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Preterm births and Psychopathology.

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Abstract

Aims: In our study we investigate how the parent's traumatic experience affects the development of the emotional regulation of the child, through the evaluation of parental reflexive functions.
Materials and Methods: In this study the sample was reduced to 90 subjects (ages 4 to 6 years). We investigated the behavioural functioning through the administration of CBCL scales and the evaluation of parental reflexive functions through the questionnaire RFQ 8.
Results: We found an inverse correlation between the sub-scale Certainty and internalizing disorders. We then found an inverse correlation between the Uncertainty sub-scale and the externalizing disturbances.
Conclusions: In this study we also demonstrated that parental reflexive functions had an implication in determining dysfunctional behaviour in children. Our analyses have shown that as parents become more certain about their mental states, internalizing behaviour of children decreases, while parents become more uncertain about their mental states, reduce the externalising behaviour of children.

Keywords: Preterm infants, Psychopathology, Externalizing disorders, Reflexive functions.

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Introduction

Premature birth is considered a risk factor for the development of the child: the preterm infant is in fact "at risk" both from the neurobiological and psychopathological point of view, due to prolonged hospital stay and separation from the mother, as well as the deriving difficulties. Preterm birth is defined primarily by a Gestational Age (GA) less than 37 weeks new-borns present difficulties especially from a physiological point of view, which result in serious damage, (including vascular damage), to the central nervous system [1,2]. Its causes may include individual behavioural and psychosocial factors, environmental exposures, medical conditions, infertility treatments, biological factors, and genetics. Many of these factors occur in combination, particularly in those who are socio-economically disadvantaged or who belong to ethnic and racial minority groups. Therefore, premature birth is characterized by the interaction of multiple variables and risk factors, both biological and socio-environmental, which impact on neuropsychological development. Despite the significant nosography difficulties in the field of neurodevelopment thanks to the numerous formalized and screening tools, recently studies that reveal how children born with VLBW (Very Low Birth Weight), are more likely to develop psychiatric disorders than children born on term [3,4]. The neurobiological, hormonal, social and psychological processes that affect an early delivery can be considered the reason why, during the development process, premature infants, would be more prone to certain psychiatric problems could be explained through, as matter of fact, many preterm parts can alter the typical development of the brain and physiological systems that participate in emotional and behavioural regulation [5]. Therefore, several studies have reported a significant association between very preterm birth and a series of psychiatric disorders such as depression, anxiety, schizophrenia, bipolar disorder, affective disorder [6-8]. During development, in school age, the symptoms of behavioural disorders gain more homogeneity, so much that it is possible to talk about a real "behavioural phenotype", that is a set of behaviours characterized by inattention, emotional, communicative and relational problems [9]. Behavioural disorders and socio-emotional difficulties at the age of five become significant predictors for psychiatric disorders at the age of seven and 11 years [10]. Finally, higher risks of internalising disorders diagnosis were observed at 1, 6 and 13 years old, becoming important markers for a diagnosis of anxiety disorder in adolescence [11-13]. It has been shown that the so-called VLBW (subjects born prematurely at 6 months) present greater difficulties in emotional regulation compared to a group of peers born at term [4]. Through the administration of questionnaires to parents such as the Infant Toddler Socio-Emotional Assessment-ITSEA and Child Behaviour Check List–CBCL, more significant rates were detected linked to disorders internalisation such as anxiety, depression, inhibition, separation and regulation problems (sleeping cycle, diet, altered sensory reactivity) in VLBW [14,15]. In particular, the parents (especially the mothers) described a traumatic experience referring to the preterm birth, but the information reported was rather general and implicit. In our study we investigate how the parents traumatic experience affects the development of the emotional regulation of the child, through the evaluation of parental reflexive functions and the behavioural aspects experienced by children through the administration of the CBCL Scales, in particular, the significant correlations between parental reflexive functions and behavioural alterations at the CBCL scales were sought [16,17].

