

Presented at The Sixth Annual Mentoring Conference, The University of New Mexico, Albuquerque, November 2013

TITLE: Probing Neurobiology for Insight into Mentoring Relationships

AUTHORS: Eve Leeman, MD, Susan Leeman, PhD

ORGANIZATIONS: Columbia University, Boston University

ABSTRACT:

Connection and successful interaction with other neurons is a biological imperative for neuronal survival. In other words, for a neuron to develop and thrive, it must both be individually robust, and capable of forming successful connections, or relationships. The essentiality of neuronal connections can be seen by the frenetic activity which dissociated neurons in culture exhibit in an attempt to re-establish functional connections. Through cellular interactions, neurons gain access to growth factors that determine whether they live or die. The properties of neurons are determined both by their genetic program and by changes in their genetic expression induced by cell-to-cell interaction. Since it is reasonable to assume that human emotional experience derives from the biological properties of their brain cells, it is fruitful to probe the basic biology of these cells for metaphors that might yield insight into psychological properties. Mentoring is based on the understanding that change occurs in both parties as a consequence of the mentoring relationship. Understanding the underlying neurobiology of neuronal development and function provides a new framework for a deeper understanding of these powerful human connections. This paper introduces basic neurobiological data, and includes examples of human relationships that can be interpreted in a new way based on a metaphorical analysis of the neurobiological underpinnings of human interaction. These ideas might be used to develop a new framework to strengthen the teaching of mentoring relationships.

CONTENT:

The theoretical framework we use to give meaning to the work we do, whether it be as a teacher, a psychiatrist, a scientist or an artist, greatly affects both how we view what needs to be done, and what we think we are doing. Theories often make use of metaphor, since few complex occurrences can be fully measured and observed. For example in psychiatry, the term ‘chemical imbalance,’ a term frequently used as if it were scientific fact, is a metaphor; no one has yet been able to measure the myriad of chemicals active in the brain in an instant, never mind over time, to even guess what a normal ‘balance’ might be. Yet this metaphor powerfully affects how both patient and doctor view the cause of the patient’s suffering and the likely treatment.

Similarly, theoretical ideas and metaphors that elucidate our understanding of mentoring deeply affect what we think is important and how we behave in the mentoring relationship. Mentors might view themselves as coaches, advisors, confidantes, and/or champions of their mentees, and each of these attitudes will likely engender different attitudes and elicit different responses. No matter the orientation, it is generally understood that successful mentoring is based on a successful relationship.

Some of what is known about neurobiology, specifically the biological properties of nerve cells, or neurons, can yield metaphors that help to elucidate human relationships. Clearly, nerve cell behavior cannot be directly extrapolated to explain human behavior. Yet it is reasonable to assume that human emotional experience derives from the biological properties of

brain cells, and it may therefore be fruitful to probe the basic biology of these cells for metaphors that might provide insight into psychological properties. Additionally, it may be helpful to keep these notions in mind when difficulties are encountered in the mentoring relationship. Hopefully, these metaphors will encourage a prioritization of relationships in the context of myriad mentoring concerns, and may allow for a more empathic interpretation of relational difficulties when they arise.

One of the most fundamental principles of neurobiology is the essentiality of connection. In other words, for neurons to survive, it is a biological imperative that they form and maintain functional connections. During development, an excess of neurons are generated, and a considerable fraction die as a result of failure to establish functional connections with other cells. These neural connections are not fixed, and they undergo active rearrangement not only during the developmental years, when such rearrangements are most pronounced, but also during the adult years, in response to environmental changes. Because the addition of cells to which they may connect increases their rate of survival, it is clear that the neurons that die are not fundamentally unfit for survival. Rather, contact with other cells, either neurons, or for example muscle cells, increases the neuronal survival rate. Conversely, removal of some of these recipient cells, and severing synaptic connection, can lead to cell death.

When neurons are dissected and grown in culture, they exhibit frenetic activity in an attempt to reestablish connections. In the absence of other cells, neurons attempt to connect with whatever is available, including artificial objects or themselves. To repeat, neurons are not self-sufficient; they must interact with other cells and form functional connections. These connections determine whether they will thrive, or even whether or not they will survive.

