstrate the existence of a continuity of psychopathology from childhood, to adolescence, to adulthood. Furthermore, it will be useful to conduct similar observations on larger samples of children and adolescents in order to understand the preliminary data presented above. Particularly, it will be necessary to extend these findings performing comparisons between groups with high and low levels of proneness to major psychiatric diseases.

The thesis was intended to provide empirical data about the assessment of psychopathology in children and adolescents from the *developmental psychopathology* perspective. In particular, reported data were collected both with a cross-sectional methodology and with a longitudinal one. Psychopathology was assessed mainly through instruments oriented to a *dimensional/quantitative approach.*

A sample of 1366 children and adolescents clinically referred to neuropsychiatric services for behavioural-emotional problems was selected and described, showing higher frequency of dimensional-assessed problems than in normal population. Internalization difficulties and socialization problems resulted to continuously increment with age (in a cross-sectional observation), while externalization ones didn't prove to be associated with age of the participants, but partially with gender. It was also reported that the cognitive level of the participants affected the presence of attention and, partly, thought problems.

Then, neuropsychological characteristics of children and adolescents from the presented clinical sample were analysed in their associations with specific profiles of behavioural-emotional problems. Participant with a *Dysregulation Profile* showed poorer performances in a motor control task than the comparison group, as well as better scores in a motor imitation test. Children and adolescents with an *Autistic Spectrum Disorder Profile*, instead, presented unexpected reduction of performances in administered mnesic tests with respect to the comparison group, controlling for cognitive characteristics of participants.

Then, a longitudinal observation was conducted on 218 children and adolescents from the clinical sample, between 11 months and eight years and six months after the first assessment. Behavioural-emotional problems resulted stables from

childhood to adolescents, with small effect of the amount of time passed between the two assessments. Problems in socialization at the first assessment showed to be associated to a wide range of difficulties, predicting behavioural-emotional problems at the second evaluation. Furthermore, female gender was related to more internalizing problems.

From a different perspective, personality scales were proposed to assess risk of severe psychopathology. One hundred and forty-one participants were assessed with these instruments, showing a probable link between proneness to *Bipolar Disorder* and externalization problems, as well as between internalization problems and pre-psychotic traits connected to perception, but not to ideation.

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Tesi di dottorato di Marco Garzitto, discussa presso l'Università degli Studi di Udine

# Subject index

Tesi di dottorato di Marco Garzitto, discussa presso l'Università degli Studi di Udine