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## Advances in family-based interventions in the neonatal ICU

Welch, Martha G.; Myers, Michael M.

### Author Information

<sup>a</sup>Department of Psychiatry

<sup>b</sup>Department of Pediatrics

<sup>c</sup>Department of Pathology and Cell Biology, Columbia University College of Physicians and Surgeons

<sup>d</sup>Department of Developmental Neuroscience, New York State Psychiatric Institute, New York City, New York, USA

Correspondence to Martha G. Welch, MD, Nurture Science Program, 51 Audubon Ave, Suite 100, New York City, NY 10032, USA. Tel: +1 212 342 4400; e-mail:

[mgw13@columbia.edu](mailto:mgw13@columbia.edu)

### Abstract

**Purpose of review:** Despite advances in medical care, preterm infants remain at risk for many adverse outcomes. This article reviews findings from several recent neonatal ICU (NICU) interventions and a trial of a novel nurture-based approach, Family Nurture Intervention (FNI).

**Recent findings:** Recent trials reviewed here find positive effects of a variety of family-related interventions focused on parental guidance. These interventions target prescribed physical activities with infants, parents' stress, and the parents' ability to recognize their positive and negative behaviors with their infants. Beneficial effects include reductions in parenting stress, maternal anxiety, and depression. A different approach, FNI, is aimed at establishing mother–infant emotional connection. As in other trials, FNI also decreased maternal symptoms of anxiety and depression, and increased maternal sensitivity. Additionally, FNI led to positive short and long-term effects on infant neurobehavioral outcomes at term and 18 months.

**Summary:** A number of recent parent-based NICU interventions have been effective at reducing preterm parent stress. Another, FNI, has positive effects on both maternal and infant outcomes and promises to be cost-effective. Future decreases in long-term morbidity in preterm infants will increasingly rely on nonmedical interventions. Therefore, the rigorous development and testing of such interventions should be a high priority in perinatology research.

## INTRODUCTION

The article reviews findings from several recent neonatal ICU (NICU)-based interventions. Approximately 10% of infants in the USA are less than 37 weeks gestation at the time of delivery [1,2]. Despite advances in neonatal medicine that decrease mortality, preterm infants are at increased risk for cognitive and language delays, autism spectrum disorder, attention deficits, executive dysfunction, depression, and psychotic disorders [3–8]. Genetics, medical complications, and physical and emotional separation of infant and mother in the NICU contribute to adverse outcomes. Parents of preterm infants are also at risk. Up to 40% of mothers of these infants suffer from postpartum depression [9] and many mothers suffer symptoms of trauma and posttraumatic stress [10–12]. Fathers of preterm infants are also at increased risk for postnatal depression [13]. Additionally, mothers of preterm infants have increased cardiovascular complications [14] and both parents report increased parenting stress when their premature infants reached 7 years of age [15].

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## KEY POINTS

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- New advances in preventing long-term morbidities associated with preterm birth may be nonmedical, and instead focused on mother and family involvement in the care of the infant and support of the family.
  - Recent interventions to improve family involvement in the NICU offer instrumental approaches to either the parent or the infant, without addressing them as a pair during intervention.
  - FNI in the NICU is unique in its treatment of the mother and infant as an inseparable unit, whose emotional connection, once established, can restore biological mechanisms from which sensitive parental care and optimal infant development flow.
  - Even small reductions in the risk of adverse neurodevelopment outcomes such as autism would save hundreds of millions of dollars each year in the USA alone.
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Box 1. no caption available

## PRIOR NEONATAL ICU-BASED INTERVENTIONS

As summarized in recent reviews, a number of behavioral interventions enhancing the environment and family participation in the NICU have been proposed to improve preterm outcomes and reduce parental stress [16,17]. These include, Creating Opportunities for Parent Empowerment, didactic sessions with parents, which reduced the length of stay and postdischarge levels of maternal anxiety and depression [18–21], Newborn Developmental Care and Assessment Program [22,23], an individualized intervention designed to support development and minimize infant stress using a relationship-based, family-integrated approach, skin-to-skin care [24,25], and massage therapy [26–28]. These studies report the effects on weight gain [27], length of stay [28], and neurobehavioral function [29], all with no significant adverse effects reported.

