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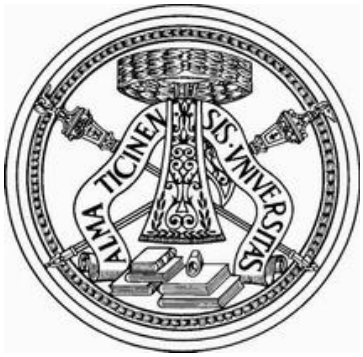

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CICLO XXIX

Early intervention in preterm babies: development and experimental trial of an easy and low-cost program

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Summary

Introduction

This PhD project is based on the definition of a protocol of Early Intervention on preterm babies and their mothers and the trial study to evaluate applicability and efficacy of the protocol proposed.

Prematurity represents today an increasing problem for public health. According to OMS data every year 15 million births are pre-term. The last published USA Perinatal Health report referred that in 2013, the preterm birth rate (infants delivered at <37 completed weeks of gestation per 100 births) was 11.39%, down for the seventh straight year. The rate was 11.55% in 2012. The preterm rate rose until 2006, increasing by more than one-third from 1981 to 2006 (Osterman, Kochanek, MacDorman, Strobino, & Guyer, 2015).

However more than 11% of total births occurred before the thirty-seventh gestation week. The Low Birth Weight (LBW, birth weight <2500 g) rate was 8.02% in 2013, essentially unchanged from 2012. The very low birth weight (VLBW, birth weight <1500 g) rate was essentially stable at 1.41% in 2013, whereas the moderately low birth weight (birth weight from 1500 to 2499 g) rate increased slightly to 6.61% of the total number of births (Blencowe, et al., 2012).

The huge number of preterm born babies urged more interest in the study of sequelae of a pre-term birth event. It is now well established that pre-term infants are associated with higher risks of organic problems (like respiratory distress, apnoea, instability of body temperature, hypoglycaemia, jaundice, feeding difficulties, periventricular leukomalacia PVL, intraventricular haemorrhage IVH) resulting frequent treatments in hospitals (Sigal & Doyle, 2008).

A possibly even major risk related to premature birth is damage of the Central Nervous System (CNS). In preterm babies the damage of CNS can cause a number of consequences. Pre-term birth hinders neurobiological maturation of new born being

the period when more intense development of the brain takes place during the last gestational period (Volpe J. J., 2009).

Nevertheless, the outcome of an original damage of CNS is not an exclusive consequence of the event of preterm birth, but it is a multi-factorial effect, that highlights the resilience or the vulnerability of the CNS in a specific subject. So it is necessary to focus on the CNS damage as the result of different pathways (i.e. ischemic and inflammatory), which give out a result depending by the exposure to different risk and protective factors modulated by genetics and environmental factors (Volpe J. J., 2009). A target was to establish pathways to endeavour better environmental factors. Continuous advances in obstetric techniques and intensive and neonatal care increase the share of children surviving preterm birth without serious cerebral damages, however there is an increase in minor difficulties (e.g. language problems, behaviour difficulties, attention deficits, etc...). These aspects may likewise adversely affect the quality of life for children and families and involve a cost to the healthcare system. A major goal is to detect as early as possible altogether subjects highly prone to risk and subjects associated with selective weaknesses (which could occasionally be supported with essential actions), and subjects who are likely to be able to build up an appropriate outcome (in order to avoid unnecessary recurrent check-ups and redirect resources to weaker subjects). In this field epigenetic is an innovative and promising approach (Cao-Lei, et al., 2017), (Provenzi, Guida, & Montirosso, 2017), (Provenzi, Scotto di Minico, Giorda, & Montirosso, 2017).

There is a wide range of intervention in terms of approach, theoretical reference, timing and duration of intervention, target of intervention (high risk population or not, children with clinical/health problems or low socio-economical status). Consequently, there are many reviews on this theme, that try to evaluate the best kind of intervention, the best period and duration, the more favourable cost/effective ratio based on different population target. It is quite evident that earlier intervention is better, with some studies that suggest the best results with antenatal programs for

mothers with positive fallout on cognitive and behavioural aspects in toddlers and children (Doyle, Harmon, Heckman, & Tremblay, 2009). It's widley known that intervention in the zero to five age period is more successfull at improving cognitive ability and educational outcomes, than school-age intervention. The zero to three age period is vital for the production and subsequent retention of synapses, therefore inadequate or better stimulation in this period can have a large and lasting effect on subsequent development. In particular "senstive periods" or "windows of opportunity" for certain developments to take place, have been identified (Hadders-Algra, 2001).

In a wide and in-depth review on early intervention in preterm babies (Spittle, Orton, Anderson, Boyd, & Doyle, 2015) the authors underline how intervention that began when infants were inpatients were more homogeneous, as they all focused on improving the parent-infant relationship and on enhancing parents' abilities to read and respond appropriately to infants' behavioural cues. This kind of family centred intervention demonstrated a greater impact on congitive outcomes at infancy and preschool age. Parenting intervention seems to have the higher cost/effectiveness ratio. They have the potential to create sustained effects on child development at a relatively low cost change in the family system. The influence on parenting practice on development of all children is well known. The beneficial effect of parenting practice becomes even more striking, for those more vulnerable children like preterm babies (Landry & Smith, 2006), (Treyvaud, et al., 2009). Moreover, parents of infants born very much preterm are at high risk of parenting difficulties. The premature birth is traumatic both for the baby and the parents. For the baby that has to adapt to a hostile and difficult environment starting to endeavour with many new tasks earlier than physiologically due, such as control breathing, temperature, hunger, external stimuli at a time of extreme fragility and vulnerability. For the parents that have to manage worries connected to the unexpected event of a birth taking place prior to the expected time, in particular worries about survival and sequelae of their child and face the difficulties of creating early bonds with a child so fragile and

seemingly less competent than expected, we can define them "Preterm parents". Some studies analysed pre term birth equating the difficulties after a premature birth to a post traumatic stress disorder (Kersting, et al., 2004), (Muller-Nix, Forcada-Guex, Pierrehumbert, Jaunin, Borghini, & Ansermet, 2004), (Kersting, et al., 2004), (Borghini, et al., 2014). In fact, "preterm moms" are more often depressed or withdrawn, and they have low levels of maternal coordination with the infant (Feldman & Eldelman, 2007), (Murray, Fiori-Cowley, Hooper, & Cooper, 1996 a). Isolation between parents and infants, often attributed to the complex technological support crucial for the infant's viability, can lead parents to feel less confident and more alienated from their infants and incompetent in the parental role (Arockiasamy, Holsti, & Albersheim, 2008), (Reynolds, et al., 2013). Other studies have found higher levels of intrusiveness, lower levels of sensitivity and more difficulties scaffolding (e.g. gradually supporting and guiding as needed to achieve higher levels of problem-solving) for mothers of preterm compared with term infants (Clark, Woodward, Horwood, & Moor, 2008), (Field, Hernandez, & Diego, 2006), (Field, et al., 2001). Cronin et al reported that parents of very low birth weight infants continue to manifest stress even up to 5 years after the birth of the child (Cronin, Shapiro, Casiro, & Cheang, 1995). Family bonding in the Neonatal Intensive Care Units (NICU) is often a very difficult process, due to separation from the child and continued physical restraints of the complex critical care environment. It is well known (Hurst, 2001 a) that mothers of preterm babies in NICU activate a series of strategies to safeguard their babies. The challenge for mothers is to increase their position of authority relative to the institution and individual caregivers, thereby protecting their babies. This kind of attitude was called "vigilant watching over": mothers are always alert to indication of safety and wary of circumstances that signal danger. They believe that their active presence at their babies' bedside is critical to ward their babies. Often they fear of being labelled as a "difficult mother", they know that they lack empowering information about their babies (about procedure, prognosis, risks and so on), they are afraid of variation, contradictions or omissions

in the care of their babies, and they are aware of having to trust the staff. (Hurst, 2001 b) Furthermore, premature infants don't engage in the social interaction typical of full term infants, their cues and interaction signals are often weak and disorganised and frequently go unnoticed. The interaction of mothers and their prematurely born children were related to child characteristics, maternal psychological well-being, and paternal support. Both maternal and child variables were related to three interactive dimensions: maternal positive involvement, maternal developmental stimulation and child developmental maturity. Mothers provide more interaction to compensate for the behaviour of sicker infants, but the mother's perception of how sick her infant is may be more important for mothering than the actual severity of the infant illness (Holditch-Davis, Schwartz, Black, & Scher, 2007).

Also, the loss of parental role has been reported as a major source of stress (Miles, Carlson, & Brunssen, 1999), (Muller-Nix, Forcada-Guex, Pierrehumbert, Jaunin, Borghini, & Ansermet, 2004). In a recent paper (Provenzi, et al., 2016) focused on the role of postnatal maternal bonding, it was hypothesized that mother-to-infant bonding would affect infants' socio-emotional regulation via the priming of an altered pattern of bonding-related care giving during the first months of life. The mothers' repertoire of actions to safeguard their babies in NICU include: negotiate actions with health care provider, judicious use of challenging institutional authority, use of institutional knowledge to challenge the institution's authority, authoritative weight of peer practice, seeking a higher authority, building supportive relationships with other mothers and garnering support from significant others (Hurst, 2001 b). Involving parents in the care of their infants and supporting them to better understand their baby's level of communication through his/her behaviour may help them to feel more comfortable with their infant and may promote positive bonding. Mothers of preterm infants have more concerns about their infants, especially in areas of attachment, health and growth, than mothers of full-term infants. These maternal emotional responses, combined with the immature and disorganized behaviours of premature infants, may interfere with parenting at least through the

first year of life (Miles & Holditch-Davis, 1995). Mothers of 3-year-old prematurely born children have been reported to view their children as more vulnerable than mothers of full-term ones (Perrin, West, & Culley, 1989). The perception of vulnerability was associated with more problems related to discipline, peer relationships and self-control. Mothers of these children are more likely to be overindulgent, but not overprotective, than mothers of children born at term (O'Mara & Jhonston, 1989). Furthermore, it is to be considered that a higher quality of maternal interaction is related to increases in infant positive emotionality, and this may in turn act as a protective factor for the infant socio-emotional development (Costa & Figueiredo, 2011).

Several years ago, Tronick, Chon and Lyons-Ruth (Cohn, Matias, Tronick, Connell, & Lyons-Ruth, 1986), (Tronick, Olson, Rosenberg, Bohne, Lu, & Lester, 2004) in the context of studying depressed mother-infant interaction described two different styles of maternal behaviour, which they identified as withdrawn and intrusive. Mothers whose behaviour style was predominantly intrusive typically showed rough physical contact such as tickling, poking and tugging, and loud, fast verbal behaviour when interacting with their infants (overstimulating). These findings were re-described many times in different works about different fields of study also in that about mother infant interaction in very-low birth weight (VLBW) preterm babies (Field, Hernandez, & Diego, 2006). Research has identified how mothers of preterm infants may be more controlling, actively engaged and/or intrusive with their infants, perhaps compensating for guilt/shame for not having been the caregiver they wanted to be during hospitalization, or for compensating preterm infants' inactive interaction (Flacking, Ewald, Nyqvist, & Starrin, 2006), (Forcada-Guex, Pierrehumbert, Borghini, Moessinger, & Muller-Nix, 2006), (Garel, Dardennes, & Blondel, 2007), (Howe, Sheu, Wang, & Hsu, 2014), (Holditch-Davis, et al., 2015). Compensatory parenting style was deeply described in 1995 by Miles and Holditch-Davis (Miles & Holditch-Davis, 1995). In this parenting style the mothers of 3 year-old prematurely born children provided special experience and avoided other experiences in attempt to compensate

the children for their neonatal experience. The children are viewed as both special and normal. Many mothers described their children as "miracle children", resulting from the children having survived a period of critical illness and having endured the related suffering. At the same time mothers have worked hard at viewing the children as normal, often denying serious health problems. Compensatory parenting involved alterations in the following four aspects of parenting: protection, stimulation, attention and limit setting. The normal maternal protective behaviours of keeping the children safe from harm are intensified. Maternal activities involved in fostering the children's development also are heightened. Mothers are intensely concerned about providing enough stimulation and thus reported providing more stimulation, as well as special experience that aren't ordinarily affordable to the children than to siblings. The mothers reported that the level of attention paid to the children is also increased greatly. The children became the focus of attention in the family, receiving more attention than siblings. Although this is fostered by mothers, it is also encouraged by many relatives and friends. In addition, behaviours related to limit setting and making demands to encourage development of responsibility are altered. The mothers believe that the children had been through too much already and thus are unable to set age-appropriate limits. Mothers are reluctant not to respond to the child's every want. As a result, children are described as dependent, stubborn, wilful, hard-headed, whiny and determined to get their own way. Mothers reported intense emotional responses to the NICU experience 3 years after, including guilt, helplessness, fear of death, anxiety and depression. These memories directly affect later parenting, and the normal process of maternal role attainment, that is becoming involved with the infant, assuming maternal care giving and developing a strong identity as a mother. Several mothers reported delaying involvement and attachment until the infant could come home.