Materials and Methods

Participants

In this study we considered a population of 150 preterm-born children, specifically those born between the 26th and the 30th week of gestation. All children born with infantile cerebral palsy, neurological deficits, and non-coding motor disorders or who had reported ischemic abnormalities to MRI were excluded from the sample. Therefore, the sample was reduced to 90 subjects (ages 4 to 6 years). The data were collected at the Pediatric Psychiatry clinic of FINDS (Fondazione Italiana Neuroscienze Disordini del Neurosviluppo) in collaboration with the TIN (Neonatal Intensive Care) and the Caserta Civil Hospital and whit the University of Salerno. We investigated the behavioural functioning through the administration of CBCL scales and the evaluation of parental reflexive functions through the questionnaire RFQ-8. Thus, to identify any defined psychopathological disorders, we performed the K-SADS-PL diagnosis-oriented test, whereas, for autistic spectrum disorder, ADOS and ADI-R tests were used, for ADHD, evaluation was performed with Conner's (Table 1).

Table 1: *Subdivision of sample.*

Total Sample
Mage 5.34 **SD** 0.21 **M/F** 59/31

Methods

Neuropsychological assessment included the administration of standardized tests such as: K-SADS-PL, RFQ (Reflective Functioning Questionnaire), CBCL (Child Behaviour Checklist) [17,18].

K-SADS-PL DSM 5: Diagnostic interview for the evaluation of psychopathological disorders (past and present) in children and adolescents according to the criteria of DSM-5. In particular, it allows detecting the presence of mood disorders, psychotic disorders, anxiety disorders, attention deficit and disruptive behaviour disorders, substance abuse.

RFQ: To assess the level of mentalization obtained through two sub-scales, which evaluate certainty (RFQ_C) and uncertainty (RFQ_U) on the mental states of oneself and others. The highest subscale score indicates two distinct RF disorders, respectively, hypomentalization and hypermentalization. Hypomentalization reflects concrete thinking and poor understanding of mental states of oneself and others, while hypermentalization describes the attitude to identifying with overly certain and detailed patterns and states of mind unsupported by evidence.

CBCL: Structured questionnaire around 8 syndromic scales: Anxiety/depression, retirement/depression, somatic complaints, social disorders, thought disorders, attention disorders, rule transgression behaviour, aggressive behaviour, grouped into two other general dimensions *i.e*, internalising and externalising disorders. Moreover, the questionnaire allows evaluating the behaviour through six scales that are based on the diagnostic criteria of DSM 5.

DSM 5: Affective disorders, anxiety disorders, somatic disorders, attention and hyperactivity disorders, oppositional-provocative disorders and behavioural disorders. Behavioural scales are an essential element in the evaluation and diagnosis of children with emotional and behavioural problems as they enable information to be collected from people who have spent months or years with the child.

Further study for the diagnosis of autism spectrum provided for the evaluation of ADOS and ADI-R, while for ADHD the evaluation of Conners. The ADI-R follows the structure of an interview protocol and five algorithms, usable at various ages for diagnosis or intervention. The ADOS test is a standardized and semi-structured assessment of communication, social interaction, play and imaginative use of materials for individuals with autism spectrum disorders. The Conners investigate psychopathological or problematic behaviours of children and adolescents, with a focus on ADHD and a broad spectrum assessment of disorders and/or difficulties that can occur in comorbidities, such as: conduct, learning, anxiety problems, depression, family and social issues.

Results

Data analysis was carried out using the SPSS 26.0 (2019) statistical survey software. Significance was accepted at the 1% level ($\alpha<0.01$). From the analysis of the subjects who did not present nosografically defined diagnoses, it was possible to correlate and identify the correlation of internalizing scale and whether there was a correlation with the externalizing. The correlation is a relationship between two variables such that each value of the first corresponds to a value of the second, following a certain regularity. The correlation can be defined direct (or positive) when the variation of an element affects, directly, and the other, or indirect (also inverse or negative) namely, to the variation of an element corresponds, in the opposite sense, to the other. The degree of correlation between two variables is expressed by the correlation index; the value assumed is between-1 (inverse correlation) and 1 (direct and absolute correlation), with an index equal to 0 resulting in the absence of correlation. In this case, the Pearson correlation index is calculated as the ratio between the covariance of the two variables and the product of their standard deviations.