## CURRENT NEONATAL ICU-BASED INTERVENTIONS

Current family-centered NICU interventions mainly target parental, and especially maternal, outcomes. As these studies note, parents of NICU infants are at risk for many adverse emotional outcomes including, but not limited to, depression, anxiety, and posttraumatic stress. Two studies in particular, one by Abdeyazdan *et al.* [30] and one by Shaw *et al.* [31] focused on alleviating parental stress using parent-centered interventions. Abdeyazdan *et al.* used a two-stage support program that included a 60-min NICU training session to inform parents about NICU care and their preterm infant, and a 2-h support session with other NICU families. It was successful at lowering parental stress in the short term, but did not address long-term outcomes and did not look at intervention effects on infant development, or on parent–infant interactions. Shaw *et al.* used trauma-focused cognitive behavioral therapy to change mother's negative perceptions of their infants and the parenting experience. Findings at 6 months infant age showed that mothers in the intervention group reported a greater reduction in trauma symptoms, depression, and anxiety compared with the control group. Future research using this intervention would benefit from an examination of the effects of mother-focused interventions on mother–infant interaction and infant outcomes.

Some interventions have targeted parental stress and anxiety by providing feedback on the parent–infant interaction. Two such studies, one by Hoffenkamp *et al.* [32] and one by Borghini *et al.* [33] used video recordings of parent–infant interactions to instruct parents on responsiveness to contact-seeking behavior, and on infant-specific reactions and adjustments to stimuli, respectively. Hoffenkamp and colleagues used three sessions of video feedback during the week after birth, an intervention that was particularly effective with mothers characterized as traumatized, and fathers, both of whom showed enhanced sensitivity and diminished withdrawal behaviors after the intervention. The intervention did not improve parental depression, anxiety, or stress, and did not look at infant outcomes. However, it was associated with sustained effects in father–infant bonding at a 6-month follow-up. The second of these studies used video feedback at three clustered time points over the first 4 months of the infant's life. All sessions were aimed at increasing parent awareness of, and sensitivity to, infants' specific needs. The findings showed decreases in maternal posttraumatic stress symptoms and improvements in the quality of mother–infant interactions. However, the study's small sample size and disproportionate time spent with the intervention group preclude positive conclusions about this intervention. Future studies using video feedback might also benefit from incorporating measures of effect on infant development.

Other studies have used a program of specific Auditory, Tactile, Visual, and Vestibular stimulation as the bases of the intervention (ATVV). Holditch-Davis *et al.* [34[black small square]] assessed the effects of this intervention on maternal distress, infant behaviors, and mother–infant relationships in comparison to kangaroo care. White-Traut and colleagues used ATVV in tandem with maternal social support and education on infant behavioral cues [35[black small square]]. Both groups noted beneficial effects of ATVV on short-term infant outcomes. In the White-Traut study, infants had increased weight gain at discharge and increased length over the course of the hospital stay, both of which are predictive of improved long-term outcomes. There were significant positive effects of ATVV on infant attention at 2 months of age in the Holditch-Davis study, but these effects were no longer significant at 6 months. In the Holditch-Davis study, both ATVV and kangaroo care were effective in reducing parenting stress. Interestingly, these researchers found that any form of infant massage, including ATVV, resulted in a more rapid decline in maternal depressive symptoms across all groups.

In a recent trial by Milgrom *et al.* [36[black small square]][black small square]] of the Mother–Infant Transaction Program (MITP), parents were trained to recognize and minimize stress responses in their preterm infants. Once the infants reached term, intervention mothers were noted to be more sensitive, and stressed their infants less during interactions. At 6 months corrected age, intervention infants scored higher on the Communication and Symbolic Behavior Scales Developmental Profile Infant-Toddler Checklist. This intervention was most effective on infant symbolic behavior.

