

# RECOGNIZING THE POTENTIAL EFFECT OF STRESS AND TRAUMA ON PREMATURE INFANTS IN THE NICU: HOW OUTCOMES ARE AFFECTED?

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**Abstract:** Extensive research of the long-term outcomes of premature infants has shown significant risk for emotional, behavioral, and psychological problems. Chronic stress and trauma have not been researched specifically in this population. However, studies of the neurobiological impact of traumatic stress on infants and children in the general population show noteworthy parallels in symptomatology. Careful consideration should be given to practitioner caregiving, parent education, future research, assessment, and interventions while being mindful of the impact that chronic stress and trauma may have on the developing brain of the preterm infant.

**Introduction:** Almost half a million premature babies are born in the United States each year. The number of infant born weighing less than five pounds, as well as the survival of those who might have previously died, has steadily increased since 1984(1). Every year we learn more and more about the impact that prematurity has on the infant and the family. We now clearly understand that premature infants are at higher risk for long-term medical and developmental problems such as chronic lung disease, poor growth, feeding problems, cerebral palsy, and learning disabilities(2).

We are also developing a better understanding of the greater risk that premature infants have of developing psychological, emotional, and behavioral disturbances. One study carried out by Botting et al(3) looking specifically at psychiatric outcomes in very low birthweight infants (VLBW, less than 1500 g at birth) at age 12 found these former premature infants to be “more vulnerable to psychiatric sequelae.” This study showed a significantly greater risk of attention-deficit/hyperactivity disorder (ADHD), generalized anxiety, and symptoms of depression. In all, 28% displayed some type of psychiatric disorder compared to nine percent of their peers. A meta-analysis carried out by Bhutta, et al(4), showed that 81% of the studies done on cognitive and behavioral outcomes of school-aged preterm infants indicated increases in internalizing and externalizing behaviors, and more than twice the risk of developing ADHD.

The cause of these psychological, emotional, and behavioral disturbances, and learning disabilities is not clearly understood. The following preterm research review proposes that there may be a correlation between the psychiatric sequelae and the chronic stress and trauma experienced by premature infants in the Neonatal Intensive Care Unit (NICU), as well as after discharge.

**Defining Stress and Trauma:** We often use the term “stress” loosely. Most of us talk about feeling stress in reference to managing everyday problems such as full schedules, traffic jams, rude people, and juggling responsibilities. However, stress truly becomes an issue when one’s equilibrium is pushed out of balance due to environmental factors that cause bodily or mental tension from a stress response (5). A premature infant can become easily “imbalanced” due to their persistent exposure to “stress” from daily occurrences such as invasive procedures, pain, interruption of sleep states, and even alterations in less complex issues such as temperature, noise, and hunger. After the NICU, a former premature infant can experience stress when coping with frequent illness, developmental delays, feeding problems, etc.

If we take stressful situations one step further, we may question whether or not preterm infants experience traumatic stress, or “trauma,” in the NICU and beyond. Bessel A. van der Kolk defines trauma as “the result of exposure to an inescapably stressful event that overwhelms a person’s coping mechanism”(6). Dr. Perry, a leading researcher in the

area of trauma in children, uses the terms “multiple painful medical procedures and life-threatening medical procedures” in his list of life events that could traumatize a child(7). Although not all premature infants experience life-threatening situations, many do, and most will endure painful medical procedures and situations that challenge their underdeveloped coping mechanisms. Barker and Rutter (8) discovered that during a premature infant’s admission to the Neonatal Intensive Care Unit, the infant can undergo an average of 60 procedures, many of them painful and invasive.

Even more significant is the fact that the preterm infant is exposed to intense or persistent stress, and/or traumatic events, during a time when brain development is occurring at a profound rate, and at a time when the brain is especially vulnerable.

**Neurobiology of stress/trauma in infancy:** For many years, conventional wisdom declared that infants and small children could not cognitively remember chronic stress or trauma. As a result, professionals assumed that children would not experience long-term problems from traumatic incidents that occurred before their cognitive memory was functioning (around the age of 3). In the past decade, researchers have made tremendous strides in negating this belief based on their improved understanding of the long-term physiological impact that chronic stress, as well as traumatic incidents, have on the developing brain(9).

The brain triples in size over the first 5 years of life. Much of this growth is in the myelination of neurons and their synaptic interconnections. Genetics determine the basic architecture of the brain, but its final form is dictated by experiences in the environment. If an infant’s or child’s experiences are abnormal, non-nurturing, traumatic, and/or chronically stressful during a time of immense change in the development of the brain, then this impact may leave a permanent imprint on the structure and mechanisms of the functioning brain throughout life(10,11).