Some of these findings were recently connected to fMRI patterns of activation in a study by Montirosso et al (Montirosso, et al., 2017). In this paper findings suggest differences in the neural processing of infant cues, which are related to parental

experience. In preterm mothers, irrespective of the infant identity (own versus unknown), the neutral infant viewing elicited an increased activation of the right putamen. Activation of putamen signals are described in perception of infants' faces and it has a role in the rewarding feature of infants' faces (Glocker, et al., 2009), (Luo, et al., 2015). Maybe in light of the scarcity of preterm infants' signals during mother-infant interaction, the infant face might be a more relevant social stimulus for preterm mothers than of full term ones. Furthermore, infant emotional expressions (distress or happy faces), even of an unknown baby, evoked a strong response in the bilateral inferior frontal gyrus (IFG) in preterm mothers, but not in the full-term ones. Interestingly, IFG is part of the mirror-neuron system (Rizzolatti & Craighero, 2004), that is triggered when individuals observed and executed an action or imitate and observe emotions. Thus, in line with the compensatory parenting hypothesis the putative role of the IFG might reflect the greater engagement of preterm mothers in understanding what infants feel. It is also to be considered that preterm mothers probably get more time to interact with their infants than do full-term mothers. Thus, it cannot be excluded that brain pattern activations observed might be due to the elapsed time with their infants, instead of the parenting experience associated with the birth and hospitalization of their own preterm infant.

The aim of this project in researching this field was to act on environmental protective factors. The most promising strategy available to compensate weaknesses and to promote growth potential of pre-term born babies seems to be to act on the environment, possibly through early intervention programs.

First of all, it is necessary to introduce what is meant by "Early Intervention" with preterm babies; in fact this term is indifferently used if the intervention starts during hospitalisation in NICU or even after hospital discharge or else in the first 2-3 years of life. Every kind of "early" is reasonable but we chose to try an intervention as soon as possible, so during hospitalization, and we aimed to demonstrate that this approach carries better chances of success in improving the performance and quality of life of pre-term born babies and their families. By a review of scientific literature a

classification of different kind of intervention already tried and their aims is available (Spittle, Orton, Anderson, Boyd, & Doyle, 2015), (Herd, Wittingham, Sanders, Colditz, & Boyd, 2014), (Symington & Pinelli, 2002), (Spittle, Doyle, & Boyd, 2007), (Vanderveen, Bassler, Robertson, & Kirpalani, 2009), (Evans, Whittingham, Sanders, Colditz, & Boyd, 2014), (Bozzette, 2007). Various approaches and intervention protocols have been described including support meetings at hospital and home visits to families or distribution of information, including videos and booklets about prematurity and off site support by telephone calls (Melnyk, et al., 2006), (Melnyk & Feinstein, 2009), (Kaaresen, Ronning, Ulvund, & Dahl, 2006), (Kaaresen, Ronning, Tunby, Nordhov, Ulvund, & Dahl, 2008), (Melnyk, et al., 2001), (Kleberg, Hellström-Westas, & Widström, 2007), (Kynø, Ravn, Lindemann, Smeby, Torgersen, & Gundersen, 2013), (Koldewijn, et al., 2009), (Meijssen, et al., 2010), (Borghini, et al., 2014), (Holditch-Davis, Withe-Traut, Levy, O'Seha, Geraldo, & David, 2014).

We found particularly interesting the Family Centred Care model in NICU, that is an approach that encourages and provides the necessary resources for families to participate as fully as possible in caring and making decisions for their hospitalized babies and respect the diversity of families and their values and beliefs, thereby facilitating the formation of mutually beneficial and supportive partnerships in the NICU and beyond (Harrison, 1993), (Dobbins, Bohlig, & Sutphen, 1994).

In this area we looked at the "Triple P approach" (Colditz, et al., 2015) an intervention that focuses on sustained environmental enrichment through enhanced parenting practices. However, the "Baby triple P for preterm infants" can be effective when integrated into an existing and well organised community-based parenting program (Triple P "Positive Parenting Program") (Sanders & Dadds, 1993), (Sanders, 1999). Another interesting model is the Creating Opportunities for Parent Empowerment (COPE) program (Melnyk, et al., 2006), (Melnyk, et al., 2001). This program was designed to enhance parent-infant interactions and parent mental health outcomes for the ultimate purpose of improving child developmental and behaviour outcomes. Participants received four intervention sessions of audiotaped and written materials,

with information and behavioural activities about the appearance and behavioural characteristics of preterm infants and how best to parent them.

At the beginning of this study we had in mind to structure a clear and effective intervention, which would have to be simple in application and inexpensive so as to be easily introduced into the daily care routine of these children. We set the protocol taking inspiration from The Newborn Individualized Developmental Care and Intervention Program (NIDCAP) (Als, A synactive model of neonatal behavioral organization, 1986), (Sizun, Ratynski, & Boussard, 1999) and The Mother-Infant Transaction Program (MITP) (Rauh, Nurcombe, Achenbach, & Howell, 1990), (Landsem, Handegård, Tunby, Ulvund, & Rønning, 2014).

NIDCAP is an early intervention in the form of family-centred developmentally supportive care. This program was widely adopted and tested. The major tool employed is formalised, naturalistic observation of the infant before, during and after caregiving procedures. The observer assesses the infant's current ability to organise and modulate the five highly interactive subsystems formulated in the synactive theory, i.e. the autonomic physiological, motor, state organisational, attention-interactive and self-regulatory systems. The infant's behavioural reactions to internal (e.g., bowel movements, proprioceptive input) and external (e.g., light, sound, touch) sensory stimuli are noted and analysed. On the basis of these observations, recommendations concerning individualised care and environmental changes based on the current developmental stage of the infant are given. As the infant matures, these recommendations are altered in an appropriate manner. The care plans are discussed with the parents and hospital staff and their ability to interpret the weak signals of and care for the fragile infant thus improve. In conclusion, care of VLBW infants according to NIDCAP appears to have certain positive long-term effects on the child's behaviour and mother-child interaction (Kleberg, Westrup, & Stjernqvist, 2000).

MITP is a brief, economic neonatal intervention based on the transactional model of development and influenced predominantly by the conceptual design of the

Neonatal Behavioral Assessment Scale, initially implemented in an intensive care nursery with the mothers of a group of low-birth-weight infants. It appeared that the two low-birth-weight groups (one that received the intervention and the other that received standard care) had progressively diverged after 12 months, the intervention group rising until it approximated the normal-birth-weight group in cognitive development, whereas the low-birth-weight control group deteriorated. Each intervention consisted of 7 hour-long sessions with parents and their baby during the last week before discharge, and 4 home visits at 1, 2, 4, and 12 weeks post-discharge.

We also got ideas from the scheme of a Dutch study published in 2007 (Maguire, Bruil, Wit, & Walther, 2007), but with the background of the "Close Collaboration with Parents™" experience (Ahlqvist-Björkroth, Boukydis, Axelin, & Lehtonen, 2017). The Dutch paper also comprises an instructive "guide" helping to plan an early developmental intervention protocol in NICU. In that trial researchers met parents 4 times over two weeks during baby hospitalisation, each session lasted about 20-30 minutes. Those "teaching sessions" are described as interactive and individual at the infants' bedside, using photos to explain infant behaviour, with care to be easily understandable and supportive for parents. Before and after the session parents were asked to complete a pre- and post-test on knowledge of what was illustrated. This protocol was very similar to the one we wanted to experiment but we found this approach focused too much on training and less on supporting and sustaining parents. In a quite recent work by Montirosso (Montirosso, et al., 2012) it was highlighted that mothers' emotional needs could go far beyond practical information about prematurity, and that they might need a more psychological oriented informed support, since they do not need to be "medically trained", instead they need to build up better competence during a difficult period of their life. In order to reach this goal it is necessary to smooth worries and enhance resources with particular attention to subjects who are facing a highly challenging experience. A kind of intervention not necessarily bound to the presence of a psychologist but to a researcher with a specific sensitivity for the themes acquired through experience and specific training. This

could be crucial in promoting the quality of mother-infant interaction, which decreases the risk of developmental difficulties in children.

We decided to follow the suggestion proposed by Zack Boukydis in his book "Collaborative consultation with parents and infants in the perinatal period" (Boukydis Z. , 2012). His approach won us over because it is oriented to suggest and propose, to observe the natural resources of babies and parents, to help them in taking care of their baby, a kind of "maieutic" attitude with the idea of the researcher as a facilitator of existing skills (Boukydis C. F., 2008). The starting point is enclosed in the title, the "collaborative consultation" is a peculiar perspective that allows the consultant to help parents on the same level and being helped by parents suggestion and natural feeling with their baby.

Aims

The aims of this project were:

- To design an experimental protocol to sustain parents in their role during NICU hospitalization
- To assess this protocol and evaluate if it could be both effective and easy to apply in the NICU "usual care"
- To assess the effect of an early parenting intervention in the NICU on maternal caregiving behaviour
- To evaluate the effects of an early parenting intervention in the NICU on maternal well-being
- To inquire the effects of an early parenting intervention in the NICU on infants' developmental outcomes
- Finally, to evaluate the early relationship between mothers and children, to assess the role of maternal presence in the NICU on the association between the early educational parenting intervention and maternal intrusiveness

Method

Study design

In the Study design high attention was posed to identify an easy and rapid protocol, with a low-cost application and a solid correlation with previous approaches as illustrated before. In particular it was chosen to target the intervention on mothers, to start it during NICU hospitalisation, with the aim of precociously sustaining the maternal role and to keep on meetings until 3 months of corrected age of the baby.

For the intervention core (meetings with mothers and observation at babies' cradles), the method described in the Boukydis book "Collaborative consultation with parents and infants in the perinatal period" was applied as cited before.

The consultant has to take time to observe the baby together with the parents, with a parity attitude with them, he isn't a teacher but he tries to recognize and support intrinsic parenting skills, innate parental attitude and he tries to show them to the parents themselves. Underlying how much parents know about their baby and how well they could imagine what is happening or why he/she is reacting in a particular way is part of helping parents in better understanding their infant to support in their role of primary figure of care. The proposed strategy includes evaluating first of all, parent availability, it isn't useful to involve parents that don't want to try this experience or that in a peculiar moment cannot see it as useful for their baby. As already written NICU's environment it is particularly stressful for parents and usually, especially in the very early period, parents are focused on the survival and clinical condition of their children, so it is necessary to wait until they can consider other aspects of baby well-being. Hence is crucial to start with a parity attitude, asking parents' permission to observe their child together, to involve them in a positive and satisfying experience. During joint observation is better to say less and to listen more to what parents already had observed about their baby, stimulating

them with open questions on what they think about their child's behaviour, on what is happening in some moments of the observation and why he/she had reacted in that peculiar way. It is useful that the consultant expresses his own ideas and comments at the end of the session, leaving time for parents to reflect, suggesting alternative views and above all point out everything that parents are already able to understand about their child's temperament and behaviour. It could be necessary to explain to parents some particular characteristics of very preterm infants and to help them to notice how much effort their babies are making in order to manage all the environmental requests and stimuli. This kind of approach was very close to our group attitude and training, so it was also easier for us to propose it.

We asked some experts for an opinion about protocol program and especially about which instruments to propose to parents and children to assess the effectiveness of intervention and at which time. After establishing a clear idea of the project we started to define the informed consent that have been approved by two Ethical committees. We proposed our project to the NICU staff in the San Matteo Hospital in Pavia, with whom we have been collaborating on a weekly basis for many years. We also proposed to some colleagues of the 0-3 Center for the Study of Social Emotional Development of the at-Risk Infant, IRCCS Eugenio Medea in Bosisio Parini, to analyse data and to perform statistical analysis without knowing the group assignation.

The Informed consent was therefore approved by Mondino Institute (where worked the researchers) and San Matteo Hospital (in which NICU we recruited patients and families) Ethical committees.

Assessment instruments

We chose to use some different outcome measures for different purposes according to our aims.

Assessment of the effects of early parenting intervention in the NICU on maternal care giving behaviour and on maternal well-being

To assess the effect of an early parenting intervention in the NICU on maternal care giving behaviour and to evaluate the effects of an early parenting intervention in the NICU on maternal well-being, we need to evaluate parental stress and feeling during NICU stay and after discharge, maternal depression, parents' perceived support by family and significant others and by staff.

