Adolescent brain development and behavior

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The symposium on ‘The Adolescent Brain Development and Behaviour’ was organized in honor of the 40th anniversary of Youthdale Treatment Clinics in Toronto. The idea for a symposium dedicated to the adolescent brain was conceived over a year ago and was stimulated by recent rapid progress in neurobiological research focused on this developmental period. Puberty is a time of dramatic physiological, cognitive and emotional changes associated with increased risk for psychiatric disorders as well as increased risk-taking behavior. The increase in risk for psychiatric disorders may be a function of changes in gonadal hormones, or may result from increased emotional stress, or an interaction of these factors. Brain structures show dramatic changes in myelination, synaptogenesis and synaptic pruning from late childhood to early adolescence. Learning and experience probably interact with the biologically programmed developmental influences modifying synaptic connections and region-specific structure and function. Adolescence presents significant challenges and also unique opportunities for intervention regarding psychiatric and behavioral disorders.

How environment & genes shape the adolescent brain

Thomas Paus (Brain & Body Centre, University of Nottingham, UK & Montreal Neurological Institute, McGill University, Quebec, Canada) began his lecture by describing the emergence of a new field – population neuroscience – which merges neuroscience, imaging, genetics and population epidemiology. This field allows for the study of large cohorts that have the power to quantify the relationship of brain structure and function with genetic and environmental factors. Brain morphology is a window into an individual’s history with a view of experience-influencing activity and brain morphology, thus this can be used as a key to examine the effects of the environment. For example, studies of musicians and individuals trained to juggle have demonstrated to us that we can identify morphological changes related to learning in the human brain in vivo.

Paus described the Saguenay Youth Study that is examining the long-term effects of prenatal exposure to maternal smoking [3]. The study design uses 500 sibling pairs, half of whom are children whose mother smoked during pregnancy [3]. The families are French-Canadian and the mothers were matched for education to minimize socio-economic status factors. The most interesting result from the study thus far is the finding of sexual dimorphism in white matter between males and females [3]. Females were found to have little change from 12 to 18 years of age whereas males showed a dramatic increase in white matter during this age period. Including testosterone levels in the analysis, the researchers were able to account for much of this change. Furthermore, there was a relationship between the numbers of (CAG)n repeats in the androgen-receptor gene and the amount of white matter. Previously, it was demonstrated that the length of the repeat correlates inversely with expression of the receptor [4]. Perrin et al. found that in boys with short repeats, testosterone levels explained greater than 20% of the variance in white matter levels. When they examined what specific part of the white matter increased, it was not the myelin but the axonal caliber that was getting thicker. The authors suggested that testosterone is increasing the cytoskeleton of the axon but not the myelin. The functional consequences of this are unknown.

With regard to maternal smoking, the results revealed that the birth weight was lower in the children exposed to smoking; however, IQ was measured as similar across both groups and there was no detectable difference in cognitive abilities at puberty [3]. The exposed group did, however, have higher rates of substance abuse and psychopathology. The volume of the orbital frontal

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cortex (OFC) was smaller in the exposed group and the corpus callosum was smaller in females exposed to parental smoking. A thinner OFC correlated with an increased number of recreational drugs experimented with by the youngsters. The direction of cause and effect is not clear.

**Adolescent rhythms, circadian & otherwise**

Colin Shapiro (The Toronto Western Research Institute, and, Youthdale Treatment Centers, Toronto, Canada) pointed out the role of circadian rhythms in different physiological functions including pain sensitivity, alertness, growth hormone release and cortisol release. Many disorders also have circadian peaks, for example, temporal lobe epilepsy and nocturnal asthma. Psychiatric disorders often show disruption in circadian rhythms, notably depression with disruptions of sleep, changes in cortisol secretion and a flattening of temperature rhythm during sleep. Sleep disruption causes changes in circadian rhythm, which results in distorted thought, impulsivity and aggression. There is a strong relationship between sleep disturbances and psychiatric disorders. Depressed youth with suicidal ideation are three-times more likely to have insomnia. Shapiro also reviewed the role of melatonin in sleep and the use of melatonin to treat sleep disorders [6]. Normally melatonin levels rise between 7 and 8 pm, signaling the body to sleep 4 h later. Treatment with melatonin should be given during this time. Melatonin has an acute hypnotic effect, but the effect is primarily chronobiotic, once the body adjusts and is synchronized. Shapiro presented several cases where correction of sleep disorders improved mood and daytime behavior.

**Can we treat adolescents with SSRIs?**

Nathan Scharf (Youthdale Treatment Centers, Toronto, Canada) began his presentation by commenting that psychiatry is influenced by societal issues and trends. Selective serotonin-reuptake inhibitors (SSRIs) were originally lauded owing to better tolerance and safety compared with previous antidepressants. In 1987, fluoxetine entered the market, but only in 2003 were SSRIs approved for use in children. In 2004, use of SSRIs increased and the idea that SSRIs might increase suicidal ideation was introduced in the public press [7–9]. Scharf commented that the issues around suicidal ideation were complicated by commercial influences and by the selection criteria used to recruit subjects for antidepressant trials. For example, 66.7% of trials excluded subjects with suicidal ideation.

In the past few years a number of studies have challenged the findings that SSRIs increased suicidality and found decreased risk in patients taking medication [10–14]. Scharf commented that the risks of prescribing medication need to be balanced by the risks of the alternative, which in the real world means psychotherapy, or often no treatment. Scharf commented on the need to look at the risk-versus-benefit, specifically for the risk of non-treatment. Indeed, prescriptions for antidepressant medications decreased after the black box warnings issued in 2004 and the reported rates of suicidal ideation increased. It is unclear if this is related to the decrease in medication.

