Commentary

Understanding relationships - the contribution of neuroscience

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This commentary provides an introduction and overview of findings from neuroscience research over recent years that are relevant for considerations in regard to the social and emotional development of infants, toddlers and young children. Beyond physiological aspects of brain chemistry and the formation of synapses and pathways in a child's brain, the importance of a caring relationship with a primary care giver during the first months and the impact of severe strass factors on the development of young children are discussed from a neuroscience perspective.

Virtually from the moment of conception our brains begin to develop so that, by the time we are 24 weeks' gestation, our neurons have formed, arranged themselves in layers and migrated to where they need to be. By the time we are born some of these will have established connections that enable the foetus to have a heartbeat, a blood pressure, a respiratory breathing pattern - all that is necessary to sustain life. By 34 weeks, the brain is still only two thirds of the size it will be at birth, and, even more impressively, by the age of a year, it will have tripled in size and be two-thirds of an adult size brain.

From a physiological perspective, the neurotransmitters that dominate in certain layers of the brain depend on the position/area as well as the layer, so that for instance the dominant neurotransmitter in the cingulate gyrus (part of the limbic system) is serotonin, which is concerned with mood, appetite or sleep, as well as learning and memory. Low levels of serotonin, on the other hand, are associated with depression. However, dopamine, as a second example, occurs in areas concerned with movement and also reward motivated pathways. Acetylcholine is the transmitter at the neuromuscular junction and adrenaline/noradrenaline are found in parts of the brain concerned with directing alertness and sleep. Excitatory neurotransmitters are glutamate and their presence increases the chance that a neuron will fire, whereas the inhibitory neurotransmitters are GABA, which occur throughout the brain.

However, at birth only 15% of our neurons are connected to others, so that our neurons are sitting there waiting for information to process - the remaining 85% of connections between neurons in our brains are formed after birth - most in the first three years of life. This rapid surge in connectivity is genetically driven, but during that process the environment begins to have increasing effect on how it is sculptured into its final form. The most important developmental process in the human brain is 'pruning' - the processes whereby the brain retains and fortifies connections that are being used with greater intensity and frequency and loses those connections that are not being used. In this way we build a brain that equips

us for the life that we are experiencing at the time. This is the main (but not only) point whereby our environment is interacting with our genetic inheritance.

Of course not all our experience starts at birth, already in utero we are subject to the many experiences that the mother has - and we can find out now, through epigenetics, what kind of experiences she had. Drugs, alcohol, severe stress and unhappiness can also influence our brain growth in utero. Studies now show that even moderate stress during pregnancy can have a negative impact on early infant development. At this stage we think the effect is not long lasting providing the post-natal environment is optimal. And obviously, pregnancy stress is often unavoidable as the family income may reduce, there may be a move to bigger housing to accommodate a new family member, often this is a time when grandparents' health is failing and pregnancy itself is exhausting as well.

As experiences are fundamental for our brain development, the question arises: how do we experience the life that we are leading? From a neuroscience perspective, we would predominantly consider our five senses: touch and vibration, smell, taste, hearing, and vision. We are born into a somatosensory bath, where we are held, stroked, cuddled, kissed, sung to, talked to rocked, fed, and loved - i.e. nurtured. It is through these processes that we develop and feed our brain so that it grows and retains the connections we need to take us forward into our lives. It is said that a new-born baby is master of his/her environment. When they are hungry they are fed, hurting they are comforted, wet or dirty they are changed, lonely and feeling sociable they are talked to, tired they are put to bed and rocked to sleep - all they need is a responsive and available caregiver

As time goes on we form a very important relationship with our main caregivers – usually our parents - the attachment relationship. This relationship forms with the people who feed us, change our nappies, comfort us and touch, hold and cuddle us. This relationship becomes the template for all of our relationships in our future and it is therefore very important that it is a secure one that we can trust and know that the caregiver is there for us at all times. It is also predictive in telling us how successful we might become in many aspects of life, and a strong and secure attachment relationship also provides resilience in hard times for whatever reason. As we form that attachment, our brains lay those related connections down in the parts of our brain that are associated with our memory and emotions - the limbic system, which is formed by the cingulate gyrus, the hippocampus the amygdala and parts of the thalamus.