The correlation does not depend on a cause-effect relationship but on the tendency of one variable to change as a function of another. In this study we performed a Correlation analysis to investigate whether the reflective parental functions may influence the behavioural aspects of their children. From our analysis it emerged that 17 subjects out of 90 included in the total sample, were affected by disorders externalizing (18.8%) of these, 5 subjects were diagnosed with Autistic Spectrum Disorder (5.5%), and 9 were diagnosed with ADHD (Inattentive Deficit and Hyperactivity) (10%), 3 subjects instead had undefined externalizing disorders (Figure 1). We therefore excluded 14 subjects from the Correlation analysis because they had a Neurodevelopment Disorders (Neurobiological Disorder) (Figure 2). Specifically, we found an inverse (or negative) correlation between the sub-scale Certainty and internalizing disorders ($r=-0.86$; $p<0.01$). This data indicates that as the confidence about the mental states of the parent's increases,

the internalizing behaviours of the children decrease. Certainty represents the ability of parents to understand their own and their child's mental states defined as hypermentalization.

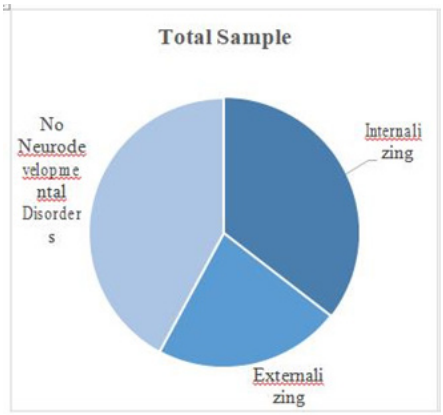

Figure 1: *Total sample.*

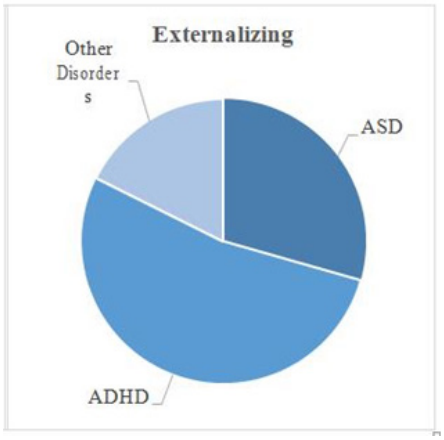

Figure 2: *Subject with externalizing disorders.*

A difficulty in mentalization skills therefore reflects the parents' inability to act as scaffolding for the child's anxieties and fears. We then found an inverse (or negative) correlation between the Uncertainty sub-scale and the externalizing disturbances ($r=-0.34$; $p<0.01$). This data indicates that as uncertainty about the mental state increases among parents, the externalizing behaviours of children decrease. A high level of uncertainty is called hypomentalization and reflects the tendency to carry out concrete reasoning and unable to grasp one's own and others' mental states (Table 2).

Table 2: *Correlation between RFQ and CBCL.*

RFQ_C			RFQ_U		
	r	*p*		*r*	*p*
CBCL_IN	0.86	.000*	CBCL_EX	0.34	.000*

Discussions

The amount of stress in the first days of life, isolation and the lack of early maternal contact are all risk factors for premature births according to Imafuku's study, aiming to investigate the gaze and attention of children born preterm; especially in children between 6 and 12 months, it was noted that the latter were much more attracted by geometric patterns, rather than by images of people, and also presented more difficulties when comparing the gaze-following behaviour with children born on term, consequently demonstrating how the different plan and evolutionary continuum between born on term and preterm births differs substantially especially in the first year of life. There is also clear evidence that extremely preterm-born children tend to have less accomplishments in tasks that assess attentive abilities and these children themselves are at greater risk of developing ADHD symptoms than peer's born-on-term.