What happens in the connection that is essential to neuronal survival? The recipient cell, often referred to as the 'target' cell though this metaphor belies the bi-directionality of the relationship, releases trophic, or nutritional, factors and other signaling molecules. One of the first such substances to be characterized was initially designated Nerve Growth Factor (Hamburger, 1976). It is now known that there are a myriad of agents, including some that alter gene expression, referred to as transcription factors, which are released in the context of these connections. These substances are transmitted from the recipient cell to the connecting cell and influence the development of the relationship. These substances protect the cell during the normal phase of cell pruning; cells that don't receive growth factors die off. The provocative notion here is that input from the target, or recipient cell, is critical to neuronal survival. That is, the recipient cell is a crucial player in the development and maintenance of a viable synaptic connection, or relationship, without which the neuron cannot survive.

Many studies in the nervous system demonstrate that when target cells are removed, the projecting cells undergo hypoplasia, reflecting an inability to grow. Conversely, enlarging the target cell area allows some cells that would have died to form connections and survive. These studies demonstrate that when given the appropriate stimulation these cells can in fact thrive. It is also interesting to note that most cells can change dramatically in the context of new connections. One dramatic example of this is recent work demonstrating a challenge to the outdated notion that neurons each release a specific neurotransmitter, or chemical signal. It is now clear that neurons can be induced to release an alternative neurotransmitter based on their interaction with a target cell, and that production of new neurotransmitters by neurons can induce new behaviors (Birren, 2013).

Until now we have been talking about neurons on the cellular level, where the development of viable relationships determined by both the outreaching and the recipient cell is

critical to survival and growth, and influences neuronal behavior. On the human level, there is also a plethora of information that parallels the fundamental importance of connection. Early studies, such as those of Rene Spitz in the 1940s compared children who were raised from birth in a foundling hospital with little adult attention to those who were cared for in a nursing home with access to their incarcerated mothers. The differences were marked; the children cared for by their mothers appeared normal, while the others were severely delayed. Only 10% were able to walk by age three, and only they could speak even a few words (Spitz, 1945).

The Harlows inadvertently developed an animal model of infant social isolation in the 1960s when they separated infant monkeys from their mothers at birth to raise them in a sterile environment. After only 6 months in social isolation these monkeys did not play or groom each other, and did not defend themselves when attacked. They spent their time rocking back and forth, hugging themselves and chewing their fingers and toes. They did not mate, and females who were later artificially inseminated ignored their offspring. (Harlow et al, 1965). Interestingly, in 1975, experiments demonstrated that this syndrome could sometimes be fully reversed with the introduction of another monkey who stubbornly insisted on continued interaction (Suomi et al, 1975).

More recently, the critical importance of early connection and nurturance has become widely understood and incorporated into early childhood policy discussions. (Shonkoff et al, 2010; Shonkoff, 2011). Compelling evidence demonstrates that interactions among genes, early experiences, and environmental influences shape the architecture and function of the developing brain (Fox et al, 2010; Meaney, 2010). This means that the prior notion that genes alone predetermine fixed outcomes is no longer seen as true. We now understand that developing cells, and developing organisms, do not simply follow fixed genetic trajectories. Environment and relationships do matter. Significant early adversity or critical positive nurturing relationships can have lifelong consequences for learning, behavior, and health (Loman, 2010).

Studies on early experiences in rodents demonstrate some mechanisms that explain *how* early parental care profoundly influences brain development, regulates gene expression, and shapes neural systems. Changes caused by maternal deprivation in rats have been shown to reflect permanently altered gene expression, which can then be transmitted to offspring (Meaney, 2005). In humans as well there is a vastly increasing database that supports the notion that environmental factors plays a crucial role in coordinating gene expression, influencing neuronal, and therefore brain, development.

Because certain specific experiences have greatest influence at key developmental stages, these time frames are described as ‘sensitive periods’ (Fox, 2010, p. 28). There are multiple physiological systems, for example in the visual and auditory cortices, where these sensitive periods had been thought to be permanent. Once these times had passed, according to these theories, it was thought to be too late for correction. Newer research has yielded many contradictions to this earlier notion, illustrating how new connections, even those made later in life, can elicit remarkable plasticity in brain function.