Therefore we selected the Parental Stressor Scale Neonatal Intensive Care Unit PSS-NICU (PSS:NICU) (Miles, Funk, & Carlson, Parent stressor scale: neonatal intensive care, 1993) and the Parenting Stress Index (PSI) (Abidin & Wilfong, 1989) to evaluate the level of stress in parents and consequently their attitude to care giving.

PSS:NICU is a 26-item self report measure of stress assessing three dimensions of parental experience during NICU stay: Sights and Sounds (SS 6 items) -stress related to the NICU physical environment; Infant behaviour and appearance (IBA; 13 items) - stress because of the infants' appearance and behaviour; parental Role Alteration (7 items) - stress related to the alteration in the expected parental role and the postponement of the actual parental care. Parents are asked to rate each item on a five-point Likert scale from 'not stressful' to 'extremely stressful'. An overall stress level score is computed for each subscale by the number of items making up a subscale. Each subscale ranges from 0 to 5, with lower scores reflecting minor perceived maternal stress.

PSI try to identify stressful aspects of parent-child interaction. This is a screening and triage measure for evaluating the parenting system and identifying issues that may lead to problems in the child's or parent's behaviour. Focuses on three major domains of stress: child characteristics, parent characteristics and situational/demographic life stress. It was designed for use with parents of children ranging in age from 1 month to 12 years. We used the PSI short form (PSI-SF): this is a self-administered instrument in which, for each item, the level of parenting stress is rated on a 5-point scale ranging from 1 (strongly disagree) to 5 (strongly agree). The items are divided

into three subscales: Parental Distress, which measures the distress that a parent is experiencing for personal reasons; Parent-Child Dysfunctional Interaction, which measures parents' perceptions of their interaction with their child; and Difficult Child, which measures parental perceptions of the child's temperament and disposition. The subscale scores, which range from 12 to 60, are summed to give a total score ranging from 36 to 180. High subscale and total scores indicate greater levels of stress. The 85thpercentile has been established as the cut-off point for the subscale and total scale scores. Scores equal to or above this cut-off point are considered clinically significant. Child and Parent domains combine to form Total Stress Scale. Parent subscales: Competence, Isolation, Attachment, Health, Role Restriction, Spouse/Parenting Partner Relationship. Child subscales: Distractibility/Hyperactivity, Adaptability, Reinforces Parent, Demandingness, Mood, Acceptability.

To evaluate maternal depression that is known as a negative factor in the mother child interaction, augmenting stress and intrusive attitude, we chose the Edinburgh Postnatal Depression Scale (EPDS) (Cox, Holden, & Sagovsky, 1987). EPDS has a strong construct validity with good internal (α = 0.8) and test-retest (α = 0.77) reliability, it's widely used in the world of research on non-clinically depressed samples. It's rapid and easy to administer, it's a 10-item self-report questionnaire designed to measure emotional and cognitive symptoms of depression. Each item is rated on a four-point scale (0 to 3), total score range from 0 to 30 with the higher score indicating high level of depressive symptoms (Benvenuti, Ferrara, Niccolai, Valoriani, & Cox, 1999).

To assess the perceived support by parents from staff and from significant others that could influence maternal well-being and consequently the care giving attitude, we selected the Nurse Parent Support tool (NPST) and the Multidimensional Scale of Perceived Social Support (MSPSS)

The NPST is a 21-itemself-report scale designed to measure the mother's perception of medical-nurse staff support during her infant's hospitalization. Items' scores range

from 1 to 5, with higher scores reflecting a greater amount of perceived support from the staff (Miles, Carlson, & Brunssen, 1999). The MSPSS is a brief research tool designed to measure perceptions of support from 3 sources: Family, Friends, and a Significant Other (Zimet, Powell, Farley, Werkman, & Berkoff, 1990). The scale is comprised of a total of 12 items, with 4 items for each subscale. Across many studies, the MSPSS has been shown to have good internal and test-retest reliability, good validity, and a fairly stable factorial structure.

Inquiring the effects of an early parenting intervention in the NICU on infants' developmental outcomes

To evaluate this aspect the Attention (Orientation) subscale of the Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNNS) (Lester & Tronick, 2004) and the Sensory-motor scale for neonates (Martinet, Boradori Tolsa, Rossi Jelidi, Bullinger, Perneger, & Pfister, 2013) were chosen.

NNNS explores the neurobehavioral organization, neurological reflexes, motor development - active and passive tone, and signs of stress and withdrawal of the at-risk infant. It was designed to provide a comprehensive assessment of both neurological integrity and behavioural function. This neurobehavioral assessment is applicable to term, normal healthy infants, preterm infants and infants at risk due to factors such as prenatal substance exposure. The exam is performed on infants who are medically stable in an open crib. Although a precise lower gestational age limit has not been set, the exam is probably not appropriate for infants less than 34 weeks of age. The upper age limit may also vary depending on the developmental maturation of the infant. A reasonable upper age limit is approximately 45 weeks (conceptional age), but it may prove useful with even older infants. As such, it is a useful tool for both researchers and clinicians, the most difficult aspect is the time required to apply all the Scale. For this reason, it was chosen to perform only the Attention (Orientation) subscale, that analyses motor and behavioural responses to different kinds of stimuli, in order to evaluate the infant resources respecting the

original idea of a rapid and easy protocol to apply in the ordinary clinical contest. (Sullivan, Miller, Fontaine, & Lester, 2012).

Sensory-motor scale for neonates is a descriptive tool, based on behavioural observation of the infant, it was created to evaluate the effects of intervention on the baby's self-regulation and neurodevelopmental stage during hospitalisation. It is based on the concept of sensory-tonic regulation of the infant. In accordance with one of the authors we try to administer it after neurological examination which is one of the possible "interventions" with a baby. It is composed of 23 items and requires 3-5 minutes to fill it in by a clinician a therapist or a nurse. The items are grouped into 6 domains: alertness, cardio-circulatory and respiratory status, postural manifestations, emotional expressions, sensory responses and oral activity.

We also try to find a biochemical measure of the baby's stress considering cortisol in hair or nails. We found two articles (Khelil, Tegerhoff, Meinlschmidt, Jamey, Ludes, & Raul, 2011), (Tegethoff, Raul, Jamey, Khelil, Ludes, & Meinlschmidt, 2011) about analysing cortisol levels in preterm nails like a biochemical index to evaluate medium term stress in these babies. In the first two years of the project we also involved a Biochemistry Professor of Molecular Medicine Laboratory of Pavia University and two her collaborators asking them to try to replicate a method published, in fact we thought that would be the right completion to our study. Unfortunately, all the attempts to find the right analysis were inconclusive because of the very small amount of nails collected (about 1 mg of nails per baby) and at the end we decided to stop these efforts.

Evaluation of the early relationship between mothers and children, the role of maternal presence in the NICU on the association between the early educational parenting intervention and maternal intrusiveness

To evaluate the maternal presence, a daily diary was chosen to note the presence in NICU/holding/kangaroo therapy like the one described and tested from the Separation and Closeness Experiences in the Neonatal Environment SCENE group (Flacking, et al., 2012), (Raiskila, et al., 2017).

The SCENE diary is composed of single pages on which to note the time present in NICU, time passed by the baby's cradle holding him/her, time passed performing kangaroo therapy. Each page covers a week of and it is possible to note the presence of both parents, this instrument was found in research studies as clear and easy to fill in by parents.

To assess the early relationship and interaction, the Maternal Postnatal Attachment Scale (MPAS) (Condon & Corkindale, 1998) and the Global Rating Scales of Mother Infant interaction (GRS) were chosen.

MPAS is a 19-item self-report questionnaire measuring maternal feelings toward the infant. All items are rated with a score of 1 (low bonding) to 5 (high bonding), with higher scores indicating higher feelings of attachment toward the infant. The MPAS is composed of three scales: (1) Quality of attachment (score range 9-45) includes nine items and indicates maternal feelings of confidence and satisfaction in being a mother; (2) Absence of hostility (score range 5-25) includes five items and indicates the lack of feelings of irritability and distress when interacting with the infant; (3) Pleasure in interaction (score range: 5-25) includes five items and refers to maternal desire of proximity and interaction with the infant. The MPAS has received adequate validation for consistency and reliability (Condon & Corkindale, 1998) and construct validity, and it was found to correlate significantly with other measures of mother-infant bonding (van Bussel, Spitz, & Demyttenaere, 2010). In the MPAS, the term attachment is used to refer to behaviours, processes, and representation of mother toward the infant, namely maternal post natal bonding, which starts to develop soon after delivery. In order to avoid misunderstanding, as suggested by van Bussel (van Bussel, Spitz, & Demyttenaere, 2010), in this study we used preferentially the term *mother-to-infant-bonding*, confining the use of the term attachment only to findings related to MPAS scale *Quality of attachment*.

GRS is a tool to code a 5 minutes video of mother and child interaction. This method has shown a predictive validity regarding infant and child cognitive outcome at 18 months and 5 years of age, and a good discriminant validity for a number of clinical

groups. It also proved to be valid cross-culturally: it has been used in studies in South Africa, Venezuela, Japan and many European countries (Cooper, Tomlinson, Swartz, Wooglar, Murray, & Molteno, 1999), (Gunning, et al., 2004). Moreover, GRS has been used to investigate associations between infant psychological profiles, temperament and quality of mother-infant interaction. The GRS comprises 25 5-point scales, 7 for describing the infant, 13 for describing mothers and 5 for describing joint interactive behaviours occurring within a 5 minute period. Scale scores were clustered in summary measures (three infants, four maternal and one dyadic). Maternal dimensions describe mother's overall sensitivity, intrusiveness, remoteness and signs of depression. Infant dimensions describe level of communication, involvement and positive emotionality. finally, interactive dimensions describe mutual engagement (Costa & Figueiredo, 2011), (Fiori-Cowley, Murray, & Gunning, 2000), (Murray, Fiori-Cowley, Hooper, & Cooper, 1996 a), (Murray, Hipwell, Hooper, Stein, & Cooper, 1996 b), (Murray, Stanley, Hooper, King, & Fiori-Cowley, 1996 c). See Appendix 1 "Outline of the summary indexes by Global Rating Scales (GRS) Encoding System"

Descriptive measures

An anonymous socio-demographic questionnaire investigates age, marital status, educational level and kind of work of parents, distance from Hospital, presence of siblings and in which health conditions and any reasons for refusing to participate. We ask parents to complete it to assess the socio-economic status (SES) following the Hollingshead scale (Hollingshead, 1975), and to verify any differences in families who have denied the consent than those who accepted to participate.

Neonatal clinical conditions were assessed through the Vermont Oxford Network Risk Adjustment index (VON-RA). It considers among others kind of delivery, sex, gestational age, birth weight, Apgar at first minute (Zupancic, et al., 2007), brain ultrasound classified according to Papile (Papile, Burstein, Burstein, & Koffler, 1978) and Volpe (Volpe, 1995) classification and duration of stay.

Procedure

This was a clinical trial study, proposed in a tertiary care NICU in north Italy between January 2015 and December 2016, the study ended in May 2017 when the last babies were 3 months of corrected age (CA). The paediatric neuropsychiatrists and the neurodevelopmental therapists recruited families, applied the intervention and entered data in the dataset, so they knew affiliation to clinical or control group but data analyzer and coders of the videos were masked to group allocation. Each family was pre-assigned to one group, according to birth order, we recruited controls from January 2015 to July 2015, then clinical babies from September 2015 to July 2016, then controls from September 2016 to December 2016.We took advantage of summer holidays (August 2015 and 2016) to have a wash out period, to minimize risk of interaction between parents belonging to different groups.

NICU facility description

The NICU is a traditional open space level III unit, where parents had 24 hour access. Developmental care is not clustered in protocols (e.g. Newborn Individualized Developmental Care and Assessment Program NIDCAP) (Kleberg, Hellström-Westas, & Widström, 2007). There are two sub-intensive units where babies are moved to when stable. There are two rooms next to the Units that are usually offered to mothers for a few days before hospital discharge to help them to familiarize more with their baby before going home or for specific clinical needs of the mother, there aren't family room facilities. Standard or reclining chairs are available for parents next to incubators or cradles in all the three units. Usually we collaborate with NICU's staff, and on a weekly basis, we perform observations and neurological examinations of high risk preterm babies nearing to hospital discharge and preterm follow up in a close department, we give extra care suggestions to mothers when needed. In our Unit the standard neuropsychiatric follow up is based on a neurological examination and some care suggestion (illustrated in a booklet given to families) soon before discharge from hospital and then visits (with neurological examination and information about any difficulties) at 3-6-9-12-18 and

24 months of corrected age, then a visit per year until 6 years of age. In these meetings the therapist's presence is not always guaranteed.