Impairment is not limited to the ability to paying attention to stimuli selectively (selective attention), as performance was also lacking in tasks of sustained attention, coding, executive attention, and divided attention. Attention difficulties can also affect the modus operandi of other cognitive domains, the level of education and social functioning. Therefore, it is crucial that these children are monitored in early childhood [19]. In line with these aspects, there is a high percentage, about 23% of cases, of diagnosis of Attention Deficit and Hyperactivity Disorder (ADHD) in VLBW subjects, especially in the subtype "Inattentive", where there are more emotional issues, such as anxiety or mood disorders, shyness and isolation [20,21]. Moreover, this subtype of ADHD is often found in comorbidity with Learning Disorders and therefore perfectly in line with the problems expressed by VLBW and ELBW [22,23]. Despite practical difficulties, there are some longitudinal studies that investigate the pathogenesis in premature births: Treyvaud et al. analyse a sample of preterm born children, thus calling attention to problems and predictive indices in different age groups [24].

A cognitive profile characterized by externalizing symptoms at 2 years, is predictive of a diagnosis of ADHD by the age of 5 years; socio-emotional problems, however, predict relational difficulties in such age group. Specifically, internalizing behaviours describe a wide class of issues, associated with "internal" dynamics: anxiety, depression and isolation. The externalizing symptoms, on the other hand, mostly refer to the social, interactive, and relational dimensions: aggressive behaviour, impulsiveness, low tolerance to frustrations, reduced adaptability [25]. An interesting study by Rogers et al. highlighted that neonatal variability between the left amygdala and the prefrontal cortex, the posterior cingulate cortex, and the right anterior insula, caused more internalizing symptoms for 2 years old children [26]. Functional connectivity between the amygdala and these regions was found to be implicated in pathophysiology of anxiety disorders, affective states, and depression in older children and adults. These results have been extended to infants.

The regional specificity of the neonatal left amygdala with specific symptoms at 2 years is similar to the associations found in older populations, suggesting that such patterns in childhood are relevant for the subsequent development of psychopathology. Therefore the observation of the neonatal amygdala could predict the appearance of externalizing symptoms at the age of 2 years with regional specificity consistent with the known pathophysiology in older subjects: connectivity with the anterior insula, related to depressive symptoms, with the

anterior cingulate spine related to generalized anxiety, and with the medial prefrontal cortex related to behavioural inhibition. Therefore, the differences in the functional connectivity of the brain between prematurely born and born-on-term babies show that there is already a predisposition to symptomatic groups related to the social and emotional sphere from birth. Our analysis showed that out of the 90 subjects included in the total sample, 17 subjects had externalizing disorders (18.8%) of these 17, 5 subjects were diagnosed with Autism Spectrum Disorder (5.5%), 9 subjects were diagnosed ADHD (Attention Deficit and Hyperactivity Disorder) (10%). These data are in line with what has been expressed by the literature according to which, especially in school age, the increase in a symptomatology attributable to the Autism Spectrum is present in children born Extremely Preterm (EP) (born with GA less than 28 weeks), with evident communication deficits, stereotypies and relationship difficulties, with an incidence percentage that varies from 4% to 8% [27]. It is also hypothesized how structural and functional abnormalities at the brain level, can often predict the development of syndromes such as that of Autism, highlighting the need to identify bio-markers for Autism Spectrum Disorder, for a better diagnosis in very premature born children, due to the overlapping of other developmental disorders symptoms, which have deficient manifestations in the communicative and social area [28].