The stress response system is activated by a centrally located area in the right hemisphere of the brain, the area of the brain that is dominant in controlling the functions that are used for survival, processing bodily information, reception and regulation of emotion, and the regulation of affect. In the early development of the brain (postnatally), the right hemisphere is also more deeply interconnected (than the left hemisphere) with the limbic, autonomic, and arousal systems, all areas of the brain that are important in the modulation of stress(12). When an infant encounters stress, these areas of the brain are primary in telling the body how to respond, that is, when and what hormones to release (corticosteroids, vasopressin, oxytocin, etc.), when to increase the heart rate, how to mobilize energy, etc. When the threat has passed, the same regions of the brain communicate, via the same or similar neurons and neurotransmitters, when and how to return to baseline(6).

We have known for years the importance of, and how the brain responds in acute stress. Just in the last decade, however, researchers have found that chronic stress or trauma (especially when it occurs while the brain is developing) can have detrimental results both psychologically and biologically(13). As the brain is developing structurally and mapping its neuropathways, these pathways are frequently compelled to take abnormal directions in order to deal with constant stress and/or trauma (such as those in the NICU and/or after discharge), which in turn can cause brain function to become abnormally integrated.

When discussing an infant’s or child’s response to trauma, Perry et al(10) explains, “in the developing brain, these states [temporary responses] organize neural systems, resulting in traits. Because the brain changes in a use-dependent fashion and organized during development in response to experience, the specific pattern of neuronal activation associated with the acute responses to trauma are those which are likely to be internalized. The human brain exists in its mature form only as a byproduct of genetic potential and environmental history”. Streech-Fischer and van der Kolk(13) believe that “chronic childhood trauma interferes with the capacity to integrate sensory, emotional and cognitive information into a cohesive whole and sets the stage for unfocused and irrelevant responses to subsequent stress.”

Theoretically, as a premature infant grows, he/she may not be able to distinguish, on a subconscious or conscious level, between the here and now of a stressful event and the past events of the NICU due to the atypical development of his/her brain. In addition, if a premature infant’s brain is programmed to respond to constant stress, subsequently as he grows older, he may have a difficult time sorting out how to respond normally to everyday circumstances. It is important

for us to abandon the myth that infants and children can “get over it because they didn’t even know what was happening.” Dr. Perry, et al (10) believes that “children are not resilient, children are malleable.” We must recognize the potential effect from the difficult events in the lives of premature infants and children.

**Correlation of the symptoms of chronic stress and trauma and the preterm outcome research:** Stress in the premature infant is fairly well documented in the literature. However, the long-term psychological effects of stress on the premature infant is not clearly understood. We know that in the NICU, preterm infants can show marked changes in oxygen levels and cerebral blood flow during stressful procedures. When these occur in the first few days of life, they can have devastating long-term effects on the infant because they increase the risk of intraventricular hemorrhage and periventricular leukomalacia(14). Whitfield and Grunau(15) examined the long-term sequelae of painful procedures and the premature infant, demonstrating that former ELBW 18-month old toddlers showed an abnormal response to normal bumps and bruises of toddlerhood, indicating an abnormal response to stressful stimuli. Perlman(16) concluded that there are a substantial number of former VLBW infants, who develop cognitive and behavioral problems, who do not have neuroimaging abnormalities and, therefore, the potential contributing role to these problems is the chronic stress on the NICU environment.

When we look further at the research and literature around stress, we move toward traumatic stress or “trauma.” There is very little written in the premature infant literature regarding trauma and the preterm infant. In his chapter in *Frontiers of Infant Psychiatry* published in 1983, Dr. Herzog writes of his observations of former premature infants who were clients as demonstrating an “abnormal attachment to pain and unlust”(17). He questions whether or not these former premature infants are presenting a “neonatal intensive care syndrome, a pain complex reflecting neuroplasticity and psychic trauma”(17). As the premature infant research regarding trauma is so limited, it is important, and interesting, to examine and compare trauma research in other populations and realms of life.

When researchers investigate traumatic stress after events such as natural disasters, abuse, neglect, car accidents, and even medical trauma they generally define and measure the impact by using the term post-traumatic stress disorder or PTSD. However, using an exclusive diagnosis of PTSD when diagnosing and treating children with trauma symptoms is not recommended because most children exposed to traumatic events never develop PTSD(11). Understanding the long-term effects of trauma without committing specifically to a PTSD diagnosis is even more important, because traumatized children who do not fit the criteria for PTSD often have as many or more overall problems than those who do fit the criteria(11).

