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Overview of the Early Experience, Stress, and Prevention Science Network

Summary. The goal of this network is to establish the conceptual and empirical basis for translating research on early experience and stress neurobiology to prevention/intervention efforts with young children who have experienced neglect, maltreatment, and relationship disruption. Preliminary work of our network has made us hopeful that this translation will yield important insights into the behavioral and emotional problems of these children and into the neurobiological pathways through which intervention efforts may operate. However, we are also highly cognizant of the many unanswered conceptual and empirical issues that need to be addressed in order for such translational efforts to be successful. We recognize that adequate translational efforts will require training prevention/intervention researchers in the literature and techniques of developmental psychobiology and neuroscience and will require us establish paradigms at the prevention/intervention research locations that will allow us to integrate physiological/neuroscience techniques into future prevention/intervention research designs.

Sommario: L'obiettivo di questa rete di ricercatori è stabilire una relazione tra le ricerche sulle esperienze precoci e la neurofisiologia dello stress e gli interventi per bambini maltrattati e trascurati. Dati preliminari fanno sperare che queste ricerche possano illuminare i problemi comportamentali ed emozionali di questi bambini e le vie neurobiologiche attraverso cui si possa intervenire. Molto c'è ancora da capire e molte conoscenze di base sono necessarie ai ricercatori in questo campo translazionale per arivare a integrare utilmente le tecniche delle neuroscienze con la traduzione operativa in interventi.

Parole chiave: cortisolo, studi translazionali, esperienze sfavorevoli infantili

A large body of literature confirms an important biological basis in affective disorders, including depression and post-traumatic stress disorder (PTSD; Gold, Goodwin, & Chrousos, 1988; Yehuda, 2000). Likewise, stressful events are common in the life histories of adults and youth who develop anxiety and depressive disorders (Goodyer & Altham, 1991). Alterations in stress-sensitive neurobiological systems have been proposed to link stressful experiences and the development of affective pathology in genetically vulnerable individuals (Rosen & Schulkin, 1998). In this regard, considerable research has focused on alterations in functioning of the limbic-Hypothalamic-Pituitary-Adrenocortical (LHPA) system and its primary releasing hormone, corticotropin-releasing hormone (CRH; Johnson, Kamilaris, Chrousos, & Gold, 1992; Nemeroff, 1996; Schulkin, McEwen, & Gold, 1994).

Abundant evidence shows that disrupting normal caregiver-infant interactions in rodents and non-human primates alters activity of the developing LHPA system producing potentially maladaptive neuroendocrine stress responsivity (see for reviews Heim, Owen, Plotsky, & Nemeroff, 1997; Sanchez, Ladd, & Plotsky, in press, see Appendix). The ontogeny of the stress response in animals has recently been described in detail (Walker, Anand, & Plotsky, 2001). In all of the animal models, the early experience manipulations that affect the LHPA stress response also produce behavioral disturbances, including fearfulness, impulsivity, and increased consumption of alcohol (Caldji et al., 2001; Huot, Thrivikraman, Meaney, & Plotsky, 2001; Kaufman, Plotsky, Nemeroff, & Charney, 2000; Ladd et al., 2000). These experiences also alter brain morphology, neurochemistry, and the expression of genes in the central nervous system that are believed to be related to the etiology of anxiety and mood disorders (e.g., Sanchez et al., in press). This animal research may serve as a model of how early psychosocial adversity in humans creates vulnerability to affective disorders. However, the translational research addressing this vital question is just beginning. The goal of our network is to stimulate translational efforts by developing the appropriate paradigms, enhancing the training of those who would perform the human studies, and addressing critical theoretical and

methodological issues. These activities should help us ultimately to apply successfully for a program project grant or a multi-site center grant to study the psychobiology of early intervention.

Physiology of the LHPA System. The LHPA system exhibits a circadian rhythmicity with a peak around the time of waking and a trough during the quiescent period of daily activity. The ontogeny of the circadian rhythm has been described in rodents in detail; less information is available for non-human and human primates, but in humans and Rhesus macaques, an early morning peak and evening trough can be demonstrated within a few weeks of birth (Price, Close, & Fielding, 1983; Suomi, unpublished data). Superimposed on this diurnal pattern is activation by interoceptive and exteroceptive cues relating to threat, violation of expectancies, pain, infection, or metabolic crisis that are communicated to the hypothalamus via stressor-specific pathways (e.g. Swanson, Sawchenko, Rivier, & Vale, 1983). These signals are integrated in the hypothalamic paraventricular nucleus (PVN) where neurons expressing the CR11 secrete this peptide that, in collaboration with other secretagogues (e.g., AVP), stimulate the synthesis and release of adrenocorticotrophic hormone (ACTFI) from the anterior pituitary. When released into circulation ACTH stimulates the adrenal cortices to synthesize and release glucocorticoids (cortisol in primates, corticosterone in rodents, hereafter referred to as CORT). These are steroid hormones that mobilize energy substrates and regulate gene expression in the body and the brain.