Further study conducted on a group of VLBW children about 1 year of age, evaluated with psychiatric examination based on the Diagnostic Classification 0-2 (zero to two, 2016), shows a higher incidence of psychiatric disorders than children in the control group: 13% of VLBW had received a diagnosis of Multisystemic Development Disorder (DMSS-Relationship and Communication Disorder), 4% for regulation disorders (emotional and behavioural difficulties in response to a sensory stimulus), 24.6% for emotional disorders [29,30]. In this study we also demonstrated that parental reflexive functions had an implication in determining dysfunctional behaviour in children. Our analyses have shown that as parents become more certain about their mental states, internalizing behaviour of children decreases, while parents become more uncertain about their mental states, reduce the externalising behaviour of children. This shows that parental reflexive functions are very important for functional development in the child. In fact, the Reflective Function (RF) is defined as that mental function that organizes our behaviour as well as other individuals. It is an evolutionary acquisition that allows the child to respond not only to the people behaviours but also to his conception of their feelings, beliefs, and expectations. By attributing mental states, the child gives meaning and prediction to people behaviours and will be capable to implement, in a flexible way, the most appropriate actions, such as to be able to respond adaptively to the various interpersonal exchanges. The latter, also as a result of the variety of self-representative models, built based on previous relational experiences [31-33]. Preterm-born children, compared to born-on-term peers, have a higher risk of developing behavioural problems therefore, with these children, it is necessary to enhance the parental reflective functions in order to allow a healthy development and the reduction of social problems of the child [34,35].

Future studies could include a larger sample and a follow-up evaluation to investigate how many people maintain the disorder, especially those who experience externalizing disorders at an early age and if these will represent a full-blown psychopathological disorder. Furthermore, mentalization skills could be deepened not only through the evaluation of the RFQ but also through the deepening of the parents' second-order TOM skills.

References

1. March of Dimes, PMNCH. Born too soon: The Global action report on preterm birth. Genova, World Health Organization. 2012.
2. Volpe JJ. Cognitive development in preterm infants. N Engl J Med. 1991;325(4): 276-78.
3. Ferrari F. Il neonato pretermine. Disordini dello sviluppo e interventi precoci, Franco Angeli, Milano. 2017:p 206.
4. Wolf MJ, Koldewijn K, Beelen A, et al. Neurobehavioral and developmental profile of very low birthweight preterm infants in early infancy. Acta Paediatr. 2002;91(8):930-8.
5. Dickerson F, Severance E, Yolken R. The microbiome, immunity, and schizophrenia and bipolar disorder. Brain Behav Immun. 2017;62:46-52.
6. Lund LK, Vik T, Skranes J, et al. Low birth weight and psychiatric morbidity; stability and change between adolescence and young adulthood. Early Hum Dev. 2012;88(8):623-629.
7. Nosarti C. A dimensional approach to assessing psychiatric risk in adults born very preterm. Psycho Med. 2018;48(10):1738-44.
8. D'Onofrio BM, Class QA, Rickert ME, et al. Preterm birth and mortality and morbidity: A population-based quasi-experimental study. JAMA Psychiatry. 2013;70(11):1231-40.
9. Johnson S, Marlow N. Preterm birth and childhood psychiatric disorders. Pediatr Res. 2011;69:22-28.
10. Treyvaud K, Doyle LW, Lee KJ, et al. Social-emotional difficulties in very preterm and term 2 year olds predict specific social-emotional problems at the age of 5 years. J Pediatr Psychol. 2012;37(7):779-785.
11. Braarud HC, Slinning K, Moe V, et al. Relation between social withdrawal symptoms in full-term and premature infants and depressive symtoms in mothers: a longitudinal study. Psychiatr Enfant. 2013;34(6):532-41.
12. Hall J, Wolke D. A comparison of prematurity and small for gestational age as risk factors for age 6-13 year emotional problems. Early Hum Dev. 2012;88(10):797-804.
13. Somhovd MJ, Hansen BM, Brok J, et al. Anxiety in adolescents born preterm or with very low birthweight: a meta-analysis of case-control studies. Dev Med Child Neurol. 2012;54(11):988-94.

14. Spittle AJ, Ferretti C, Anderson PJ, et al. Improving the outcome of infants born at <30 weeks' gestation - a randomized controlled trial of preventative care at home. 2009;9:73.