The NICU staff was informed of the project (we exposed the project to nurses and doctors in two meetings before starting), but no particular kind of different intervention or care by them is required; they only have to manage the presence of diaries next to cradles (filled in by parents) and that we can arrange meetings with parents.

Operational procedures

The paediatric neuropsychiatrist or the neurodevelopmental therapist approached the eligible families soon after the baby was in a stable condition. At first contact the researchers outlined the key elements of participation (including the voluntary nature of participation), and gave information on both risks and benefits and on the specific research activities of the study. Parents were given a copy of the informed consent which includes an abstract of the project and a detailed plan of the intervention, the anonymous socio-demographic questionnaire had already been given. Parents could, after a few days, give the two forms filled in a closed envelope to nurses or researchers.

Study design phases

For both groups four check-points were planned: soon after obtaining written informed consent from parents (T0), at hospital discharge (T1), at 40 weeks of gestational age (T2) and at 3 months of corrected age (T3).

- At T0 we proposed a daily diary to note the presence in NICU/holding/kangaroo therapy like the one described and tested from the Separation and Closeness Experiences in the Neonatal Environment SCENE group (Raiskila, et al., 2017)
- At T1 the neurodevelopmental therapist proposed some care suggestions and delivered an information booklet "Piccoli passi per crescere insieme" regarding characteristics and development of preterm babies until one year of age. This illustrated booklet was developed by our group collecting several

care suggestions to apply at home, derived from clinical experience and inspired by neurodevelopmental care programs (i.e. NIDCAP). The Parental Stressor Scale Neonatal Intensive Care Unit (PSS:NICU), the Edinburgh Postnatal Depression Scale (EPDS), the Multidimensional Scale of Perceived Social Support (MSPSS), the Nurse Parent Support tool (NPST) were also proposed

- At T2 the Maternal Postnatal Attachment Scale (MPAS) and the Parenting Stress Index (PSI) was given
- At T3 a Life events form, the PSI-SF, the EPSD, the MSPSS was given.

At T1, T2 and T3 a Neurological examination, General Movements videotaping and Behavioural examination of the baby were performed by the paediatric neuropsychiatrist and the neurodevelopmental therapist.

At T1 and T2 (hospital discharge and 40 weeks of GA) the Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNNS) Attention (Orientation) subscale, and the Sensory-motor scale for the neonate were also performed.

At T2 and T3 a 5 minute video was made of the mother-infant interaction following the Global Ratings of Mother Infant Interaction Scale (GRS) instructions. The infant was placed in a baby bouncer when awake and calm, the mother was placed in front of him/her, and they played together for 5 minutes. Video recording was made using a mirror behind the baby bouncer to have a double image (of the baby's face directly from the video camera and of mother's face reflected in the mirror), and to allow us to exit the room to make moms more comfortable in playing with their children.

Description of the Early intervention protocol

Only for the experimental group (Early Intervention Protocol):

- from recruiting to hospital discharge 2 meetings have been planned (lasting about 60-90 minutes each) with a small group of mothers (fathers were also invited), the paediatric neuropsychiatrist and the neurodevelopmental therapist to describe some typical characteristics of preterm babies, some

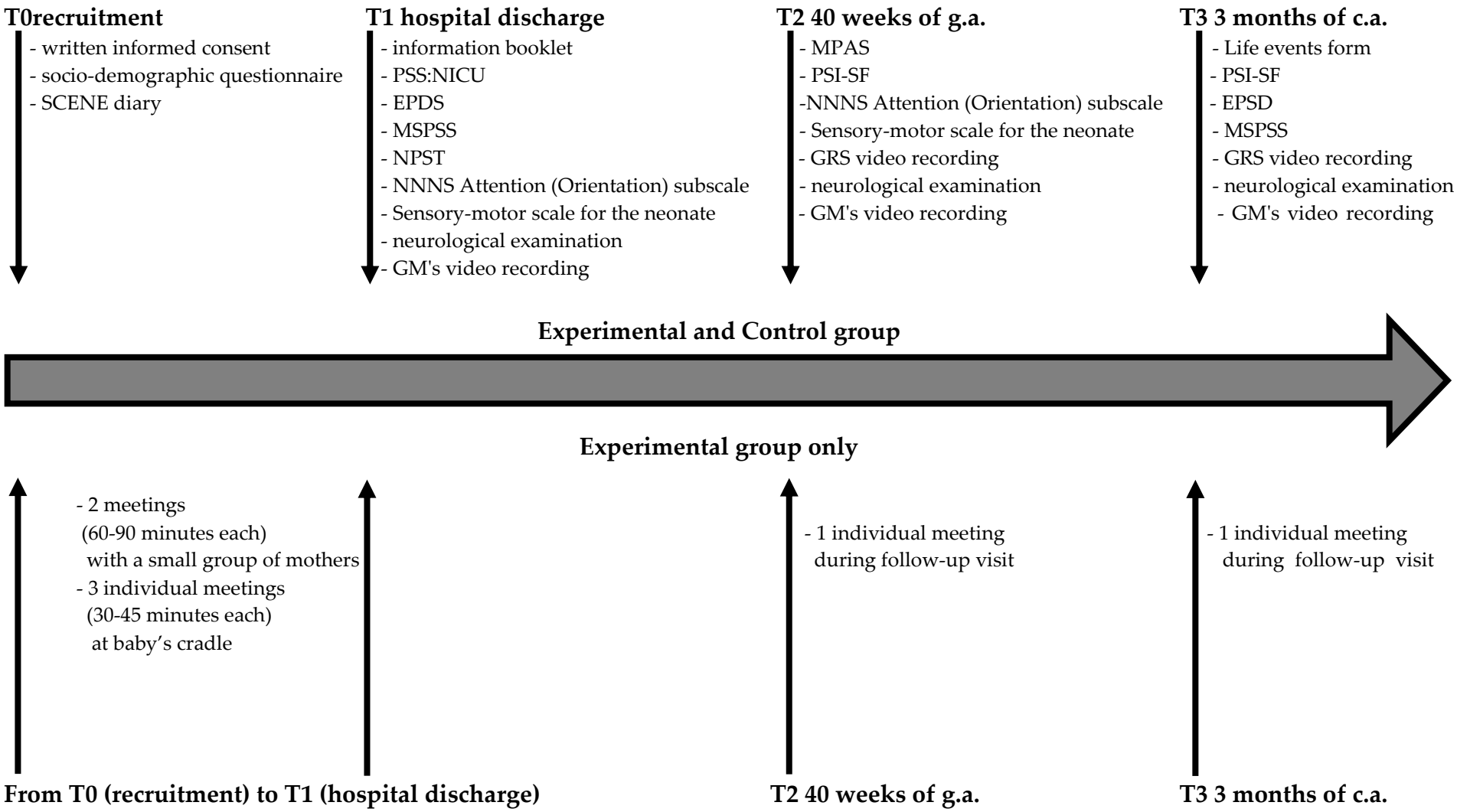
special needs in care habits and to talk about prematurity. If group sessions were not possible, individual ones were provided.

- in the same period 3 individual meetings (lasting 30-45 minutes each) with every mother and the neurodevelopmental therapist at the baby's cradle to observe together that single baby: his/her attitude, behaviour, temperament, ability to call for help and to accept external intervention, his/her way of showing stress, and his/her own way of coping
- at 40 weeks and at 3 months of corrected age one individual meeting with each mother, the paediatric neuropsychiatrist and the neurodevelopmental therapist, was carried out to discuss about changes in the baby and in the mother's attitude

(See Figure 1 Visual representation of the early intervention protocol)

To complete the program, we needed at least two weeks to plan meetings and give parents some time to reflect about what we were saying, so we decided to exclude children who would have been discharged before. The group meetings and specially the individual ones with the neurodevelopmental therapist were based on Zack Boukydis theory (Boukydis Z. , 2012), as already explained above. In the group meetings the aim was to share knowledge and information on preterm newborn infants with parents. We talked about preterm babies competence, Brazelton's infant behavioural states (Als, Tronick, Lester, & Brazelton, 1997), correct age, signs of stability or of stress, environmental changes, holding and handling suggestions. In the individual meetings at the bedside the aim was to recall what emerged in the group meetings, recognize stress and the self-regulation signals of the baby, find the individual characteristics of that single baby. Behavioural state, motor patterns, stress or self-regulation signals and interactive attitude were observed together by parents and neurodevelopmental therapist.

Figure 1 Visual representation of the early intervention protocol

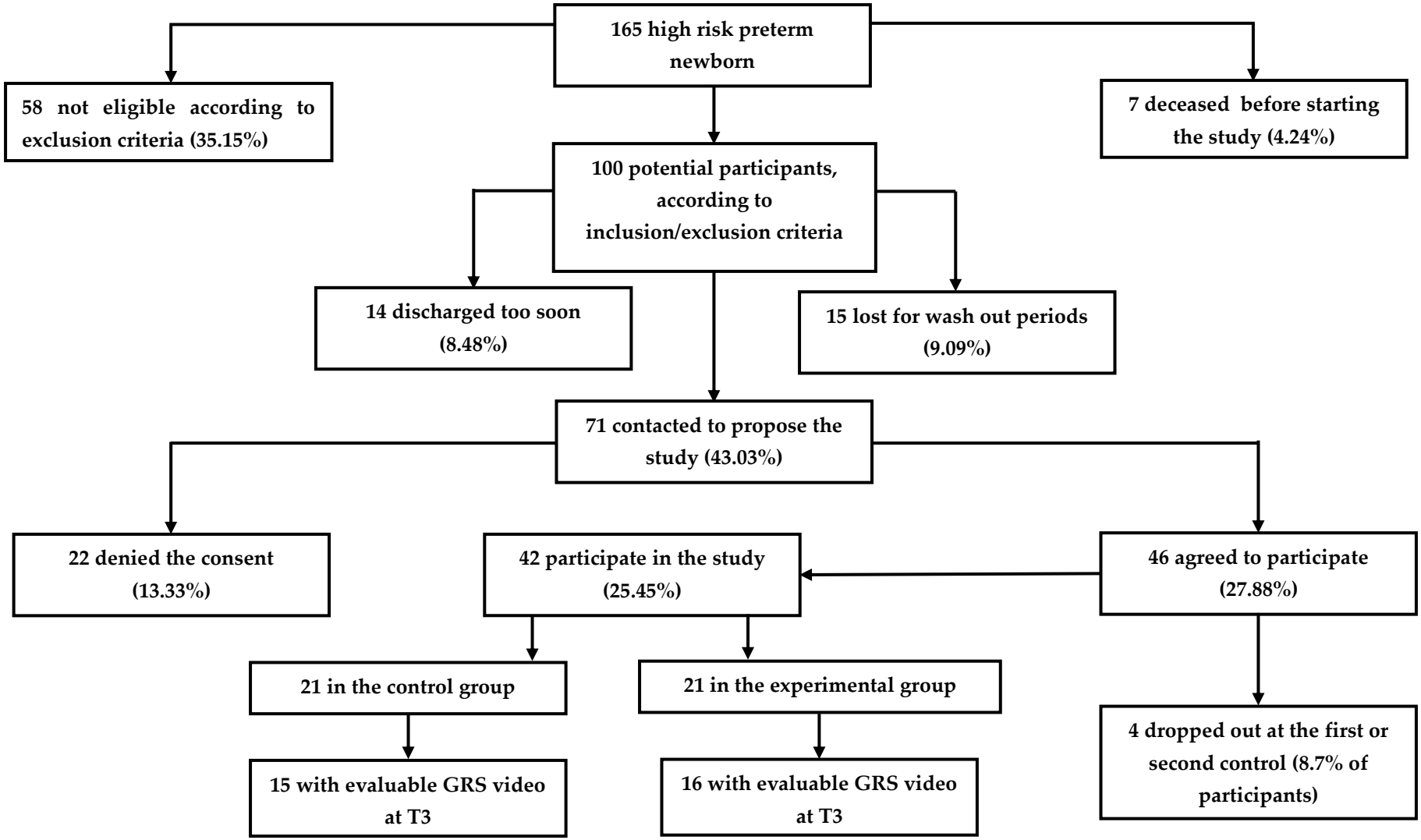


Data collection

Of 165 high risk preterm newborn from January 2015 to December 2016 in this NICU 58 babies weren't eligible for this study (35.15%) and 7 deceased (4.24%), of the remaining 100 potential participants, 14 had been discharged from hospital too soon after being in a stable condition (8.48%, primarily "small for gestational age" babies) and 15 (9.09%) were lost due to the wash up periods.