Prolonged CORT and CR11 secretion can lead to pathological states, including immuno-suppression and cognitive impairment (e.g., McEwen, 1998). Normally, this is prevented by CORT-mediated negative feedback inhibition at pituitary and central (brain) sites via two receptor types (MR and GR). MR tend to be occupied at basal CORT levels; these receptors play a role in modulating the circadian rhythm (e.g., Dallman et al., 1987). *A normal circadian rhythm appears to facilitate termination of the LHPA response to stressors, indicating that disturbances in the daily rhythm may contribute to LHPA stress dysregulation.* GR tend to be occupied at the peak of the circadian rhythm and as CORT concentrations rise in response to stressors. GR occupation, primarily in the hypothalamus and hippocampus, also helps contain the LHPA stress-response. MR mediate many of the health promoting functions of CORT, while GR mediate many of the effects that threaten neuronal integrity.

GR and MR distributions differ between rodents and primates. In primates (compared to rodents), MR and GR are widely distributed in the prefrontal cortex, suggesting a potentially important role for CORT in the development and modulation of frontally mediated cognitions, moods, and social behaviors (e.g. Lopez, Akil, & Watson, 1999; Sanchez, Young, Plotsky, & Insel, 2000). Lesions to the frontal cortex and anterior cingulate cortex are known to disturb regulation of both neuroendocrine and autonomic responses to stressors (Brake et al., 2000). These frontal regions are also hypothesized to play critical roles in behavior and emotion regulation (e.g., Posner & Rothbart, 2000).

In addition to its major role as an ACTH secretagogue, CR11 acts as a neurotransmitter. CR11-containing neurons and receptors are widely distributed in cortical, limbic, and brain stem regions (Sawchenko & Swamson, 1990). CRH neurocircuits, particularly those from the hypothalamus and amygdala to medullary noradrenergic nuclei, have been implicated in behavioral and autonomic expressions of stress (e.g Heinrichs, Menzaghi, Pich, Britton, & Koob, 1995). Increasing anatomical and functional evidence suggests that the amygdala may play a pivotal role in central CRH neurotransmission. Activation of the amygdala is modulated via peptidergic and aminergic projections from numerous limbic and midbrain structures, which, in turn, receive reciprocal CRH projections from the central nucleus of the amygdala (Gray & Bingaman, 1996). Repeated or chronic elevations in CORT appear to result in increased CR11 expression in the amygdala, providing one mechanism whereby stressor exposure may heighten behavioral and autonomic (e.g., sympathetic and parasympathetic) reactivity to threat (Rosen & Schulkin, 1998). CRH activity in the amygdala and in the bed nucleus of the stria terminalis (BNST) also is known to mediate the acoustic startle reflex, stress-induced freezing, defensive withdrawal, and stress-induced emotionality. Currently, evidence suggests two receptors for CRH, one that mediates fear/anxiety and one that mediates feeding and other vegetative functions, are disturbed during periods of chronic stress. CR11 and CORT also interact with the growth system, suppressing growth of the long bones during periods of chronic physical or psychological adversity (Chrousous, 1992).

Because *of the numerous effects of CORT and CRH on brain regions involved in emotionality, cognition, and basic vegetative functions, disturbances to this system during periods of rapid development are expected to have wide-ranging consequences for the organism.* Most of the focus has been on disturbances that produce chronic elevations in CORT and/or CORT hyper-responsivity to stressors. However, unexpectedly low basal CORT due to a lack of a morning peak in hormone production and/or a blunted

CORT responses to stressors (described as "hypocorticolism") have been noted in a number of conditions associated with stress in human adults, including PTSD, chronic fatigue syndrome, and chronic pain syndrome (Heim, Ehlert, & Hellhammer, 2000). Similar patterns have been noted following disturbances in early rearing. Maternal separation in rodents produces hyper-reactivity of the LHPA system if imposed early in ontogeny, but appears to reduce ACTFL responses to stressors if imposed later (van Oers, de Kloet, & Levine, 1997). In addition, early weaning combined with isolation housing produces a pattern of LFIPA activity highly reminiscent of the human hypocortisolism pattern (Sanchez, Aguado, Sanchez-Toscano, & Saphier, 1998). As discussed below, neglect in human and non-human primates may also result in a loss of a daytime rhythm in CORT production, although it is not clear whether this is accompanied by hypo- or hyper-CORT responses to stressors.