15. Stoelhorst G, Rijken M, van Zwieten P, et al. Developmental outcome at 18 and 24 months of age in very preterm children: A cohort study from 1996 to 1997, Early Hum Dev. 2003;72(2):83-95.

16. Fonagy P, Target M. Attaccamento e Funzione Riflessiva. Milano: Raffaello Cortina Editore. 2001.

17. Achenbach TM, Rescorla LA. Manual for the ASEBA school-age forms & profiles. Burlington: Research Centre for Children, Youth and Families, University of Vermont. 2001.

18. Fonagy P, Luyten P, Moulton-Perkins A, et al. Sviluppo e validazione di una misura self-report di mentalizzazione: il Questionario sul funzionamento riflessivo. 2016;11(7):e0158678.

19. Anderson PJ, De Luca CR, Hutchinson E, et al. Attention problems in a representative sample of extremely preterm/ extremely low birth weight children. DevNeuropsychol. 2011;36(1):57-73.

20. Johnson S, Marlow N. Growing up after extremely preterm birth: lifespan mental health outcomes. Semin Fetal Neonatal Med. 2014;19(2): 97-104.

21. Stanford LD, Hynd WG. Congruence of behavioral symptomatology in children with ADD/H, ADD/WO, and Learning Disabilities. J Learn Disabil. 1994;27(4):243-253.

22. Grunau RV, Whitfield MF, Davis CD. Pattern of learning disabilities in children with extremely low birth weight and broadly average intelligence. Arch Pediatr Adolesc Med. 2002;156(6):615-20.

23. Ammaniti M. Maternal representations during pregnancy and early infant-mother interactions. Psychiatr Enfant. 1991;12(3):246-55.

24. Rogers C, Sylvester C, Mintz C, et al. Neonatal amygdala functional connectivity at rest in healthy and preterm infants and early internalizing symptoms. J Am Acad Child Adolesc Psychiatry. 2017;56(2):157-166.

25. Arpi E, Ferrari F. Preterm birth and behavior problems in infants and preschool-age children: a review of recent literature. Dev Med Child Neurol. 2013;55(9):788-96.

26. Ure A, Treyaud K, Thompson DK, et al., Neonatal brain abnormalities associated with autism spectrum disorder in children born very preterm. Autism Res. 2015;9(5):543-52.

27. Janssens A, Ulvin K, Van Impe H, et al. Psychopathology among preterm infants using the diagnostic classification zero to three. Acta Paediatr. 2009;98(12):1988-93.

28. Healy E, Reichenberg A, Nam KW, et al., Preterm birth and adolescent social functioning-alterations in emotion-processing brain areas. J Pediatrics. 2013;163(6):1596-1604.

29. IBM to acquire SPSS Inc. to provide clients predictive analytics capabilities. 2009.

30. Imafuku M, Kawai M, Niwa F, et al. Preference for dynamic human images and gaze-following abilities in preterm infants at 6 and 12 months of age: An eye-tracking study. Infancy. 2016;22(2):223-39.

31. Kroll J, Froudist-Walsh S, Brittain PJ, et al. A dimensional approach to assessing psychiatric risk in adults born very preterm. Psycho Med. 2018;48(10):1738-44.

32. Shirley M. A Behavior syndrome characterizing prematurely-born children. Child development 1939;10(2):115-128.

33. Sogos C, Di Noia SP, Fioriello F, et al. K-SADS-PL DSM-5. Intervista diagnostica per la valutazione dei disturbi psicopatologici in bambini e adolescent. Edizioni Erikson. 2019.

34. Thomason M, Scheinost D, Manning J, et al. Weak functional connectivity in the human fetal brain prior to preterm birth. Scientific Reports. 2017;7:39286.

35. Wolke D, Eryigiy-Madzwamuse S, Strauss V, et al. Personality of adults who were born very preterm, Arch Dis Child Fetal Neonatal Ed. 2015;100(6):F524-9.

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