Again, all we need for this important attachment relationship to happen is a responsive and available adult caregiver, which are usually our parents. Not a brilliant mind (orphanage studies using mentally retarded young women as caregivers instead of orphanage personnel showed better outcomes) or a super parent is needed – just a 'good enough' parent, someone who will love and care for that child. There is usually one or maybe two primary attachments and a couple of secondary attachments in a child's world at that stage. Bronfenbrenner's well known quote "all it needs…is a progressively more complex exchange between a child and somebody else – especially somebody who is crazy about that child" sums up the importance of having an involved and caring person in a child's early life.

In relation to the above, there has recently been interest in a theoretical model of empathy – the mirror neuron system. This derives from an animal study by Singer

and colleagues in 2004 whereby it was demonstrated that empathy recruits similar neural networks as the direct experience of the emotion one is showing empathy for. These studies were looking at motor functions rather than social/emotional processing and although it is an appealing concept to think that social mirroring and empathy can result from mirror neuron function, subsequent studies have not been able to show this empirically in humans.

More recently there has also been interest in the microbiome in infant brain development. Each of us is essentially an ecology and carries on and inside of us about 1.5-2 kilogram of bacteria. This is on our skin and in our intestines mainly. In fact, 90% of the cells we carry on and within us are bacterial (10 times our own natural cells) so that we are really an ecosystem. We acquire our microbiome from our mothers as we come through the birth canal or by being physically in contact with them when breast feeding, and so on. This microbiome is initially unique to our parent and is composed mostly of lactobacilli and bifidobacteria - organisms that are essentially probiotics and promote health at the expense of pathogenic organisms that might be the alternative. Delivery by Caesarean will therefore result in a slightly different set of flora in the microbiome than if there has been vaginal delivery and broad spectrum antibiotics will also alter our microbiome – fortunately only temporarily. Within 24 hours of caesarean delivery the infant microbiome is identical to the mothers and no different than if there had been a vaginal delivery. As we experience more of life, the microflora becomes more diverse and there is constant modification and alteration of the microbiome until about three years of age, when we achieve a more adult microbiome.

This is relevant, as the infant microbiome is having ‘conversations’ with the developing brain – via circulating bacterial toxins, via vagal nerve sympathetic/parasympathetic connections (there are many more nerve cells in the gut than the brain, especially dopaminergic and serotonergic – relating to mood and behaviour), and by influencing cellular output of cytokines and other metabolites that reach the central nervous system (CNS) in circulation. They may prime or educate circulating immune cells that then travel to the brain. They influence a range of complex human behaviours, including learning and memory, mood and emotion, and appetite and satiety. They have also been linked to disorders of the central nervous system including anxiety, depression, autism and multiple sclerosis, which may be a consequence of an ecosystem that has fallen out of balance. Modern changes in lifestyle, including improved sanitisation, caesarean sections, antibiotic usage, and immunisations are among some of the factors that can shift the microbiota, and are being studied as potential drivers of the sudden increase in immune-mediated diseases in the developed world. It has been hypothesised that there is a “critical window” early in life during which the microbiota can be disrupted in a way that may favour the development of disease later in life.

We do not know exactly what these conversations between the microbiome and the developing brain are, but almost certainly they will hold the answers to some of our newer diseases such as autistic spectrum disorder, schizophrenia and ADHD. Stress in particular is modified or created by the microbiome. Mood influences biology and the reverse. However, most of the information we have about this is from studies in mice – for example, cognition in germ free mice is reduced compared to normal.