To summarize, the physiology of the LHPA and extra-hypothalamic CR11 systems strongly suggests that activity of these systems support behavioral and emotional responses to stressors. During early development in rodents and non-human primates, contact with responsive, nurturing caregivers appears critical in the development of this neuroendocrine system and its central hormone, neuropeptide and receptor systems. Numerous researchers have speculated that adverse early rearing environments in humans enhance vulnerability to behavior disorders, affective pathology, and drug abuse, in part, through disturbing the development of stress-sensitive neurobiological systems, including the LHPA system (e.g. Dawson & Ashman, 2000; Gunnar, 2000; Heim et al., 1997). *However, the many differences between rodents, non-human primates, and human in the neuroanatomy and physiology of this system suggest that adequate translation of the early experience-stress research from animals to humans, and from the level of basic science to applied prevention, will require an iterative interdisciplinary approach where (1) results from research on human infants and children guides the refinement of models/theories based on the animal research, and (2) the animal research on neurobiological mechanisms guides the methods and issues addressed in the human research.* Of particular note, it will require integration of the animal research with human studies of emotion, temperament, self-regulation, and early attachment relationships.

Relevance of LHPA Stress Research to the Field of Prevention. Over past decades, prevention research in mental health has become a mainstream, multidisciplinary science. This is in part due to large-scale, longitudinal studies that have documented the association between disturbances in parent-child relationships and later psychopathological outcomes (Reid & Eddy, 1997). For example, microsocial observations of family interaction have documented that high rates of harsh and inconsistent parenting as early as toddlerhood are predictive of child behavior problems, school failure, and juvenile delinquency (Patterson, Reid, & Dishion, 1992). These sorts of longitudinal studies have provided the theoretical bases and specific proximal targets for many current prevention efforts. Subsequently, theory-driven randomized prevention trials have shown that it is possible to intervene with families, thus deflecting children from depression/suicide (e.g., Bums, Hoagwood, & Mrazek, 1999), substance abuse (e.g. Aktan, Kumpfer, & Turner, 1996), and antisocial behavior (e.g. Reid, 1993) trajectories. In spite of recent advances, prevention research has rarely attempted to connect with research on the neurobiological systems that may be affected by disturbances in parent-child relationships and/or may contribute to disordered behavior. Along with the possibility that biological factors may increase risk for psychopathology comes the equally important question of whether prevention efforts, if instituted early enough, can effectively impact immature, developing neurobiological systems. Early experience/LHPA research is highly applicable to prevention research as it suggests ways that adverse social experiences, coupled most likely with genetic vulnerability, may contribute to the behavioral targets of prevention/intervention efforts.

We propose to focus much of our translational efforts on infants, toddlers, and preschoolers within the U.S. foster care system. We make this choice for three reasons.

1. Current statistics show that the foster care population is increasing in size and is highly vulnerable for psychopathology, thus, efforts to develop comprehensive strategies for preventive intervention are warranted. Indeed, the most rapidly expanding segment of the foster care population is under age 5 (Ruff, Blank, & Barnett, 1990). Psychopathology in this population is on the rise (National Committee to Prevent Child Abuse, 1996; U.S. General Accounting Office, 1995). Klee, Kronstadt, & Zlotnick (1997) reported that over 80% of children under age 6 in the foster care have developmental or emotional problems, and over 50% have problems in both areas.

2. Children in foster care have experienced both prolonged separations from primary care givers (i.e., disturbed attachment relationship) and, frequently, pervasive patterns of maltreatment-two factors which

are known to affect the developing neurobiology of stress in animal studies. Children entering foster care have by definition received inadequate parental care (albeit in newborns, these experiences occur prenatally). Neglect of physical and psychological needs combined with episodic and unpredictable trauma and numerous transitions in residence and significant adult caregivers combine to create a context that has potential to significantly compromise development, but to which the child must adapt in order to survive. These circumstances are compounded via the relationship disruption that occurs as a result of placement in foster care.