According to van der Kolk et al(18), a central quality of a traumatized child is “a loss of the ability to physiologically modulate stress responses which leads to a reduced capacity to utilize bodily signals as guides to action, and this alteration of psychological defense mechanism is associated with impaired personal identity.” Clinical presentation of a child who has experienced trauma includes symptoms such as “impulsivity, distractibility, attention problems (due to hypervigilance), dysphoria, emotional numbing, avoidance behaviors, fears, dissociation, sleep problems, aggressive play-outbursts, school failure, difficulty concentrating, memory impairment, complex reenactment of the event, exaggerated startle response, withdrawal, overly friendly behavior, and regressed or delayed development”(19,20). Perry also notes that children with post-traumatic signs and symptoms “have altered sensitivity and functioning of neuroendocrine and autonomic nervous systems. This sensitivity may predispose them to the development of various medical conditions such as asthma, hypertension, cardiac arrhythmias, endocrine disorders, gastrointestinal disorders, and various other somatic complaints”(19). Other researchers have shown that “exposure to violence and trauma-related distress in young children were associated with substantial decrements in IQ and reading achievements”(21).

Research of the long-term outcomes of premature infants shows an interesting parallel to the clinical symptoms already presented. One study carried out to examine the functional abilities of extremely low birthweight (less than 800 g) infants at school age showed significant increases in distractibility, activity levels, anxiety, and withdrawal from difficult situations when compared to non-premature infant cohorts(22). This study also demonstrated that these former premature infants had difficulty in problem-solving, they retreated and gave up easily, distrusting their own ability. In the Botting et al(3) study mentioned earlier, of psychiatric outcomes of premature infant born less than 1250 g and studied

at age 12, results showed that 28% of these premature infants had a psychiatric disorder compared to 9% of their peers. The most common disorder found was ADHD, the second was generalized anxiety, and these premature infants showed more symptoms of depression and oppositional defiant disorders, all symptoms commonly seen in children who have experienced traumatic stress.

Many studies, including one carried out by Brandt et al (23), have demonstrated that former premature infants have an increased risk of learning disabilities. Most studies report findings indicating approximately 50% of all premature infants having learning disabilities, compared to 9% of their peers. Saigal et al(24) confirmed that former extremely low-birth-weight premature infants (less than 1000g) had decreased IQ scores of 11 to 22 points compared to their non-premature infant peers.

A noteworthy study that may correlate to the premature infant population was conducted by Aaron et al(25). This group examined post-traumatic stress in children following acute injury. At 1 month after the injury, 22.5% of these children (ages 8 to 17) presented with the full diagnosis of PTSD. Almost half met at least two of the three symptom clusters necessary for the PTSD diagnosis.

One other area that is important to mention is the correlation between post-traumatic stress disorder in the parent of a premature infant and the subsequent effect on the child. The amount of PTSD shown by parents of premature infants remains unclear; however, a study carried out by DeMier et al(26) demonstrated that mothers of infants at high risk in the NICU reported significantly more PTSD symptoms than mothers of healthy, term infants. A study carried out by Manne et al(27) of children who were diagnosed with PTSD following survival of childhood cancer showed that those children whose parents had symptoms of PTSD had a greater incidence of PTSD themselves. Educating parents about the symptoms of PTSD in adults such as flashbacks and/or recurrent memories of a traumatic event, avoidance of stimuli associated with the event and/or numbing of responses, and hypervigilance(27) can help them to know when to seek help for themselves.

Other research shows us that acute injury predisposes a child to PTSD. We also know that chronic stress and one or more traumatic events in infancy or childhood can cause a child to develop neurobiological changes that alter a child's everyday response to his/her environment, regardless of whether or not they have a cognitive memory of the event. Therefore, as health professionals working with premature infants, we should look more carefully at the long-term outcomes of these infants and how they relate to their NICU experience.

What can be done in the NICU?: If caregivers do accept and address the possibility that exposure to extreme stress and/or trauma may have a direct relationship to the outcome of premature infants, what can be done to help? Three areas come to mind as a means of intervention: recognition, prevention, and support.