Although each of these family/mother-oriented interventions provides support for the efficacy of such approaches, none of these NICU interventions are in general use because of cost, staffing concerns, and lack of supporting evidence [37]. The following sections describe a new approach that is intended to address these concerns, Family Nurture Intervention (FNI) [38].

## **FAMILY NURTURE INTERVENTION: A NOVEL NEONATAL ICU APPROACH**

The randomized controlled trial of FNI studied 150 preterm infants (26–34 weeks postmenstrual age) from 115 families who were assigned to FNI or standard care by randomized block design. A total of 72 infants received standard care, and 78 infants received standard care plus FNI.

As soon as possible after delivery and throughout the stay, nurture specialists facilitated FNI mothers and infants in the following activities: mutual scent cloth exchange, firm and sustained touch, speaking in soothing or emotional tones (in native language), and eye contact. When the infant was medically able, the nurture specialists helped FNI mothers to engage in skin-to-skin, and nonskin-to-skin, holding with continuation of vocal soothing, emotional expression of affect, and eye contact.

During the NICU stay, FNI mothers exhibited increases in maternal sensitivity during caregiving [39[black small square]]. At term age, FNI infants exhibited changes in electroencephalogram (EEG)-based frontal brain activity consistent with advanced maturation [40[black small square],41[black small square]]. At 4 months infant age, FNI mothers had decreased symptoms of anxiety and depression [42[black small square]]. At 18 months, FNI infants had improved cognitive and language scores on the Bayley III, fewer attention problems on the child behavioral check list, and decreased risk for autism spectrum disorders [modified checklist for autism in toddlers (M-CHAT)] [43[black small square]][black small square]].

## **DISCUSSION**

Sensory stimulation embedded in mother–infant nurturing interactions is critical for shaping neurodevelopment. Thus, normal developmental trajectories can be altered by the environment, impacting physical and mental development and resilience at the earliest stages [44,45]. Each of the recent interventions summarized above are consonant with this construct and could contribute to the improved well-being of the infant or the mother, or both. Most of these studies aimed to shape the parents' instrumental control of the baby, or to have an interventionist help the mother cope with her stress and emotional state separate from the baby. FNI, in contrast, engages the mother and baby in affective interactions that emotionally and physiologically affect each other. Results from the FNI trial demonstrate that this is a practicable approach, with significant effects on both mother and baby. Our working model posits that the underlying mechanism of FNI works to enhance mother–infant coregulation by facilitating the baby's regulation of the mother and, reciprocally, the mother's regulation of the baby.

## CONCEPTUAL FRAMEWORK

Basic science research on early life experience, together with substantial clinical work with families of children with emotional, behavioral, and developmental problems [46], prompted the design of the FNI trial. The goal of FNI is to facilitate an emotional connection between mother and infant by establishing a 'calming cycle' routine that includes the communication of affect through comforting touch, vocal soothing, eye-to-eye contact, and skin-to-skin (or clothed) holding [38]. The construct of emotional connection is the result of physiological coregulation in mother–infant dyads. It is a dynamic state that begins *in utero*, is initially reinforced by natural birthing processes and breastfeeding, and subsequently promoted through ongoing, positive mother–child interactions. It can be interrupted by current birthing practices that separate the mother and infant immediately postpartum and other events that interrupt coregulation, threatening emotional connection during infancy. The more an emotional connection is reinforced, the more easily it is maintained or reestablished. Our model for reestablishing emotional connection uses repeated calming cycles to create and recreate coregulation to overcome the effects of repeated separations during the NICU stay. Figure 1 summarizes the concepts that underlie FNI.