Let us go back to the infant relationship with his/her primary caregiver and consider the consequences of not having this important relationship. Growing up in a deprived, abused and neglectful environment leads to the development of a brain with connections primed for negativity rather than nurturing and joy – the implications of this are obvious and sad. The determinants of a childhood steeped in negativity (see, for example, the longitudinal studies Dunedin and Christchurch and eventually the Growing Up in New Zealand study) are identifiable at birth. These include mother being young, solo parent, has had serial partners, drug/alcohol use, history of psychiatric disease, and lack of social supports. One interesting recent study of bad asthmatic attacks has shown that conflict filled marriages can also have negative effects on children's physical as well as mental health. Importantly, the lack of a secure attachment relationship has been linked to terrible outcomes, often resulting in suicide or remorseless criminal behaviours.

Thinking about the importance of the above mentioned developmental aspects, I want to look at another more long-term determinant of outcome. Imagine a health determinant that meant that we have a much higher risk of heart disease, cancer and psychiatric disease and on average a life span shorter by 20 years? We would really want to do something about it. The Adverse Childhood Experience study done by a collaboration between Kaiser Permamente, a health insurance provider in San Diego and the Centre for Disease Control in Atlanta, has looked at certain determinants of health outcome in over 17,000 of its workers and the results are sobering. About 10 factors are named as adverse childhood experiences (ACEs): physical, emotional and sexual abuse, neglect, exposure to family violence, parental divorce/separation, drug/substance use, psychiatric illness, incarceration. Four or more of these ACEs were associated with 12-fold risk of suicide and four to five-fold risk of depression and seven or more ACEs gave three times higher lung cancer risk and three to four-fold higher heart disease rates. These risks suggest that in high doses, ACEs affect brain development, the immune system, hormonal systems, and DNA transcription.

The mechanisms are not known but likely to be mediated via cortisol, a stress response hormone that is released in times of stress. Small amounts of cortisol are probably beneficial - they enable us to get the energy to take on challenging tasks and to push ourselves and test limits. However, larger amounts repeatedly can have damaging effects on the developing nervous system. Our CNS responses become blunted or muted so that eventually we are unable to respond appropriately.

Another probable mechanism is that ACEs lead us to make lifestyle choices depending upon our circumstances which predispose to adverse health outcomes, such as smoking, alcohol, drugs, and fast foods. One of the ways in which certain traits are transferred down generations is via epigenetic transformation, i.e. gene switches. This is the process whereby, although our genetic code is unchanged, gene function can be altered by environmental factors. What happens is that environmental influences slightly alter the chemicals in the microstructure of the DNA which either blocks its function and switches it off or opens it up so that the gene can then make its proteins in the target cell. This could relate to some of the information we hold about our early experiences. This change in the microstructure of the DNA but not the genetic code can be carried through to the next generation (for example - mice trained to fear the smell of cherry blossom carried this fear through to the next generations of mice).

One aspect that needs mentioning in this context are the obvious social implications for the association between adverse early life experiences and adverse outcome relating to poverty. Currently approximately 150,000 children are living in poverty in New Zealand – missing out on warm clothing, housing, nutrition, vulnerable to chronic illness, child abuse, neglect. While being poor does not automatically mean you will have abused and neglected children, there is an association between poverty and poor outcomes – being poor adds huge stresses to parents' and children's lives.

In summary, the early childhood years are a period of massive brain growth with arguably more brain development occurring than at any other time of post-natal life. We know about the importance of healthy diet and nutrition for brain development and the importance of warm and nurturing relationships in fostering healthy brains. The absence of a supportive emotional environment can have long lasting effects and influence our adult health, both physical and mental. However, the mechanisms through which the early life experiences exert their effect are not fully understood. Attachment relationships are of prime importance and may also help promote resilience, whereas poverty is an associated risk factor for adverse developmental outcomes. More recently, we have become aware of the importance of the gut microbiome in directing brain development and this may help answer some of the questions about brain development in response to early life course.

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