Sixty families (corresponding to 71 high risk preterm babies, 43.03% of the total sample) were contacted to propose they participate in the study, 38 mothers corresponding to 46 babies (corresponding to 64.79 % of the contacted babies and to 27.88% of the total newborn at high risk), were recruited and 22 denied the consent. All the families (mothers and fathers) filled an anonymous socio-demographic questionnaire to evaluate possible differences in the two groups. The most frequent causes of refusal was fear of taking time for the baby or to evaluate or not interested in the project. There were no significant differences in the socio-economical status or in the babies' clinical variables from the subjects that agreed to the study or the ones that didn't. Three families (corresponding to 4 babies, 8.7%), dropped out at the first or second control 40 weeks or 3 months of C.A.) when recalled, they refused to continue with the study. At the end of the project thirty five mothers and 42 high risk preterm babies were enrolled in this study, 21 babies in the control group and 21 in the experimental group. See Figure 2 Data collection flow chart.

Figure 2 Data collection flow chart



Participants

Inclusion criteria:

- gestational age ≤32 weeks and/or birth weight ≤1500 g
- mothers with a good knowledge of spoken and written Italian
- written informed consent

Exclusion criteria:

- diagnosed psychiatric disease or alcohol or drug abuse in one or both parents
- diagnosed genetic/syndromic disease in the baby/ies
- single mother or fathers
- maternal age <18 years or > 45 years

It was chosen to not exclude babies with major clinical consequences related to preterm birth (periventricular leukomalacia, intraventricular haemorrhage, retinopathy of prematurity, etc...).

Statistical analysis

Descriptive statistics were compared by means of *t*-test and Chi-squared for continuous and categorical variables, respectively. Pair wise comparisons of means for questionnaires were carried out using *t*-test for independent samples. As for the EPDS, due to two time-points being available, the comparison was done using an analysis of variance (ANOVA) 2x2 (Group: control *vs.* clinical x Time: T0 *vs.* T1). Independent-sample *t*-tests were also implied to compare the groups for the GRS scores. Finally, to test for the potential moderation role of maternal presence in the NICU on the association between intervention and maternal intrusiveness, a regression model was assessed including two steps: (1) step 1 included only the independent effects of Group and maternal presence in the NICU (expressed in hours and centred) and (2) step 2 included the interaction effect Group x maternal presence in the NICU. Despite the sample size being relatively small, a conservative $p<0.05$ was used as significance cut-off for all the analysis. The statistical analyses were carried out using SPSS 21.0 (IBM).

Results

As planned, the statistical analysis was blind, for all the variables collected for the 42 babies and their mothers. Unfortunately, not all the subjects had complete information. Socio-demographic and clinical information were available for all the infants and mothers. However, 2 subjects from the control group did not complete the questionnaires (including the MSPSS, the EPDS, the PSS-NICU, and the NPST). For these questionnaires, indeed there are 19 subjects available for the control group and 21 subjects for the clinical group. All the subjects returned the MPAS and PSI questionnaires. 17 mother-infant dyads in the control group and 15 mother-infant dyads in the clinical group had completed information for what pertains the GRS scores at T3 (3 months of baby's corrected age). In fact, for many dyads it wasn't possible to record a valid GRS video at T2 (40 weeks of gestational age) because of the great instability of babies at that age. Moreover, at T3 in some videos the mother's face was hidden by the baby bouncer, or the baby started to cry obliging the mother to take the baby in her arms, or in a few cases the video/sound quality (due to instrumental problems) was too poor to evaluate it. We decided together to analyse only the T3 GRS videos of these 31 babies (16 in the experimental group and 15 in the control one).

The two groups (clinical and control) didn't differ significantly in the socio-demographic characteristics ($p>0.5$ at *t*-test for independent variables or at the Chi-squared test) neither analysing the characteristics of the 42 babies enrolled (see Table 1) nor for the 31 babies of which we have a valid GRS video (see Table 2), except for maternal age ($p = 0.31$). The control group mothers are a little older than in the experimental one (mean 35.94 vs 32.07, SD 5.05 vs 4.559).

The analysed variables are mother age, mother educational level, mother SES, gestational age, birth weight, Apgar index, sex, type of delivery (vaginal or caesarean), multiple gestation, criterion of small for gestational age (SGA) at birth,

presence of bronchopulmonary dysplasia, retinopathy of prematurity or periventricular leukomalacia (as VON-RA).

There aren't significant differences in questionnaire results filled by mothers (MSPSS, MPAS, PSI, PSS NICU, NPST and EPDS see Tables 3 and 4), there is only a slightly significant difference in the MSPSS in the subscale "Support from Friends" score (FRI) F (1,38)= 4.40, p = 0.45, eta-squared= 0.10 of difficult interpretation (maybe due to the small sample size).

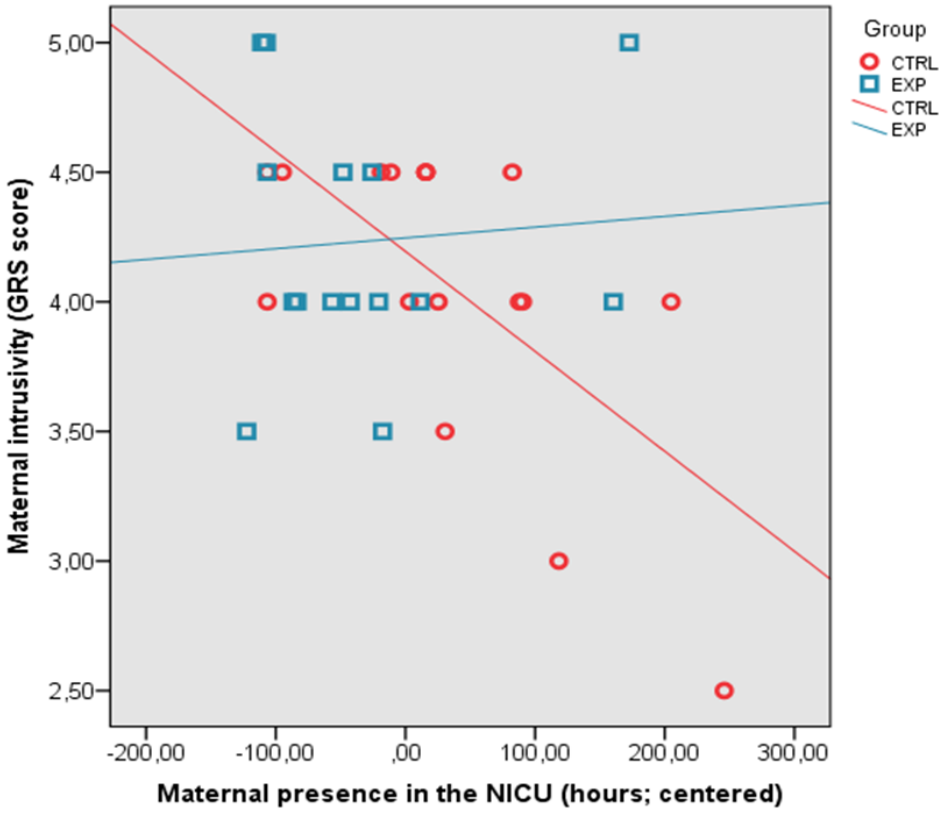
There aren't significant differences in babies' neurological examination, in GMS' scoring at T1, T2 or T3, in the NNNS score and in the behavioural scale at T1 or T2 (See Table 5, Table 6, Table 7).

There aren't significant differences in life events (specifically created questionnaire), but there is a significant difference p = 0.027 in the mother presence (SCENE diary) during the baby hospitalization with a mean of 96.98 hours (SD 75.53) in the experimental group and 178 hours (SD 98.48) in the control group (See Table 8).

There aren't significant differences in GRS scales for children or mothers' scales except for a slight significant difference in the Mother "good_poor index" p = 0.049 (See Table 9). This result is difficult to evaluate both for the small sample size and for the complexity of the index itself. Concerning GRS scales the *maternal intrusiveness* was a very interesting index for the well-known attitude of preterm mothers to became increasingly intrusive with their preterm babies (already cited Compensatory parenting style). Considering also the significant difference in hours of presence in NICU in the two groups, we choose to analyse in a regression model the three variables: group allocation, presence in NICU and intrusiveness (See Table 10). *Maternal intrusiveness* reflects the extent to which mother is over stimulating with verbal and physical intervention so that she disturbs the infant. Higher scores indicate low intrusiveness, low scores indicate high intrusiveness (See Figure 3 and Appendix 1). This model predicts 25% of variance despite using only two variables (group allocation and presence in NICU) that explain only 16% of variance. In the

control group (CTRL) greater presence predicts greater intrusiveness, while in the experimental group (EXP) this effect is not detected (see Figure 3).

Figure 3 Association between presence of mother in NICU and maternal intrusiveness in the two groups.



Note. GRS, Global Rating Scales; The maternal intrusiveness score is inverse (high scores indicate low intrusiveness; low scores indicate high intrusiveness); CTRL: control group; EXP: experimental group; the maternal presence variable was centered with mean = 0 for easier interpretation of interaction and to reduce multicollinearity in the regression model.

Discussion

We thought about an easy to perform and feasible program, with few meetings and a small workload for parents: few questionnaires to fill, only one visit more than usual follow-up for preterm babies at high risk and for the experimental group the possibility to deepen the behavioural characteristics of their child to understand it better during 5 meetings, however about 35% of families contacted refused to participate. Probably the particular situation of NICU, as already seen before, doesn't allow these parents to focus on other aspects of taking care of their child. Despite the fact that the study was proposed only when the babies were considered clinically stable, parents were obviously still very worried about the health conditions of the children, often not concentrating on the project explanation or uneasy in talking with a doctor about behaviour and prematurity. For this reason, we provided the written informed consent available to be read ahead of making a decision. We noticed already that when few parents started to refuse the project after that more other parents did the same, and on the other hand when few families agreed more families were prone to carefully listen and most likely agreed. This situation was probably related to the fact that parents talk about and influence each other, making a more or less favourable emotional climate. For the same reason we choose to take advantage of summer holidays (losing the chance to propose the study to some babies) to prevent the information provided to the experimental group from passing to the control group, therefore leading to biased results.

The scores of all the questionnaires proposed during the project (PSS-NICU, EPDS, MSPSS, NPST, MPAS and PSI) were similar in the two groups, without significant differences. Also, the EPDS and the MSPSS that were compiled at T1 (discharge from hospital) and at T3 (3 months of corrected age follow-up visit), didn't show any significant changes neither between the two groups nor separately in the two groups between the two times. We had hypothesized that the intervention could affect the

maternal emotional state or the impression of being sustained, even though the MSPSS refers to the support perceived by friends and family members not by the staff. It's interesting that all these questionnaires (including EPDS) are self-report forms and that a formal psychiatric evaluation about post-partum depression wasn't done. Clinically there was no evidence of a psychiatric disease, but surely we noticed some "depressive feelings" in those mothers. These results are however consistent with research in which self-report and behavioural observation procedures were compared (Barden, Ford, Jensen, Rogers-Salyer, & Sayler, 1989). That study documented some discrepancy between behavioural observation and self-rating scales (measuring stress, social support, parenting and general life satisfaction) in mother of infants with cranio-facial anomalies. The subjective measure doesn't always capture some negative maternal feelings, leading to some inconsistency with the interpersonal attitudes adopted by mothers in the interactions with their infants. In an original study (Jones, Field, Hart, Lundy, & Davalos, 2001) about interaction in depressed mothers and their infants, they find that self-scoring a videotape of interaction results in a good agreement in choosing one of the two proposed paradigms (over or under-stimulating) but with poor accuracy in the stimulation intensity. A study by Field (Field, Morrow, & Adlestein, 1993) found out that depressed mothers perceived their infants more negatively than other mothers, but they perceived their own behaviours more positively than other mothers. Maybe these mothers have reduction in the perception of the negative affective state that result in the self-report survey. So we can conclude that for our finding the self-evaluation of well-being, depressive symptoms or perceived support from significant others doesn't change with the intervention on parents skills.

We also expected that in the experimental group at least questionnaires on parental stress (like PSI or PSS:NICU) would have a lower score, but there wasn't any kind of effect in that way.

The same thing emerged in the NPST score. Nurses were not to have changed their attitudes towards parents, and this was a clear message during meetings with them

to explain the project. Some mothers asked us if the questionnaire was only reported to nurses or even to us (project staff), and the indication before handing it over was to refer only to nurses. During meetings with mothers, sometimes they said that they found few interlocutors well aware and sensitive about behaviour and resources of preterm babies. It has to be pointed out that the NICU where the study was carried out is technically front level with a high degree of attention on survival of children reducing as much as possible sequelae associated to preterm birth. However less focus is devoted to Developmental care approach and support to the highly fragile parent-child relationship which is stressed by the occasion of a preterm birth. There are studies which demonstrate that pre-term birth is a real traumatic event which can trigger a real distress in parents and in particular, in mothers (Kersting, et al., 2004), (Muller-Nix, Forcada-Guex, Pierrehumbert, Jaunin, Borghini, & Ansermet, 2004), (Borghini, et al., 2014).