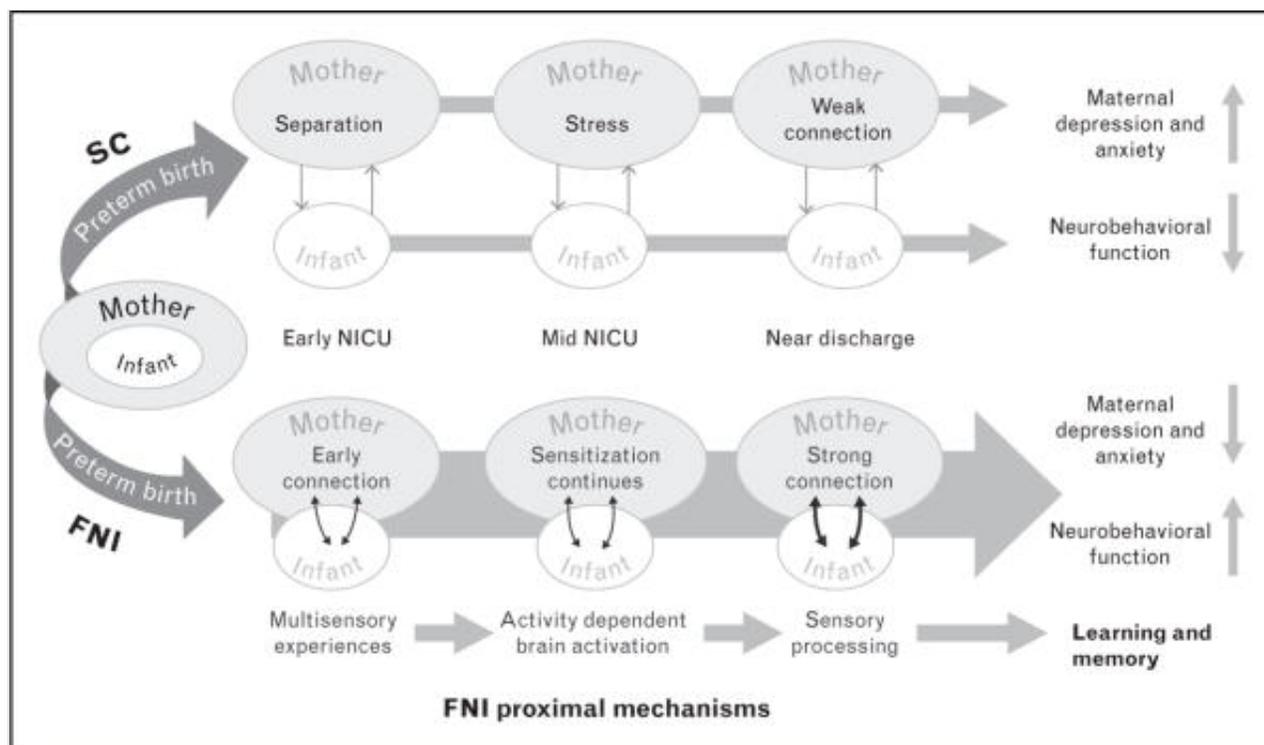


FIGURE 1. Overall conceptual framework for the Family Nurture Intervention (FNI). The scheme indicates the hypothetical developmental flow of both standard care infants (top sequence) and infants in the intervention wing of the trial, along with the proposed proximal mechanisms underlying the effects of the intervention. NICU, neonatal ICU; SC, standard care.

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We propose that the effects of FNI on brain activity at term age are consistent with the intervention's mediating accelerated frontal cortical maturation [40[black small square],41[black small square]]. These findings are of great interest because frontal regions are involved in the regulation of attention, cognition, and emotion regulation [47]; domains deficient in preterm infants [3,5,6].

FNI mothers showed significantly higher quality maternal caregiving behavior prior to discharge from the NICU. A similar effect was noted at term age in the above mentioned trial of MITP [36[black small square] [black small square]]. We strongly endorse evaluations of maternal caregiving behavior for any NICU intervention because this behavioral input is particularly important for shaping early infant development and provides a mechanism for achieving sustained effects of such interventions.