**How can we engage adolescents in psychotherapy?**

Sylvia Kemenoff (Youthdale Treatment Centers, Toronto, Canada) stressed the ecosystem model approach to treatment. In her presentation she explained the ecosystem model, which shows a series of concentric circles with the self in the center, surrounded by expanding circles of family, friends, school, community, cultures and nation. Kemenoff claimed that the world youngsters are living in today is more complicated than in previous years and that professionals working with children need to know the context in which children live. She provided examples by playing current music hits that had explicit sexual lyrics and a movie clip that provided an example of the complex social relationships of adolescents. Kemenoff highly recommended a book by Michael Bradley (2003) *Yes, Your Teen is Crazy*. Kemenoff discussed the social factors influencing teenagers, including the power of peers. Younger children are not as affected, middle-school is where they are most influenced by peers, and this influence then declines as they move through adolescence. Kemenoff said that it is not peers that apply pressure but teenagers themselves as they strive to conform. The second factor is parental attachment disruption and marital problems during these years, which increase the likelihood of behavioral problems. Kemenoff emphasized that a child’s psyche is a result of the interaction between their genetic predisposition and their environment/experience.

Kemenoff then spoke about the therapeutic techniques that contribute to successfully engaging teenagers in treatment (e.g., commenting positively on something unique about the child and treating them with respect). However, the practitioner should let the child know that she/he respects parental authority and will not undermine the child's parents.
Finally, Kemenoff also discussed the power of expression in treatment (e.g., music, poetry, dance, art and stories), and closed by emphasizing that establishing and maintaining a trusting relationship is the key to a successful intervention.

**Adolescent aggression: how & why?**
Kate Cochrane-Brink (Youthdale Treatment Centers, Toronto, Canada) began by explaining that aggression can be adaptive and does serve a purpose, particularly for self-defense. Aggression is maladaptive when it occurs out of social context; occurs without the usual social antecedents; has a long duration and or extreme intensity; and does not end appropriately [19].

Aggression is a common problem that occurs in 60% of children that present at psychiatric clinics. It is common in both girls (76%) and boys (86%). It occurs across diagnoses and is relatively refractive to treatment [16]. Adolescents are at greater risk of being aggressive for a number of reasons including:

- Adolescence is a time where a number of psychiatric disorders begin;
- Influence of peers;
- Intensity of dating relationships increases;
- Experimental and risk-taking behavior increases;
- Increased strength and access to weapons;
- Neural maturity differences between the limbic region and prefrontal cortex has been suggested as a neurobiological factor [17,18].

Aggression is heterogeneous, but there are defined subtypes. Clarifying etiological subtypes allows for the development of specific interventions and provides prognostic information. Three validated subtypes of aggression are reactive affective defensive impulsive (RADI), proactive instrumental planned (PIP), and relational. Cochrane-Brink then went on to describe aggressive behavior in girls, which is underestimated and understudied. The salient forms are indirect aggression, which takes place behind the back of the victim, or anonymous. Relational aggression has the intent to damage or manipulate, particularly in relationships where there is gossiping, exclusion and spreading rumors. This harms the social status of others. Basically, language is the weapon. This type of aggression spans all ages but is most common in adolescents, more common in girls and is the preferred modus operandi in girls.

This type of aggression is not benign and harms the perpetrators as well as the victim. There are a number of neurobiological models of aggression, in particular the top-down model, which suggests that higher cognitive functions are overwhelmed by the bottom-up limbic system. Neurobiological models of the psychopathology of aggressive behavior indicate that there may be hypofunction of the amygdala and deficits in recognizing fearful facial expressions. There is little information on the neurobiology of relational aggression as this is a relatively new frontier.

**Neurobiology of adolescent risk-taking & decision-making**
Adriana Galvan, UCLA (CA, USA) explained that risk-taking behavior in adolescents is normative and can be adaptive [19]. There are ecological reasons for risk taking, for example, leaving home. However, these behaviors can lead to long-term harmful outcomes (e.g., substance abuse). Factors for risk-taking behavior include peers, predisposition, family history, life stressors and poor impulsive control. Age-related changes in synaptic density including pruning occur during adolescence with regional specificity. The brain is 90% of its adult size by first grade (age: 6 years); however, the amount of grey matter increases until early adolescence and white matter increases into the early 20s. The prefrontal cortex development is completed last. The prefrontal cortex is involved in decision making, impulse control, future planning, goal-directed behavior and appreciation of future outcomes. This is part of the brain that adolescents need for good judgment and it develops last. So why do children not also show the same levels of suboptimal decision making as adolescents? The imbalance model of risk-taking behavior suggests that in adolescents the subcortical region (social-emotional system) is overactive relative to the frontal cortex (cognitive control system). As this dual system is involved in decision making and judgment, such imbalance may lead to dysfunctional behavior [18].

In the laboratory setting, adolescents will make rational decisions, but in real life emotions are involved. In a laboratory-based test of reward, researchers observed an increased influence of monetary reward in adolescents compared with younger children. The results suggest that brain activity relates to the significance of reward. It is also possible to interpret the data as indicating that small rewards were perceived
as punishment. These studies indicate that adolescents have heightened brain activity to incentives/rewards while cognitive control systems are still relatively immature (20).

Galvan then described a series of experiments that were conducted to find out if frontal regions actually help regulate affect (21). Galvan summarized the results by indicating that the adolescent brain is a work in progress. Adolescents predisposed to mental disorders may be at further risk during this developmental period when risky behaviors are more likely. Neurobiologically, the evidence indicates that adolescents have an imbalance between heightened sensitivity to incentives and affect and a less developed top-down cognitive control. Thus, adolescents are more likely to respond to reward in an emotional way with less opportunity to engage in cognitive control.

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