Some other studies (Flacking, et al., Closeness and separation in neonatal intensive care, 2012) and (Raiskila, et al., 2017) highlight that in order to establish an effective mother-child relationship, physical closeness and the emotional closeness must occur and how the two are interconnected. These two groups differ in a significant way in hours of presence in NICU (See Table 8), but don't in the GRS scales at 3 months of age except for Maternal "good_poor index" with a slight significance (See Table 9). This result is quite difficult to interpret due to the composite nature of this index that include: maternal emotional warmth, responsiveness to baby's signals, acceptance of baby's signals, maternal requests, maternal sensitivity. This dimension captures the extent to which the mother responds to her infant's cues in a way that is appropriately adjusted to the infant's behaviour, responding to his/her agenda, and also measures warmth and acceptance. There are a lot of different aspects synthesised in this index and with a small sample size it is very difficult to give a clear meaning to this result. Analysing the other GRS index the maternal intrusiveness was the more indicated to be combined with the hour of presence in NICU, that is significantly different in the two groups. Maternal intrusiveness was

therefore analysed in a regression model controlled by hours of maternal presence, as is well known that mothers of preterm babies tend to be more intrusive than mothers of term babies, independently from other babies characteristics and that intrusiveness is well correlated to hours of presence. In that model (see Figure 3) it is very clear that the presence (expressed in hours) in NICU is linked to maternal intrusiveness at GRS scores. In the control group (CTRL) greater presence predicts greater intrusiveness, while in the experimental group (EXP) this effect is not detected. Therefore, the intervention appears to have a protective effect in the mother-child dyads that benefited from early intervention.

We found that there aren't any significant differences between experimental and control group in socio-demographic or clinical variables, and also with the group that denied the consent, so they are comparable groups. There is a significant difference in the mother age and some slight differences in the two final groups for the maternal socio-demographic characteristics and birth gestational age and weight, in favour of the control group. Indeed, that babies were little more mature and the mothers a little more aged, with a better educational level and SES. These differences, sustain that it is the intervention that protects mothers becoming intrusive with their babies and not other factors like a higher social and intellectual level or a little more reactive baby because a little more mature.

Study limits

The most evident limit of this work is the small sample size. In fact during the 24 months we proposed the study, of 165 high risk preterm newborn (gestational age ≤32 weeks and/or birth weight ≤1500 g) only 60% (100 babies) were eligible for the study and about 30% of the total ones agreed. This is a big problem in this kind of project, we wanted to try a very early intervention (during hospitalization) but we also know that obviously parents are in a very upset mental state, they are very worried about their baby's health conditions and rightly focused more on survival than on their child's behaviour. Probably all these aspects had significantly

influenced the level of adhesion to the study, which is, however, not too far from those found in other trials.

Secondly, we didn't find any differences in neurobehavioral aspects or in the GRS scale baby oriented in the two groups. Probably three months of corrected age is a too short period to find some significant difference, the Sensory-motor scale for neonates (Martinet, Boradori Tolsa, Rossi Jelidi, Bullinger, Perneger, & Pfister, 2013) showed some discrepancy but not statistically significant, small sample size or maybe not sufficient sensitivity of the instrument, could explain this result. We are now collecting data about neuro-developmental level and behaviour of these children who will undergo the neurological and Griffiths-R evaluation at 24 months of corrected age. We also planned to assess behaviour with the Child Behaviour Check-list (CBCL) questionnaire and clinical observation to evaluate possible long term effects.

The third big question is how to assess parental (in this case maternal) well-being, perceptive support, depressive symptoms in a more effective and sensible way. We had the impression of a different mood and attitude in mothers of the experimental group (also sustained by the results of regression model about maternal intrusiveness), but we couldn't detect it. The small sample size already should be an obstacle, maybe with more data we would have some significant results.

The fact that in this NICU there isn't (as explained above) an official and collective attention and sensitivity to developmental aspects (it mostly depends on staff personal attitude and interest) may have influenced our project results. In particular, we didn't find a specific attention to help and improve parental skills and sense of effectiveness, we had the impression that parents are seen often more as a complication than a resource. Poor and restricted staff-parent interaction and communication can exacerbate parent's sense of isolation from their preterm infants. It has in fact already been suggested that parents' negative experience associated with prematurity can lead them to withdraw physically and emotionally, thereby handing over the care of their infants to staff (Arockiasamy, Holsti, & Albersheim,

2008), (Flacking, Ewald, Nyqvist, & Starrin, 2006). In recruiting families, we quite often found difficulties in finding parents beside the baby's cradle, also in extremely variable time of the day. The expert knowledge of technology, policies and procedures of the NICU placed nursery personnel in a position of authority relative to the mothers and their babies. Thus, nursery personnel could potentially use their power to rank themselves above the mothers in their interactions (Hurst, 2001 b). Yet when mothers took actions to negotiate collaborative relationships and participate as equal partners in their babies' care, the mothers' actions often went unrecognized or were misunderstood by health care providers. As a consequence, many mothers became guarded, developing varying degrees of trust in health care providers. This kind of mentality is very diffuse and already evidenced in other studies (Flacking, et al., 2012), (Ahlqvist-Björkroth, 2017), (Montirosso, Provenzi, Calciolari, Borgatti, & Group, 2012), and is very comprehensible for staff who are focused on ensuring the survival for these children. However, it's increasingly evident that a deep change in this way of seeing the NICU's work, involving in each possible occasion parents in taking care of their babies could help babies, families and staff in carrying out their roles better. A major barrier to involve parents is mothers' fears about the ramifications of their actions on their babies' care. Partnerships between health care providers and NICU families in which both are equal participants is important in addressing such fears. The mothers understood that there would necessarily be multiple caregivers for their babies. The mothers' concerns and attendant actions, properly recognized by all health care providers, provide an important opportunity to partner with families and create a mutually beneficial model (Hurst, 2001 a). It's shown that when the parents were supported to be the caregivers, the atmosphere of the unit changes to be more welcoming for the parents, which facilitated their presence and physical closeness with the infant (Axelin, Ahlqvist-Bjorkroth, Kauppila, Boukydis, & Lehtonen, 2014). Probably further multi-centre studies could help to overcome limits of the small sample size and the specificity of a single NICU,

helping to better assess the real impact of the intervention on mothers and consequently on their attitude towards their babies.

Furthermore, our intervention was consciously planned to be very easy, feasible and low cost, but could be improved. During the project we noticed that three months between the first and the second follow-up visit it's a too long a period. We didn't want to plan staff home visits, because it would be very expensive and not easy (Pavia's NICU is a third level unit and most of the families come from quite far away in the territory), but we think that we could make some planned telephone calls to give parents the opportunity of asking question and clarifying doubts. This implementation wouldn't be difficult or expensive and probably could help parents involved in feeling more sustained in their role.

There are increasing amounts of studies about environmental factors and their role in epigenetics, the elements analysed are for instance prenatal stress (Cao-Lei, et al., 2017), parental and infant interactions and maternal sensitivity (Provenzi, et al., 2017) and early protective experiences (Provenzi, Guida, & Montirosso, 2017). For these reasons we were very disappointed that it wasn't possible to carry out the analysis of cortisol in preterm nails as a biochemical marker of perinatal stress, we think that further studies in these fields would be very useful in planning care of these infants.

A biological outcome of babies stress or babies cerebral maturation would have been more quantifiable and objective. We have chose neurobehavioural measures (like NNNS or GMS' videotaping) that where less sensitive for this purpose, especially because our project has not been funded in any way, so could not include this type of exams. In further studies would be useful planning other kind of outcome like cortisol dosage or maybe cerebral RMN, as already tried (Ferrie, et al., 1999), (Milgrom, et al., 2010).

Conclusions

The intervention appears to have had a protective effect in the mother-child dyads that benefited from early intervention. Indeed, the regression model about GRS scale "Maternal Intrusiveness" lead us to sustain that the intervention played a role in changing maternal attitude towards their preterm babies and despite there not being a promoting effect (as we had wished for at the beginning of the study), probably there was a protective effect. Mothers in the experimental group didn't become intrusive after already having passed a considerable period of time in NICU.
It is not enough that mothers spend a lot of time in NICU (and therefore open it 24 hours a day), on the contrary it can become counterproductive. The mothers left alone without support and guidance, may face even more difficulties in establishing a meaningful and positive relationship with their premature babies. As theorized in the transactional model of developmental risk (Sameroff & Fiese, 2000) at any point of development, new risk conditions may worsen previous ones, at the same time, intervening protective conditions may compensate pre-existent disadvantaged conditions (Coppola, Cassibba, & Costantini, 2007). The quality of parent-child interactions is considered paramount in supporting children's development, serving as the foundation for secure attachment, development of joint attention and emotion regulation, and later cognitive and social emotional development (Ainswotrh, Blehar, Waters, & Wall, 1978), (Thompson, 2008).
Furthermore, psychological well-being of the parents of preterm infants has a long-term impact in terms of later child behaviour (Huhtala, et al., 2012). A mother's positive affective and behavioural involvement in the NICU was related to parenting two years later, which has clinical implication for supportive interventions in the NICU in a family-centred care model (Gerstein, Poehlmann-Tynan, & Clark, 2015). The Family Centred Care model in NICU is an approach that encourages and provides the necessary resources for families to participate as fully as possible in

caring and making decisions for their hospitalized babies and respects the diversity of families and their values and beliefs, thereby facilitating the formation of mutually beneficial and supportive partnerships in the NICU and beyond (Harrison, 1993), (Dobbins, Bohlig, & Sutphen, 1994). However, this kind of intervention is usually quite expensive in terms of time, cost and staff involvement, instead this small, easy, low cost program has demonstrated to have a clear protective role on maternal intrusiveness. Moms who had the possibility to understand and observe with the guide of experts their babies characteristics, behaviour and resources are more sensitive and less pressing. They are more capable of waiting for reaction times of their babies and to tune better with their child. We think that this is a very good result for such a small intervention that could be applied in every NICU and became part of the routine intervention with minimal effort.

Tables

Table 1 Babies' perinatal/clinical variables and socio-demographic variables in experimental and control group (total sample of 42 children)

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Gestational age (weeks)	CTRL	21	30,38	2,783	,607
	EXP	21	29,57	2,959	,646
Birth weight (grams)	CTRL	21	1.309,90	307,706	67,147
	EXP	21	1.244,57	345,405	75,374
Apgar (minute 1)	CTRL	21	6,43	1,630	,356
	EXP	21	5,57	1,777	,388
Apgar (minute 5)	CTRL	21	8,19	1,209	,264
	EXP	21	7,71	1,927	,421
Mother age	CTRL	21	35,24	5,059	1,104
	EXP	21	32,57	4,781	1,043
Mother educational level	CTRL	21	4,05	1,322	,288
	EXP	21	3,81	1,601	,349
Mother SES	CTRL	21	3,43	2,839	,619
	EXP	21	3,05	2,376	,519
Family SES	CTRL	21	1,81	1,030	,225
	EXP	21	2,05	1,244	,271

		t-test for Equality of Means						
		T	df	**Sig. (2-tailed)**	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
Gestational age (weeks)	Equal variances assumed	,913	40	,367	,810	,887	-,982	2,601
	Equal variances not assumed	,913	39,851	,367	,810	,887	-,982	2,601
Birth weight (grams)	Equal variances assumed	,647	40	,521	65,333	100,945	-138,684	269,351
	Equal variances not assumed	,647	39,477	,521	65,333	100,945	-138,768	269,435
Apgar (minute 1)	Equal variances assumed	1,629	40	,111	,857	,526	-,206	1,921
	Equal variances not assumed	1,629	39,706	,111	,857	,526	-,207	1,921
Apgar (minute 5)	Equal variances assumed	,959	40	,343	,476	,496	-,527	1,480
	Equal variances not assumed	,959	33,632	,344	,476	,496	-,533	1,486
Mother age	Equal variances assumed	1,756	40	,087	2,667	1,519	-,403	5,736
	Equal variances not assumed	1,756	39,873	,087	2,667	1,519	-,403	5,737
Mother educational level	Equal variances assumed	,526	40	,602	,238	,453	-,677	1,154
	Equal variances not assumed	,526	38,621	,602	,238	,453	-,678	1,155
Mother SES	Equal variances assumed	,472	40	,640	,381	,808	-1,252	2,014
	Equal variances not assumed	,472	38,801	,640	,381	,808	-1,253	2,015
Family SES	Equal variances assumed	-,675	40	,503	-,238	,353	-,951	,474
	Equal variances not assumed	-,675	38,661	,503	-,238	,353	-,951	,475

No significant differences between groups.