FNI was designed to minimize maternal psychological comorbidities of preterm birth by facilitating early emotional connection between mothers and their preterm infants. By 4 months, mean depression (CES-D) and anxiety [state-trait anxiety inventory (STAI)] scores were significantly lower in FNI mothers compared with standard care mothers. Similar effects on maternal mood were found in a trial of the maternal skills-based approach [31[black small square]] and in the ATVV trial reported above [34[black small square]]. As is the case for the assessment of maternal caregiving behavior, we strongly recommend that assessments of maternal mood be included as an outcome in any NICU trial as negative maternal mood is known to have a significant impact on infant development [48].

None of the recent studies cited have as yet reported long-term effects on the infants. However, in the FNI trial, multiple neurobehavioral outcomes at 18 months corrected age were improved by the intervention. Of particular note were robust differences between FNI and standard care infants with regard to risk scores for autism. Not only were total M-CHAT scores significantly lower in FNI infants, FNI infants had no failures on social-related items compared with 33% of standard care infants [43[black small square][black small square]]. Although the nurture specialists encouraged skin-to-skin care, we found that the long-term effects of FNI measured at 18 months were independent of the amount of skin-to-skin care [43[black small square] [black small square]].

The gains seen in the FNI trial suggest that an intervention that facilitates the emotional connection between mothers and preterm infants in the NICU may be a key to altering adverse developmental trajectories. Because they were independent of the amount of various components of the intervention, the results prompted us to obtain preliminary evidence that the construct of emotional connectedness is measuring a phenomenon that can be observed and coded. Scores for maternal care sensitivity during feeding [39[black small square]] were divided at the median into low and high maternal sensitivity. Then the trial's nurture specialists judged FNI mothers and infants as to whether the pair was emotionally connected. Figure 2 shows that the concordance between emotional connectedness and maternal sensitivity was 76%,  $P < 0.01$ .