Recognition and prevention can work hand in hand in the NICU. By recognizing the possibility that any treatment or handling of a premature infant may have a long-term effect on brain structure, the caregiver can approach and handle an infant more gently, using developmental care guidelines. Caregivers should educate themselves as to the physiologic stress indicators that premature infants demonstrate such as increased heart rate, blood pressure, and respiratory rates, hiccups, mottling of skin color, staring with glossed over eyes, and even apnea or bradycardia(12). Understanding these cues can help to know when to stop and comfort the infant.

Minimizing treatments and clustering care can help prevent stressful scenarios and allow more time for recovery between stressful events. Assessment of pain and subsequent use of nonpharmacological agents should be used to maintain a therapeutic environment(28). Comfort measures such as swaddling, nesting, playing recordings of the mother's voice, and putting something near the infant with the mother's smell on it may also be used(29). If the caregiver simply stays with the infant until he/she has recovered from the stressful event using these or other comfort measures, the infant may be helped in managing its own regulation of stress.

One of the most critical aspects of helping a premature infant in dealing with stress and trauma in the NICU and beyond is support of the parent-infant relationship. Many studies have shown that the primary factor in the normal

development of the infant brain is his/her relationship with the primary caregiver, most often the mother(30). “It is the attachment relationship that creates an inner map of the world. This map determines what image the child has of him or herself, caregivers, and the way the world works. This inner image of the world is comprised both of cognitive and affective knowledge of the world(13). If a premature infant is facing frequent stress and trauma, he needs his mother to help him regulate the stress and know that the world can be a safe place.

Begin with educating the parent regarding the needs of the infant. Many premature infant parents are afraid and unclear as to their role in the NICU. Teach parents about infant cues, both positive and negative, so they can learn how to help comfort their infant. Beyond the typical handling of a premature infant, parents should be encouraged to do Kangaroo Care and appropriate Infant Massage when their infant is ready. Both of these forms of touch are positive and have been shown to benefit the infant, while helping to create a special bond between the infant and parent that extends throughout a lifetime(31-34).

**Help after discharge:** Because the research is not available regarding exactly how much of the long-term outcomes that premature infants experience are specifically a result of the stress and trauma of the NICU, it may be inappropriate to tell parents to look for PTSD or PTSD like symptoms in their infant and child. However, it is always appropriate to educate parents regarding the statistics and possibilities of the psychological, emotional, behavioral, and learning difficulties that premature infant can face. Having a watchful eye while enjoying their baby and child is always a difficult balance. Encourage parents to understand that a loving, supportive, playful, and nurturing relationship with their child is extremely important in helping a child heal from their stress and trauma and it will improve and promote normal brain development. They can also be advised to see prompt professional evaluation and support if they see abnormal or “strange” behaviors in their child. Finally, parents should be encouraged to look after their own well-being, as this can indirectly affect their child’s well-being. When they are educated about the emotional aspects of parenting a premature infant in the NICU and beyond, they can become more aware of their own reactions and adjustment, and can see timely evaluation and support for themselves(35).

It is also important for those who work in the psychiatric/mental health field to be aware of the possibility of post-traumatic and post-traumatic-like symptoms in the former premature infant. Developmentally supportive treatment protocols might be improved if we carefully consider this possibility.

Conclusion: Although we recognize that stress in the NICU and beyond can be a factor in the long-term outcome of a premature infant, research has not clearly demonstrated all of the variables and possibilities. There are many viable options for research in this area. Evidence might be gained by testing outcomes after controlled clinical trials using gentler methods of resuscitation and CPAP instead of intubation and artificial ventilation. Studies might incorporate many measurements, including cortisol and other stress hormone levels, vagal tone abnormalities, atypical EEG readings that correlate with psychiatric sequelae, imaging structural changes in the brain that may relate to changes seen in post-traumatic stress disorder in other traumatized populations, and less invasive measure such as stress, trauma, and behavioral scales.

As we gain more knowledge of the neurobiological impact that chronic stress and trauma have on the developing premature brain, we can better understand the parameters that might predict those infants who are at risk for the symptoms that result from them. When exceptional developmentally supportive and family-centered care becomes standard practice in the NICU, for infants and parents alike, the environmental contribution to the risk of psychiatric sequelae in the premature infant may decrease significantly. For parents, receiving support and understanding the unique needs and characteristics of their premature infant may be the most valuable keys to their ability to form a responsive relationship with their baby, which may lead to an improved outcome for the child. Early assessment after the NICU leading to early interventions should be provided so that every premature infant can have the opportunity for healing and optimal health.

References: Please refer to the Journal of Perinatology for references.