3. Preliminary preventive intervention efforts targeting care giver-child interaction have yielded promising behavioral results with this population. As described under preliminary work, we also have some suggestive data on salivary cortisol activity in response to improve caregiver-child relations. Although the circumstances leading to removal of the child from the birth family--and the very act of removal itself--may present significant challenges to healthy development, placement in foster care can also represents an opportunity. Many therapeutic approaches to working with at risk families are conducted in mental health clinics in only a few hours/wk, and must attempt to change parental behavior in the face of often overwhelming odds (parental substance abuse, marital violence, psychiatric disorder). When foster parents can provide a safe, structured, responsive environment, foster care is potentially a very powerful intervention, altering the child's experiences 24 hr/day, 7 days/wk. However, many factors decrease the likelihood that foster care will prove therapeutic. First, foster children commonly enter care with behavioral strategies that, while possibly adaptive in their birth families, can have very negative consequences in their foster homes. These behaviors place them at risk for further disrupted placements (and to be labeled with diagnoses of attachment disorder and/or one of the disruptive behavior disorders). Second, the child welfare system often lacks support, training, and ongoing consultation for foster parents. To offset these challenges, in Delaware (Dozier, a network member) and in Oregon (Fisher, a network member), we have developed interventions that provide support and training to foster parents in order to enhance the therapeutic relationship between foster parent and child. These preventive interventions are being tested through randomized, efficacy trials that offer not only the opportunity to test their impact in altering child behavior and outcomes, but also to determine whether improving characteristics of caregiver-child relationships impact the development of stress-sensitive neurobiological systems. Furthermore, through examining the temporal relations between changes in caregiving, child behavior, and the activity of stress-sensitive neurobiological systems, these randomized intervention trials offer the opportunity to examine pathways through which intervention efforts are operating to alter developmental trajectories. We argue, however, that successful integration of stress neurobiology into these prevention/intervention models will require close support from basic science researchers.

Unanswered Questions and the Need for a Richer Conceptual Basis for this Translational Research.

Despite our enthusiasm for this domain of translational research, our analysis to date has made us highly cognizant of many unanswered questions. These issues (and the need to develop effective paradigms for their explication) form the basis for the work proposed in this application. We begin by describing the issues and questions still extant in research on young children, followed by our analysis of the animal modeling work needed to probe the neurobiological mechanisms underlying the human developmental phenomena.

a. The ethics of imposing stressors on young children have severely constrained research on reactivity of the LHPA system in early development, particularly with high-risk populations. Indeed, this is why the initial work described above dealt with salivary CORT levels collected under ambulatory or "basal" conditions. The relative dearth of studies of CORT responsivity to stressors, especially in high risk infants and preschoolers, leaves us uncertain of whether altered patterns of daytime CORT provide a marker for altered stress reactivity and, if so, whether conditions of neglect, abuse, and relationship disruption produce hyper- or hypo-responsivity to stressors. It is critical to answer these questions; the answers will inform the needed conceptual and empirical work. However, ethics constrain the magnitude and type of stressors that can be imposed on young children. They also constrain the invasiveness of the procedures that can be used to access higher levels of the axis (e.g., plasma is need to measure ACTH). Ethical and feasible paradigms are needed.

b. An adequate understanding of the role of experience in shaping stress neurobiology requires a broader conceptualization than provided by a sole focus on the LHPA system. The LHPA system develops in relation to other systems regulating circadian activity (e.g., sleep and feeding), physical growth,

and the development of limbic-cortical processes involved in emotions and emotion-regulation. From an ontological perspective, disturbances of the LHPA system at different points in development may index (and influence) central systems involved in neuroendocrine and autonomic responses to physical and psychosocial stressors. These ontological processes are likely to intersect with (see *Overview of Temperament, C. Polak)*genetic vulnerabilities. Having reviewed the literature, we recognize the critical need for articulation of a richer conceptual basis for research on early experiences and stress neurobiology. Articulating such a model could guide future translational efforts. We plan to approach this challenge in two ways: strengthening the empirical base of translational research and enhancing the conceptual base.
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Conceptual issues: With regard to conceptual issues, we will continue to meet with consultants and will extend attempts to network with other networks. In our 4 network meetings to date, we identified areas that we believe need conceptual work. The two we plan to address beginning in the first year of this project are as follows.