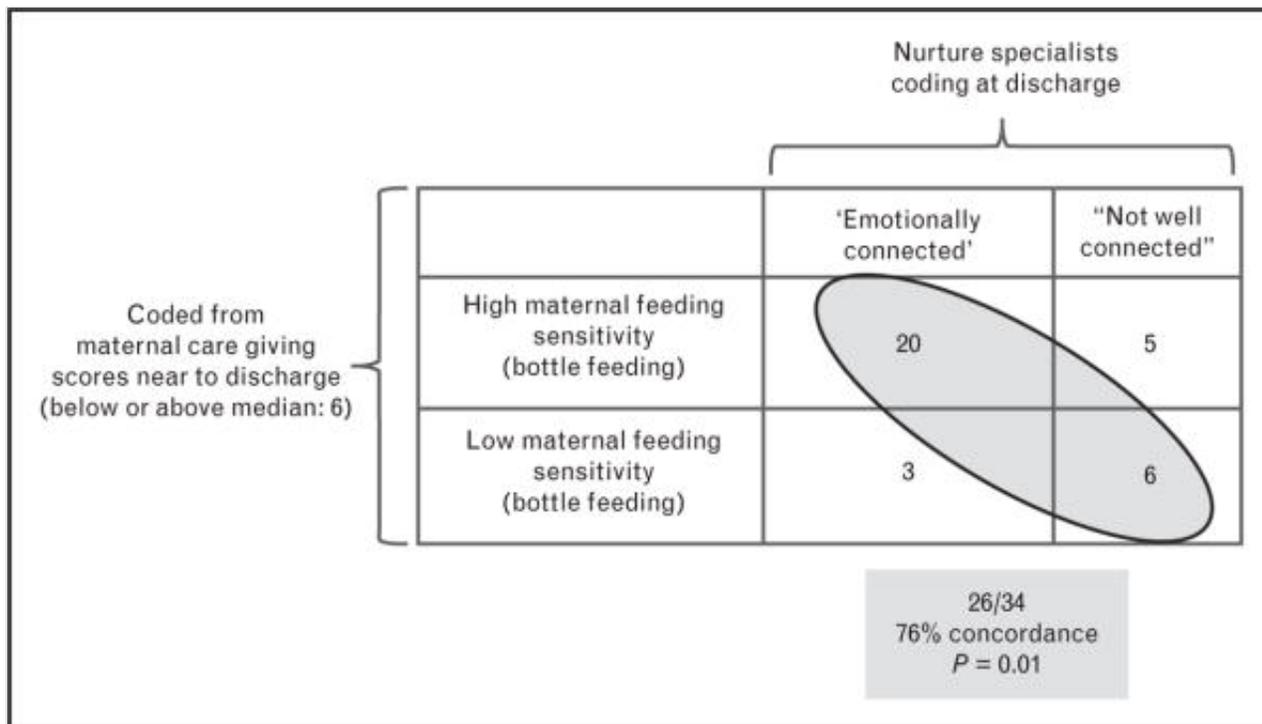


FIGURE 2. Scores for maternal care sensitivity during feeding obtained from video tapes made prior to discharge [39] were divided at the median into low and high maternal sensitivity. The trial's nurture specialists assessed Family Nurture Intervention mothers and infants as to whether the pair was emotionally connected. This figure shows that the construct of emotional connectedness and maternal sensitivity were significantly concordant.

## COST-BENEFIT ANALYSIS

In addition to reviewing findings from multiple recent family-based NICU intervention trials, we wish to highlight the potential value of preventive approaches to decreasing long-term adverse outcomes in preterm infants and their parents. Treatments administered after problems emerge are costly and certainly not totally effective.

The cost of treating the 3.5 million children and adults with diagnosed autism in the USA is computed to be more than ~\$230 billion/year [49]. Based on published distributions of birth by gestational age [50], an overall estimated rate of autism of one in 68 [51], and an estimated relative risk of three for autism in preterm infants [52], we estimate that ~7% of all autism cases were born under 34 weeks gestational age, thus costing ~\$16 billion/year. If a NICU-based intervention prevented only 10% of preterm-related autism, the ultimate treatment savings would be \$1.6 billion/year, not including the additional millions saved each year in unnecessary autism spectrum disorder workups. If FNI required a full-time nurture specialist at \$100 000/year in each of 1000 NICUs, the cost of implementing preventive FNI for each of ~130 000 preterm infants born at less than 34 weeks each year [50] would be \$800/infant, a small addition to the total cost of NICU care for these high risk infants. Although this new standard care practice would cost \$100 million/year, the ultimate projected return on investment would be 16 to 1 (\$1.6 billion in savings vs. \$100 million in costs).

## CONCLUSION

Most NICU interventions focus on either infant development or mother's mood and traumatic experience. FNI differs in that it is not didactic, rather requiring facilitated experience of mother/infant coregulation. It is the first trial from our Nurture Science Program, dedicated to testing and scaling effective interventions for emotional, behavioral, and developmental disorders. The positive results from the studies reviewed, including the FNI trial, support the effectiveness of parental interventions, encouraging further research in this area. However, in our opinion, to achieve broad effects on child development as well as on the mother and family, these interventions must specifically aim to create an emotional connection.

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## Conflicts of interest

*There are no conflicts of interest.*

## REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

[black small square] of special interest

[black small square][black small square] of outstanding interest

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The intervention found that a combination of strategies that included a video-based NICU training session and a multifamily group support session was effective in reducing parental stress.

31[black small square]. Shaw RJ, St John N, Lilo E, et al. Prevention of traumatic stress in mothers of preterms: 6-month outcomes. *Pediatrics* 2014; 134:e481–e488. [Bibliographic Links](#) | [\[Context Link\]](#)

The intervention focuses exclusively on maternal trauma and showed that cognitive behavioral therapy could improve the mother's negative perceptions of her infant and parenting experience.