A fascinating example of this phenomenon comes from the work of Dr. Pawan Sinha at MIT, who established a center for treating and studying blind children and young adults in India (Sinha, 2013). One particularly vexing question he hoped to answer was a famous one raised by the Irish scientist Molyneux in conversation with the British philosopher John Locke in the 1600s. Molyneux wondered how humans are able to link information they receive from their different senses into a unified perception of the world, and particularly whether this ability is something people are born with, or learn from experience. He also wondered whether this ability

to link information from different senses must be learned during a ‘sensitive period,’ or whether it could be learned later in life. Sinha was able to establish definitively that his blind subjects were not able to visually recognize objects they had previously perceived only by touch immediately following their corrective surgeries, which mostly involved removal of cataracts developed from vitamin deficiency. Yet to his great surprise, they were able to do so in as little as a few days or weeks. This finding implies a residual, latent ability for rapid learning to associate different senses, and suggests that congenital blindness does not preclude the development of sophisticated visual ability at a relatively advanced age (Sinha, 2013). What is most exciting for our purposes is that these studies provide evidence that neural plasticity, or the ability to develop new capacities in response to new experiences, exists even in young adults.

While there is clearly so much more in the neurobiological literature that could enlarge on this brief survey, the themes of the essentiality of connection, the dire consequences of isolation, the importance of developmental relationships and the capacity for transformative new connections even later in life all lend support to the enormous potential value of mentoring relationships. One example of how thinking about these neurobiological tenets can be used to conceptualize a mentoring interaction is as follows, based on a patient of mine in psychotherapy.

In this session SY was struggling with uncertainty regarding her current job and career path. Two years ago she had rejected several graduate school offers for PhD training to continue working for an exciting non-profit whose goal was to improve public school education in the sciences. She was disappointed by a conversation with her boss in which they both acknowledged that she had been feeling frustrated in her job over the past year because of insufficient challenge and intellectual stimulation. They briefly discussed how to address this. Her boss suggested an extended leave of absence. In considering this she ventured that perhaps that would allow her to pursue additional education. He countered that losing her during the busy season wouldn’t be in the best interest of the organization. She in turn felt confused because he had been the first to suggest a leave.

Looking at this from a relationship point of view strengthened by an understanding of neuronal metaphors allows the following interpretation. Both were saddened and perhaps threatened by the potential threat to their connection. Her boss felt that she might be on the verge of leaving and worried about the consequences to him and the organization; she in turn felt rejected by his suggestion of her taking a leave. This feeling worsened when he seemed to have a shift in outlook that made her feel sad that he wasn’t interested in fostering her growth. Reframing the discussion in terms that made it clear that she remained committed to the organization and hoped to find a way to engage her additional talents in a way that would both excite her and foster organizational growth allowed a more collaborative and animated discussion of the possibilities.

Additionally, the importance of her connection to me was central to my response. By empathically reflecting and validating her feelings, I allowed us to work together to figure out why she felt so demoralized. Because she felt supported in her hesitant initial expression of distress, she was able to access concerns she hadn’t initially realized were present. One can imagine that a more directive approach, such as telling her, as her mother had, that it would be smarter for her to quit the job and go back to graduate school, might have conflicted with her strong feelings of connection to her job. This rift would likely have extended to her relationship with me. Though she may at some point want to consider leaving her job, at the moment the threat to her connection was causing her to be too upset to contemplate such a disruption. It therefore would seem counterproductive to insist.

This clinical example, because it was about a career decision, reflects a circumstance that has special relevance to a discussion of mentoring, but reflects an attunement to the power of relationships to both ameliorate and activate distress that is generally relevant to my psychiatric work. There are many theories in psychiatry that reflect an appreciation of the power of the therapeutic alliance, as well as the critical impact of early attachment. However, mentally referring to neuronal metaphors while practicing has increased my capacity to recognize the centrality of connection to overall well-being. Thinking about symptoms of distress in this way does not preclude the use of medications, but it elicits a very different treatment approach than invoking the metaphor of ‘chemical imbalance’ that needs correction. Knowing that genes, environment and experience all interact with each other strongly debunks the old-fashioned but remarkably persistent notion that nature and nurture can be separated.