Emotions and emotion regulation *(see Emotion and Emotional Development, A. Wismer-Fries)* While negative emotions long have been associated with LHPA (and other stress-sensitive systems) activation, dissociations among measures of emotionality and neuroendocrine and electrophysiological activity are frequently found (Gunnar, Marvinney, Isensee, & Fisch, 1988). Furthermore, when emotionality and physiological reactivity covary, it is not clear that their relations are causally linked; if linked, it is unclear whether they reflect activity in common neural circuits, the effects of physiology on behavior, or the evocative effects of behavior on caregivers and other individuals that create adverse psychosocial stimulation. Finally, as the capacity to understand and regulate emotions develops, we anticipate the emergence of complex interaction between the LHPA system (its hormones, neuropeptides and receptors) and the various neural systems involved in emotion awareness and regulation (*see Self-Regulation: Overview and Critical Questions, J. Bruce*) (e.g., the cortico-limbic systems involved in attention regulation and other facets of executive functioning (Gunnar & Davis, 2001). As the result of this complexity, nearly every pattern of physiology-behavior association and dissociation has been documented, often in contrast to the results anticipated by the researcher. This state of affairs is highly disconcerting and reflects the inadequacy of the conceptual work to date.

We plan to incorporate this conceptual work into assessments appropriate for use with high-risk populations of young children. These assessments need to include a number of electrophysiological techniques available in the laboratories of our network members: (1) measures of frontal EEG asymmetry associated with negative emotionality (Fox, 1994; Fox, Schmidt, Calkins, Rubin, & Coplan, 1996), (2) measures of sympathetic (e.g., pre-ejection period; Tottenham, Parker, Liu, & Gunnar, 2001), and parasympathetic activity associated regulating cardiac reactivity to stressors (Donzella, Gunnar, Krueger, & Alwin, 2000; Fox, 1995), and (3) startle measures to index activity of the amygdala (Schmidt & Fox, 1998). The assessments also need to index the development of frontal lobe functions e.g., (attention regulation, inhibitory control, working memory) that are expected to influence emotional behavior and stress physiology. Again, a number of potentially appropriate procedures are available in the laboratories of our network members and our consultants (such as Rothbart, Posner, Kochanska, & Pollak). We argue, however, that it is inadvisable simply to import procedures used with middle- to upper-middle class, family-reared, low-risk children for use in populations of children studied by prevention/intervention researchers. For example, standard stressors (e.g., brief maternal separation) are unlikely to have the same psychological meaning for children who have disorganized/disordered attachment relationships (*see Introduction to Attachment Theory and Research, Stovall-McClough, C.)* Furthermore, many of the neuropsychological assessments of frontal lobe functioning are not appropriate for infants and toddlers, although several researchers (including network members and consultants) are currently attempting to adapt and validate measures for such populations.

Circadian rhythms, sleep, feeding, and growth. Activity of the LHPA system is intimately related to neurobiological systems regulating sleep, feeding, and physical growth, all of which are coordinated with the earth's geophysical cycles. Disturbances in these systems are common in adult affective disorders and are hallmarks of disturbance in the pediatric mental health literature. The evidence that conditions of neglect and relationship disruption in young children disturb the daytime CORT rhythm strongly suggests associations with alterations in other hypothalamic-mediated systems (e.g., circadian rhythms related to sleep and energy regulation). In addition, evidence that psychosocial neglect can impair physical development (e.g., psychosocial dwarfism) implicates interactions with the growth system (Vazquez, Watson, & Lopez, 2000). Furthermore, work by Hofer (1987), Reppert (Reppert, Duncan, & Weaver, 1987)

Blass (1996), Barr (Barr et al., 1999), and others have yielded models for understanding how caregiver-infant interactions may provide what Hofer has termed "hidden regulators" in relationships that connect with the neurobiology of these systems. We plan to examine empirical linkages with these other systems (which are critical to healthy development), extending our conceptual work in this direction. This conceptual thrust will help inform our understanding of experiential effects on the cortico-limbic level of the stress/emotion system. We argue that efforts to understand the development of emotions and stress that fail to incorporate this basic level of psychobiologic regulation will be incomplete.