32[black small square]. Hoffenkamp HN, Tooten A, Hall RA, et al. Effectiveness of hospital-based video interaction guidance on parental interactive behavior, bonding, and stress after preterm birth: a randomized controlled trial. *J Consult Clin Psychol* 2015; 83:416–429. [Bibliographic Links](#) | [\[Context Link\]](#)

The intervention, performed in the first week after birth, educated parents on infant contact-seeking behavior using NICU-based Video Interaction Guidance to increase parental interactive behavior and lower parent stress.

33[black small square]. Borghini A, Habersaat S, Forcada-Guex M, et al. Effects of an early intervention on maternal posttraumatic stress symptoms and the quality of mother-infant interaction: the case of preterm birth. *Infant Behav Dev* 2014; 37:624–631. [\[Context Link\]](#)

Uses video feedback to enhance the quality of mother–infant interactions by educating mothers about their infants' specific behavioral cues at multiple timepoints over the first 4 months of the infant's life.

34[black small square]. Holditch-Davis D, White-Traut RC, Levy JA, et al. Maternally administered interventions for preterm infants in the NICU: effects on maternal psychological distress and mother-infant relationship. *Infant Behav Dev* 2014; 37:695–710. [\[Context Link\]](#)

Compares the effect of two interventions that have previously improved infant outcomes, ATVV and kangaroo care, on maternal stress, and mother–infant relationships, thereby acknowledging the impact of infant condition on maternal well-being.

35[black small square]. White-Traut R, Norr KF, Fabiyi C, et al. Mother-infant interaction improves with a developmental intervention for mother-preterm infant dyads. *Infant Behav Dev* 2013; 36:694–706. [Bibliographic Links](#) | [\[Context Link\]](#)

Education about infant behavioral cues, ATVV and maternal social support to effectively increase infant weight and length over time from birth to discharge.

36[black small square][black small square]. Milgrom J, Newnham C, Martin PR, et al. Early communication in preterm infants following intervention in the NICU. *Early Hum Dev* 2013; 89:755–762. [Bibliographic Links](#) | [\[Context Link\]](#)

Ten psychologist-led didactic sessions aimed to heighten maternal awareness and sensitivity and reduce infant stress by training NICU mothers to recognize infant cues and stress responses with a modified version of MITP.

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First study to use maternal caregiving behavior in the NICU as an outcome variable in an intervention trial.

40[black small square]. Myers MM, Grieve PG, Stark RI, et al. Family Nurture Intervention in preterm infants alters frontal cortical functional connectivity assessed by EEG coherence. *Acta Paediatr* 2015; 104:670–677. [Bibliographic Links](#) | [\[Context Link\]](#)

First study to use coherence at term age as an outcome variable, suggesting more rapid maturation of distributed processing in intervention babies.

41[black small square]. Welch MG, Myers MM, Grieve PG, et al. Electroencephalographic activity of preterm infants is increased by Family Nurture Intervention: a randomized controlled trial in the NICU. *Clin Neurophysiol* 2014; 125:675–684. [Bibliographic Links](#) | [\[Context Link\]](#)

Trial demonstrates the utility of high density EEG as a proximal outcome variable of an NICU intervention, in this case, indicating increased power in frontal regions known to be adversely affected by prematurity.

42[black small square]. Welch MG, Halperin MS, Austin J, et al. Depression and anxiety symptoms of mothers of preterm infants are decreased at 4 months corrected age with Family Nurture Intervention in the NICU. *Arch Womens Ment Health* 2016; 19:51–61. [Bibliographic Links](#) | [\[Context Link\]](#)

Convergent evidence that NICU-based interventions decrease maternal depression and anxiety, even, as in FNI, when intervention does not target these maternal symptoms.

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