Table 2 Babies' perinatal and clinical variables and socio-demographic variables in the smaller sample (31 babies)

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Gestational age (weeks)	CTRL	17	30,76	2,538	,616
	EXP	15	29,60	3,180	,821
Birth weight (grams)	CTRL	17	1.343,18	304,799	73,925
	EXP	15	1.246,00	365,178	94,288
Apgar (minute 1)	CTRL	17	6,59	1,661	,403
	EXP	15	5,53	1,767	,456
Apgar (minute 5)	CTRL	17	8,12	1,317	,319
	EXP	15	7,47	2,134	,551
Mother age	CTRL	17	35,94	5,056	1,226
	EXP	15	32,07	4,559	1,177
Mother educational level	CTRL	17	4,18	1,380	,335
	EXP	15	3,73	1,792	,463
Mother SES	CTRL	17	3,35	2,871	,696
	EXP	15	3,07	2,576	,665
Family SES	CTRL	17	1,65	,931	,226
	EXP	15	2,20	1,320	,341

		t-test for Equality of Means						
		t	df	**Sig. (2-tailed)**	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
Gestational age (weeks)	Equal variances assumed	1,151	30	,259	1,165	1,012	-,901	3,231
	Equal variances not assumed	1,135	26,761	,266	1,165	1,026	-,942	3,271
Birth weight (grams)	Equal variances assumed	,820	30	,418	97,176	118,437	-144,704	339,057
	Equal variances not assumed	,811	27,432	,424	97,176	119,813	-148,479	342,832
Apgar (minute 1)	Equal variances assumed	1,740	30	,092	1,055	,606	-,183	2,293
	Equal variances not assumed	1,733	28,940	,094	1,055	,609	-,190	2,300
Apgar (minute 5)	Equal variances assumed	1,052	30	,301	,651	,619	-,612	1,914
	Equal variances not assumed	1,022	22,749	,317	,651	,637	-,667	1,969
Mother age	Equal variances assumed	2,264	30	**,031**	3,875	1,711	,380	7,369
	Equal variances not assumed	2,280	29,980	**,030**	3,875	1,700	,403	7,346
Mother educational level	Equal variances assumed	,789	30	,436	,443	,562	-,704	1,590
	Equal variances not assumed	,776	26,211	,445	,443	,571	-,730	1,616
Mother SES	Equal variances assumed	,295	30	,770	,286	,970	-1,694	2,267
	Equal variances not assumed	,297	29,987	,768	,286	,963	-1,681	2,253
Family SES	Equal variances assumed	-1,382	30	,177	-,553	,400	-1,370	,264
	Equal variances not assumed	-1,352	24,812	,189	-,553	,409	-1,395	,290

Not significant differences between groups.

Table 3 Parents questionnaires scores

	Group	N	Mean	Std. Deviation	Std. Error Mean
Support from significant others	CTRL	16	26,5000	3,42540	,85635
	EXP	15	27,0000	2,00000	,51640
Support from family members	CTRL	16	25.6875	2.89180	.72295
	EXP	15	25.2000	4.19524	1.08321
Support from friends	CTRL	16	24.8750	3.77492	.94373
	EXP	15	20.4000	7.60451	1.96348
Support from significant others	CTRL	17	26.1765	3.08697	.74870
	EXP	15	27.0000	1.55839	.40237
Support from family members	CTRL	17	24.5882	3.89003	.94347
	EXP	15	25.8000	3.09839	.80000
Support from friends	CTRL	17	23.9412	3.30663	.80198
	EXP	15	23.0000	5.23723	1.35225
Quality of postnatal attachment	CTRL	17	40.9235	2.99051	.72531
	EXP	15	41.0533	2.87225	.74161
Absence of Hostility	CTRL	17	19.3353	1.62786	.39481
	EXP	15	19.0400	1.81139	.46770
Pleasure of interaction	CTRL	17	23.7647	1.98524	.48149
	EXP	15	23.6000	1.18322	.30551
Defence response by mothers	CTRL	17	11.8824	3.01833	.73205
	EXP	15	13.3333	3.19970	.82616
Mothers Stress	CTRL	17	21.4118	5.09974	1.23687
	EXP	15	22.8667	5.55321	1.43383
Mother Dysfunctional relationship	CTRL	17	14.7059	4.10434	.99545
	EXP	15	15.6667	3.63842	.93944
Difficult baby (mother)	CTRL	17	18.7059	5.54262	1.34428
	EXP	15	18.0667	5.24359	1.35389
Total stress Mother	CTRL	17	54.8235	13.33808	3.23496
	EXP	15	56.6000	11.29349	2.91597
Stress Occurence Level PSS - Visual stimuli	CTRL	16	2.2333	.78909	.19727
	EXP	15	2.5422	.93753	.24207
Stress Occurence Level PSS - Aspect	CTRL	16	3.0039	.86682	.21670
	EXP	15	3.1422	1.16248	.30015
Stress Occurence Level PSS - Parental Role	CTRL	16	3.6830	1.12814	.28203
	EXP	15	3.8159	.93259	.24079
Stress Occurence Level PSS - Total score	CTRL	16	3.0229	.81671	.20418
	EXP	15	3.2069	.95541	.24669
Overall stress level PSS - Visual and hearing stimuli	CTRL	16	2.1771	.74652	.18663
	EXP	15	2.4556	.94799	.24477
Overall stress level PSS - Baby's aspect and behaviour	CTRL	16	2.2212	.95206	.23801
	EXP	15	2.6308	1.36902	.35348
Overall stress level PSS - mother-baby relationship	CTRL	16	3.6071	1.22946	.30736
	EXP	15	3.7143	1.06221	.27426
Overall stress level PSS - Total Score	CTRL	16	2.5841	.83077	.20769
	EXP	15	2.8821	1.10352	.28493
NPST Total Score	CTRL	16	3.8988	.76525	.19131
	EXP	15	3,3841	,65822	,16995

		t-test for Equality of Means						
		T	df	**Sig. (2-tailed)**	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
Support from significant others	Equal variances assumed	-,492	29	,627	-,50000	1,01653	-2,57904	1,57904
	Equal variances not assumed	-,500	24,431	,622	-,50000	1,00000	-2,56197	1,56197
Support from family members	Equal variances assumed	,379	29	,708	,48750	1,28692	-2,14455	3,11955
	Equal variances not assumed	,374	24,680	,711	,48750	1,30230	-2,19641	3,17141
Support from friends	Equal variances assumed	2,096	29	**,045**	4,47500	2,13495	,10853	8,84147
	Equal variances not assumed	2,054	20,209	**,053**	4,47500	2,17850	-,06626	9,01626
Support from significant others	Equal variances assumed	-,932	30	,359	-,82353	,88318	-2,62722	,98017
	Equal variances not assumed	-,969	24,264	,342	-,82353	,84998	-2,57678	,92972
Support from family members	Equal variances assumed	-,966	30	,342	-1,21176	1,25498	-3,77478	1,35125
	Equal variances not assumed	-,980	29,720	,335	-1,21176	1,23699	-3,73903	1,31550
Support from friends	Equal variances assumed	,616	30	,543	,94118	1,52907	-2,18160	4,06395
	Equal variances not assumed	,599	23,082	,555	,94118	1,57218	-2,31048	4,19283
Quality of postnatal attachment	Equal variances assumed	-,125	30	,902	-,12980	1,04004	-2,25384	1,99423
	Equal variances not assumed	-,125	29,764	,901	-,12980	1,03733	-2,24902	1,98941
Absence of Hostility	Equal variances assumed	,486	30	,631	,29529	,60787	-,94614	1,53673
	Equal variances not assumed	,482	28,430	,633	,29529	,61206	-,95761	1,54819
Pleasure of interaction	Equal variances assumed	,280	30	,781	,16471	,58802	-1,03618	1,36559
	Equal variances not assumed	,289	26,557	,775	,16471	,57023	-1,00623	1,33564
Defence response by mothers	Equal variances assumed	-1,319	30	,197	-1,45098	1,09968	-3,69683	,79487
	Equal variances not assumed	-1,314	28,982	,199	-1,45098	1,10383	-3,70863	,80667
Mothers Stress	Equal variances assumed	-,773	30	,446	-1,45490	1,88323	-5,30098	2,39117
	Equal variances not assumed	-,768	28,688	,449	-1,45490	1,89360	-5,32958	2,41977
Mother Dysfunctional relationship	Equal variances assumed	-,697	30	,491	-,96078	1,37938	-3,77786	1,85629
	Equal variances not assumed	-,702	29,998	,488	-,96078	1,36874	-3,75614	1,83457
Difficult baby (mother)	Equal variances assumed	,334	30	,741	,63922	1,91475	-3,27122	4,54965
	Equal variances not assumed	,335	29,837	,740	,63922	1,90791	-3,25814	4,53658

Total stress Mother	Equal variances assumed	-,404	30	,689	-1,77647	4,40182	-10,76618	7,21324
	Equal variances not assumed	-,408	29,959	,686	-1,77647	4,35521	-10,67150	7,11855
Stress Occurence Level PSS - Visual stimuli	Equal variances assumed	-,995	29	,328	-,30889	,31050	-,94393	,32615
	Equal variances not assumed	-,989	27,465	,331	-,30889	,31227	-,94911	,33133
Stress Occurence Level PSS - Aspect	Equal variances assumed	-,377	29	,709	-,13833	,36669	-,88830	,61165
	Equal variances not assumed	-,374	25,845	,712	-,13833	,37020	-,89951	,62286
Stress Occurence Level PSS - Parental Role	Equal variances assumed	-,356	29	,724	-,13284	,37318	-,89607	,63040
	Equal variances not assumed	-,358	28,572	,723	-,13284	,37084	-,89179	,62612
Stress Occurence Level PSS - Total score	Equal variances assumed	-,578	29	,568	-,18402	,31856	-,83556	,46752
	Equal variances not assumed	-,575	27,644	,570	-,18402	,32022	-,84035	,47231
Overall stress level PSS - Visual and hearing stimuli	Equal variances assumed	-,912	29	,369	-,27847	,30540	-,90309	,34615
	Equal variances not assumed	-,905	26,614	,374	-,27847	,30780	-,91046	,35352
Overall stress level PSS - Baby's aspect and behaviour	Equal variances assumed	-,972	29	,339	-,40962	,42122	-1,27111	,45188
	Equal variances not assumed	-,961	24,812	,346	-,40962	,42614	-1,28761	,46838
Overall stress level PSS - mother-baby relationship	Equal variances assumed	-,259	29	,798	-,10714	,41394	-,95374	,73945
	Equal variances not assumed	-,260	28,820	,797	-,10714	,41194	-,94988	,73559
Overall stress level PSS - Total Score	Equal variances assumed	-,853	29	,401	-,29792	,34935	-1,01242	,41659
	Equal variances not assumed	-,845	25,983	,406	-,29792	,35259	-1,02270	,42687
NPST Total Score	Equal variances assumed	2,001	29	,055	,51468	,25718	-,01131	1,04067
	Equal variances not assumed	2,011	28,800	,054	,51468	,25590	-,00885	1,03821

Table 4 EPDS score at T0 and at T3

Descriptive Statistics

	Group	Mean	Std. Deviation	N
EPDS_T0_score	CTRL	18,8125	2,76209	16
	EXP	16,8000	3,07525	15
	Total	17,8387	3,04518	31
EPDS_T3_score	CTRL	18,6875	2,62599	16
	EXP	17,3333	3,97612	15
	Total	18,0323	3,36139	31

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	Df	Mean Square	F	**Sig.**	Partial Eta Squared
Time	Sphericity Assumed	,645	1	,645	,123	,729	,004
	Greenhouse-Geisser	,645	1,000	,645	,123	,729	,004
	Huynh-Feldt	,645	1,000	,645	,123	,729	,004
	Lower-bound	,645	1,000	,645	,123	,729	,004
time * Group	Sphericity Assumed	1,678	1	1,678	,319	,577	,011
	Greenhouse-Geisser	1,678	1,000	1,678	,319	,577	,011
	Huynh-Feldt	1,678	1,000	1,678	,319	,577	,011
	Lower-bound	1,678	1,000	1,678	,319	,577	,011
Error(time)	Sphericity Assumed	152,742	29	5,267			
	Greenhouse-Geisser	152,742	29,000	5,267			
	Huynh-Feldt	152,742	29,000	5,267			
	Lower-bound	152,742	29,000	5,267			