c. Continued research using rodent and non-human primate *(see The Effects of Early Post-Natal Stress in Non-Human Primates, McCormack, K. and Reading List)* **is needed to understand the neurobiological mechanisms involved in early experience-stress effects.** However, we argue that these models need to help explicate hypo- as well as hyper-LHPA responsivity. Furthermore, to enrich translational efforts, the animal research needs to integrate "intervention" into early experience designs so that we can understand what produces disorder and what fosters remediation in early development. Cross-species comparisons, however, require careful attention to species differences in the developmental trajectories of specific neural systems and appropriately validated methods for comparing developmental status across species boundaries. Normative developmental neuroanatomy research on humans and non-human primates is still sparse, hampering translational efforts. However, although occurring at different tempos across species, within species the sequence of brain developmental events leading to organization of structures appears to be predictable. This suggests that developing organisms, regardless of species, may be sensitive to perturbations at particular stages of neural development. Thus, while our analysis of animal models suggests that care giver-infant interactions are critical to the development of the stress system in rodents, nonhuman primates, and humans, disturbances in these relations may impact different levels of the stress system in different species because of varying neural maturity at birth (however, see Clancy & Darlington, in press; Finaly & Darlington, 1995). Indeed, even within species, perturbations at different points in development may produce markedly different effects on stress neurobiology.

Cross-species comparisons also require careful attention to the social ecology of development. Interactions with other juveniles are an important developmental context in many species. Privation of species-typical social stimulation from age mates (either because of experimentally-imposed social isolation or because of disturbances in early caregiving that lead to disturbed relations with age-mates) may also affect the developmental organization of emotion- and stress-related neurocircuits. Similarly, species' normative experiences with age mates may improve the "deprived" infant's capacity to manage potentially stressful stimulation, as has been documented in isolation-reared rhesus infants (Novak & Harlow, 1975; Suomi & Harlow, 1972). In rodents, the post-weaning period is one of juvenile play, when animals engage in robust social interaction, typically in the context of exploring novel elements of the environment outside the nest. This developmental context is modeled in the "enriched environment" (EE) paradigm (Black, Jones, Nelson, & Greenough, 1998), a paradigm known to enhance neurogenesis and cognitive performance and to moderate the duration of pituitary-adrenal responses to stressors (Kempermann & Gage, 1999). Recently, Meaney and colleagues (Meaney, personal communication with P.M. Plotsky, March 2001) have shown that EF exposure in animals who were deprived of sufficient maternal stimulation, reduced many of the functional effects of early maternal deprivation (e.g., reduced fearful behavior, reduced CORT hyper-responsivity, and increased CR11 mRNA in the central nucleus of the amygdala and locus ceruleus) but did not alter reduced GR in the hippocampus. Conversely, Sanchez has shown that early weaning and social isolation (which deprives the juvenile of normal age mate and environmental stimulation) results in hypo-function of the LI-IPA system combined with hyper-fearfulness and aggressivity (Sanchez et al., 1998). Our network is striving to develop paradigms permitting explication of the neurobiological processes resulting in hyper- and hypo-LHPA functioning in relation to the neurodevelopmental stage of stress-related neurocircuits, along with an explication of the impact of more species normative 'juvenile play/exploration" in helping to reorganize these circuits. We argue that this will provide a more complete basis for translating rodent early experience-stress research.

Non-human primate research continues to offer important avenues for the explication of psychobiological processes influencing the neurobiology of stress and emotions. Notably, primate models of early disruptions in caregiving provide opportunities for exploration of altered circadian rhythms. As noted above, in infants and young children neglect produces an apparent loss of a daytime rhythm in CORT. Gunnar and Suomi have demonstrated a similar effect in nursery reared Rhesus infants (Boyce, Champoux, Suomi, & Gunnar, 1995), and others have noted circadian phase disturbances in body temperature and activity rhythms (Lubach, Kittrell, & Coe, 1992). Translational research efforts are already being conducted in the laboratories of several of our network members (Suomi, Sanchez & Plotsky). However, we argue that (in some instances) the capacity for translational research has been hampered by the failure of primate and

human researchers to closely collaborate toward complementary behavioral observational schemes and assessment procedures. Though this has been done at times to the benefit of translational efforts (e.g., the development of the monkey Brazelton in Dr. Suomi' s laboratory), we have identified other opportunities for developing integrated observational and assessment procedures to assess circadian activity, secure-base attachment behavior, executive function, and emotion-regulation. Funding during this developing grant period will be used to develop, validate, and pilot such procedures. This will also provide opportunities for cross-training prevention/intervention and primate researchers.

Take Me Home