The clinical example illustrated a successful intervention, but there are myriad reasons for failure in a mentoring relationship that might also be considered through the lens of neurobiology. For example, in an intriguing study of youth mentoring programs, several themes emerged that contributed to the disappointing fact that only about half of youth mentoring relationships established through formal programs last beyond a few months (Spencer, 2005). One of the most poignant causes for failure that the mentees gave was mentor abandonment (Spencer, 2005, p. 339). Several students spoke of the pain of waiting for mentors who never arrived; one young person was so devastated by being stood up twice that he decided not to take the risk of trying again, even though he had initially been excited by the idea of having a stable adult in his life.

Interestingly, several of the mentors reported similar feelings of abandonment toward mentees who didn’t show. They too spoke of the pain associated with the experience and expressed ambivalence about trying again (Spencer, 2005, p. 340). From what we know of the critical nature of neuronal connection, we would hypothesize that the urge to form these human connections was strong, but that the risk of a failed connection was so threatening that these people chose instead to rely on safer, already existing relationships. Certainly it is clear that just as neuronal connections are complex, so too are mentoring relationships.

In conclusion, connection is imperative to the survival of neurons, and requires active engagement from the recipient cell. Far from being predetermined by genetic mandate, cellular relationships undergo frequent rearrangement in response to environmental stimuli and experience. Neurons change dramatically in response to the connections they form. Human relationships are also critical to normal development, and also undergo recurrent rearrangement. Human beings change in response to experience and in the context of relationships, and this is true not just in childhood, but well into adulthood. Effective mentoring is based on an understanding that change occurs in both parties as a consequence of the mentoring relationship. A high level of commitment and sensitivity is needed to be successful, as is recognition that the connection itself is paramount.

REFERENCES:

- Birren, S. J., & Marder, E. (2013). Plasticity in the neurotransmitter repertoire. *Science*, 340(6131), 436-437. doi: 10.1126/science.1238518
- Fox, S. E., Levitt, P., & Nelson, C. A., III. (2010). How the timing and quality of early experiences influence the development of brain architecture. *Child Development*, 81(1), 28-40.
- Hamburger, V. (1976). The developmental history of the motor neuron. *Neurosciences Research Program Bulletin, MIT Press, vol 12*.
- Harlow, M. F., Dodsworth, R. O., & Harlow, M. K. (1965). Total social isolation in monkeys. *Proceedings of the National Academies of Science* 54 (1) 90-97.
- Loman, M. M., & Gunnar, M. R. (2010). Early experience and the development of stress reactivity and regulation in children. *Neuroscience and Biobehavioral Reviews*, 34, 867-876. doi: 10.1016/j.neubiorev.2009.05.007
- Meaney, M. J. (2010). Epigenetics and the biological definition of gene x environment interactions. *Child Development*, 81(1), 41-79.
- Meaney, M. J., & Szyf, M. (2005). Maternal care as a model for experience-dependent chromatin plasticity. *Trends in Neurosciences*, 28(9), 456-463. doi: 10.1016/j.tins.2005.07.006
- Shonkoff, J. P. (2011). Protecting brains, not simply stimulating minds. *Science*, 333, 982-983.
- Shonkoff, J. P., & Levitt, P. (2010). Neuroscience and the future of early childhood policy: moving from why to what and how. *Neuron*, 67, 689-691. doi: 10.1016/j.neuron.2010.08.032
- Sinha, P. (2013). Once blind and now they see: surgery in blind children from India allows them to see for the first time and reveals how vision works in the brain. *Scientific American*, 309(1), 49-55.
- Spencer, R. (2005). It's not what I expected: A qualitative study of youth mentoring relationship failures. *Journal of Adolescent Research*, 22 (4), 331-354.

Spitz, R. A. (1945). Hospitalism: an inquiry into the genesis of psychiatric conditions in early childhood. *Psychoanalytic study of the child*, (1) 53-74.

Spitz, R. A., & Wolf, K. (1947). Analytic depression: an inquiry into the genesis of psychiatric conditions in early childhood. *Psychoanalytic study of children*, 2, 313-342.

Suomi, S. J., & Harlow, M. F. (1975). *The role and reason of peer relationships in Rhesus monkeys*. M. Lewis & L. A. Rosenblum (Eds.). New York, NY: Wiley.