Table 5 results of behavioural evaluation and GMs videotaping

Variable	*Mean CTRL*	*SD CTRL*	*Mean EXP*	*SD EXP*	*t*	***p***
Sensory-Motor Scale	24.60	3.22	26.26	1.94	-1.97	.060
Sensory-Motor Scale	24.38	2.66	24.95	2.35	-0.71	.48
Variable	*Mean CTRL*	*SD CTRL*	*Mean EXP*	*SD EXP*	*Chi-square*	***p***
GMS_T1	.48	.68	.63	.60	1.57	.21
GMS_T2	.38	.67	.50	.71	.46	.50
GMS_T3	3.33	.58	3.47	.51	2.12	.15

Table 6 Results of NNNS Attention (Orientation) subscale at T1

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Nnisliv	CTRL	13	5,38	2,631	,730
	EXP	12	3,67	2,229	,644
Nnislia	CTRL	14	5,14	1,512	,404
	EXP	11	5,45	1,809	,545
Nnislib	CTRL	15	6,33	2,410	,622
	EXP	12	4,75	2,301	,664
Nnislav	CTRL	15	6,47	1,727	,446
	EXP	12	6,50	1,382	,399
Nnislaa	CTRL	13	5,77	1,536	,426
	EXP	10	7,00	1,633	,516
Nnislab	CTRL	15	6,60	2,324	,600
	EXP	13	6,85	1,144	,317

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	**Sig. (2-tailed)**	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
nnisliv	Equal variances assumed	,438	,515	1,754	23	,093	1,718	,980	-,309	3,745
	Equal variances not assumed			1,766	22,848	,091	1,718	,973	-,296	3,731
nnislia	Equal variances assumed	,671	,421	-,470	23	,643	-,312	,664	-1,685	1,062
	Equal variances not assumed			-,459	19,475	,651	-,312	,679	-1,730	1,107
nnislib	Equal variances assumed	,287	,597	1,730	25	,096	1,583	,915	-,301	3,468
	Equal variances not assumed			1,739	24,160	,095	1,583	,910	-,295	3,461
nnislav	Equal variances assumed	1,644	,212	-,054	25	,957	-,033	,614	-1,297	1,230
	Equal variances not assumed			-,056	24,998	,956	-,033	,598	-1,265	1,199
nnislaa	Equal variances assumed	,124	,728	-1,854	21	,078	-1,231	,664	-2,611	,150
	Equal variances not assumed			-1,839	18,865	,082	-1,231	,669	-2,633	,171
nnislab	Equal variances assumed	6,300	,019	-,347	26	,732	-,246	,710	-1,706	1,213
	Equal variances not assumed			-,363	21,004	,720	-,246	,679	-1,658	1,165

Table 7 Results of NNNS Attention (Orientation) subscale at T2

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
NNNS_T2_VI	CTRL	18	5,67	2,497	,589
	EXP	16	5,31	2,442	,610
NNNS_T2_UI	CTRL	15	4,80	1,082	,279
	EXP	15	4,33	,900	,232
NNNS_T2_VUI	CTRL	17	5,71	2,201	,534
	EXP	16	6,50	1,549	,387
NNNS_T2_VA	CTRL	19	7,05	1,177	,270
	EXP	16	7,00	1,461	,365
NNNS_T2_UA	CTRL	14	7,00	1,797	,480
	EXP	11	6,36	1,804	,544
NNNS_T2_VUA	CTRL	19	7,47	,841	,193
	EXP	16	7,31	1,078	,270

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	**Sig. (2-tailed)**	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
NNNS_T2_VI	Equal variances assumed	,001	,978	,417	32	,679	,354	,849	-1,375	2,084
	Equal variances not assumed			,418	31,688	,679	,354	,848	-1,374	2,082
NNNS_T2_UI	Equal variances assumed	,538	,469	1,284	28	,210	,467	,363	-,278	1,211
	Equal variances not assumed			1,284	27,096	,210	,467	,363	-,279	1,212
NNNS_T2_VUI	Equal variances assumed	2,391	,132	-1,191	31	,243	-,794	,667	-2,154	,565
	Equal variances not assumed			-1,204	28,772	,238	-,794	,660	-2,144	,555
NNNS_T2_VA	Equal variances assumed	,693	,411	,118	33	,907	,053	,446	-,854	,959
	Equal variances not assumed			,116	28,735	,909	,053	,454	-,877	,982
NNNS_T2_UA	Equal variances assumed	,353	,558	,877	23	,389	,636	,725	-,864	2,137
	Equal variances not assumed			,877	21,583	,390	,636	,726	-,870	2,143
NNNS_T2_VUA	Equal variances assumed	1,136	,294	,497	33	,623	,161	,324	-,499	,821
	Equal variances not assumed			,486	28,154	,631	,161	,332	-,518	,840

Table 8 Hours of maternal presence in NICU

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
PRE_h_md	CTRL	14	178,2968	98,48222	26,32048
	EXP	12	96,9792	73,53735	21,22840

		t-test for Equality of Means						
		t	df	**Sig. (2-tailed)**	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
PRE_h_md	Equal variances assumed	2,351	24	**,027**	81,31768	34,59226	9,92276	152,71260
	Equal variances not assumed	2,405	23,608	**,024**	81,31768	33,81439	11,46683	151,16853

Table 9 GRS results at T3 (3 months of corrected age)

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
M_goodpoor	CTRL	17	3,7765	,48416	,11743
	EXP	15	3,4000	,54511	,14075
M_intrusive_remote	CTRL	17	-,1912	,34832	,08448
	EXP	15	,0500	,56061	,14475
M_intrusive	CTRL	17	4,0588	,58316	,14144
	EXP	15	4,2333	,49522	,12786
M_remote	CTRL	17	4,4412	,46376	,11248
	EXP	15	4,1333	1,09327	,28228
M_depres	CTRL	17	4,0588	,34832	,08448
	EXP	15	3,6333	,82303	,21251
I_goodpoor	CTRL	17	3,1765	,63593	,15424
	EXP	15	2,8889	,91432	,23608
I_inert_fretful	CTRL	17	-,0441	,38315	,09293
	EXP	15	-,2778	,35449	,09153
I_inert	CTRL	17	3,4706	,57806	,14020
	EXP	15	3,1111	,82295	,21249
I_fretful	CTRL	17	3,5588	,39061	,09474
	EXP	15	3,6667	,61721	,15936
D_global	CTRL	17	3,3412	,66620	,16158
	EXP	15	2,7967	,92591	,23907

		t-test for Equality of Means						
		t	df	**Sig. (2-tailed)**	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
M_goodpoor	Equal variances assumed	2,070	30	**,047**	,37647	,18191	,00497	,74797
	Equal variances not assumed	2,054	28,283	**,049**	,37647	,18330	,00117	,75177
M_intrusive_remote	Equal variances assumed	-1,481	30	,149	-,24118	,16287	-,57379	,09144
	Equal variances not assumed	-1,439	22,843	,164	-,24118	,16760	-,58801	,10566
M_intrusive	Equal variances assumed	-,906	30	,372	-,17451	,19267	-,56800	,21898
	Equal variances not assumed	-,915	29,965	,367	-,17451	,19067	-,56392	,21490
M_remote	Equal variances assumed	1,060	30	,298	,30784	,29050	-,28544	,90112
	Equal variances not assumed	1,013	18,393	,324	,30784	,30386	-,32958	,94526
M_depres	Equal variances assumed	1,946	30	,061	,42549	,21861	-,02096	,87194
	Equal variances not assumed	1,861	18,373	,079	,42549	,22868	-,05425	,90523
I_goodpoor	Equal variances assumed	1,043	30	,305	,28758	,27572	-,27552	,85068
	Equal variances not assumed	1,020	24,583	,318	,28758	,28199	-,29370	,86886
I_inert_fretful	Equal variances assumed	1,782	30	,085	,23366	,13109	-,03406	,50138
	Equal variances not assumed	1,791	29,920	,083	,23366	,13043	-,03275	,50007
I_inert	Equal variances assumed	1,443	30	,159	,35948	,24905	-,14915	,86810
	Equal variances not assumed	1,412	24,740	,170	,35948	,25457	-,16510	,88405
I_fretful	Equal variances assumed	-,598	30	,554	-,10784	,18034	-,47614	,26045
	Equal variances not assumed	-,582	23,117	,566	-,10784	,18540	-,49126	,27557
D_global	Equal variances assumed	1,926	30	,064	,54451	,28268	-,03281	1,12183
	Equal variances not assumed	1,887	25,124	,071	,54451	,28855	-,04962	1,13864

Table 10 GRS and hours of presence regression

DescriptiveStatistics

	Mean	Std. Deviation	N
M_intrusive	4,0542	,53176	31
Group	,55	,506	31
PRE_h_md	132,1237	101,37079	31
GR_x_pres	54,0108	79,35097	31

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	ChangeStatistics				
					R SquareChange	F Change	df1	df2	Sig. F Change
1	,408[a]	,166 [a]	,107	,50256	,166	2,793	2	28	,078
2	,499[b]	**,249 [b]**	,165	,48584	,082	2,961	1	27	,097

a. Predictors: (Constant), PRE_h_md, Group

b. Predictors: (Constant), PRE_h_md, Group, GR_x_pres

ANOVA[a]

Model		Sum of Squares	Df	MeanSquare	F	Sig.
1	Regression	1,411	2	,706	2,793	,078[b]
	Residual	7,072	28	,253		
	Total	8,483	30			
2	Regression	2,110	3	,703	2,980	**,049[c]**
	Residual	6,373	27	,236		
	Total	8,483	30			

a. Dependent Variable: M_intrusive

b. Predictors: (Constant), PRE_h_md, Group

c. Predictors: (Constant), PRE_h_md, Group, GR_x_pres

Model		UnstandardizedCoefficients		StandardizedCoefficients	t	**Sig.**	95,0% ConfidenceInterval for B		Correlations			CollinearityStatistics	
		B	Std. Error	Beta			Lower Bound	UpperBound	Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	4,104	,216		19,036	,000	3,662	4,546					
	Group	,241	,195	,229	1,234	,227	-,159	,641	,327	,227	,213	,862	1,160
	PRE_h_md	-,001	,001	-,263	-1,413	,169	-,003	,001	-,348	-,258	-,244	,862	1,160
2	(Constant)	4,348	,252		17,249	,000	3,831	4,865					
	Group	-,187	,312	-,177	-,598	,555	-,827	,454	,327	-,114	-,100	,316	3,169
	PRE_h_md	-,003	,001	-,531	-2,232	**,034**	-,005	,000	-,348	-,395	-,372	,491	2,038
	GR_x_pres	,003	,002	,489	1,721	,097	-,001	,007	,249	,314	,287	,345	2,900

a. Dependent Variable: M_intrusive

Appendix1

Outline of the summary indexes by Global Rating Scales (GRS) Encoding System

Mother

- The *maternal sensitivity* dimension captures the extent to which the mother responds to her infant's cues in a way that is appropriately adjusted to the infant's behaviour, responding to his/her agenda, and also measures warmth and acceptance. Higher scores indicate higher competence.
- The *maternal intrusiveness* reflects the extent to which mother is over stimulating with verbal and physical intervention so that she disturbs the infant. Higher scores indicate higher intrusiveness.
- The *maternal remoteness* measures the extent of mother's capacity to participate actively in the interaction with the infant both through body and verbal channels. Higher scores indicate higher maternal involvement.
- The *signs of depression* dimension captures the outward impression of the mother' s affective state and the level of her enjoyment in interacting with her infant. The dimension is related to the depressive person's experience of low energy, psychomotor retardation and indicates the extent to which the mother is really engaged with her infant and is not thinking about her own experience. Higher scores indicate higher mother's enjoyment and fewer maternal signs of depression in the interaction with the infant.

Infant

- The *level of communication* captures infant's ability to engage with the mother through the verbal channel (positive vocalizations) and non-verbal (eye-contact, pre-speech). High scores indicate that the infant establishes high level of communication.

- The *infant involvement* measures the infant's ability to actively participate in the interaction and mother's capacity to be involved with the caregiver. Higher scores indicate that the infant is more actively engaged with his/her mother.
- The *positive emotionality* indicates if during the interaction with the mother the infant shows pleasure, smiling and laughter, level of positive effect shown by the infant. Higher scores indicate higher levels of positive emotionality.

Interaction

- The *mutual engagement* is a dimension which assesses the ability of the mother and infant to interact with each other so that their interaction is involving, dynamic, positive and mutually satisfying. Higher scores indicate higher reciprocal engagement.

(Montirosso, et al., 2012)

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