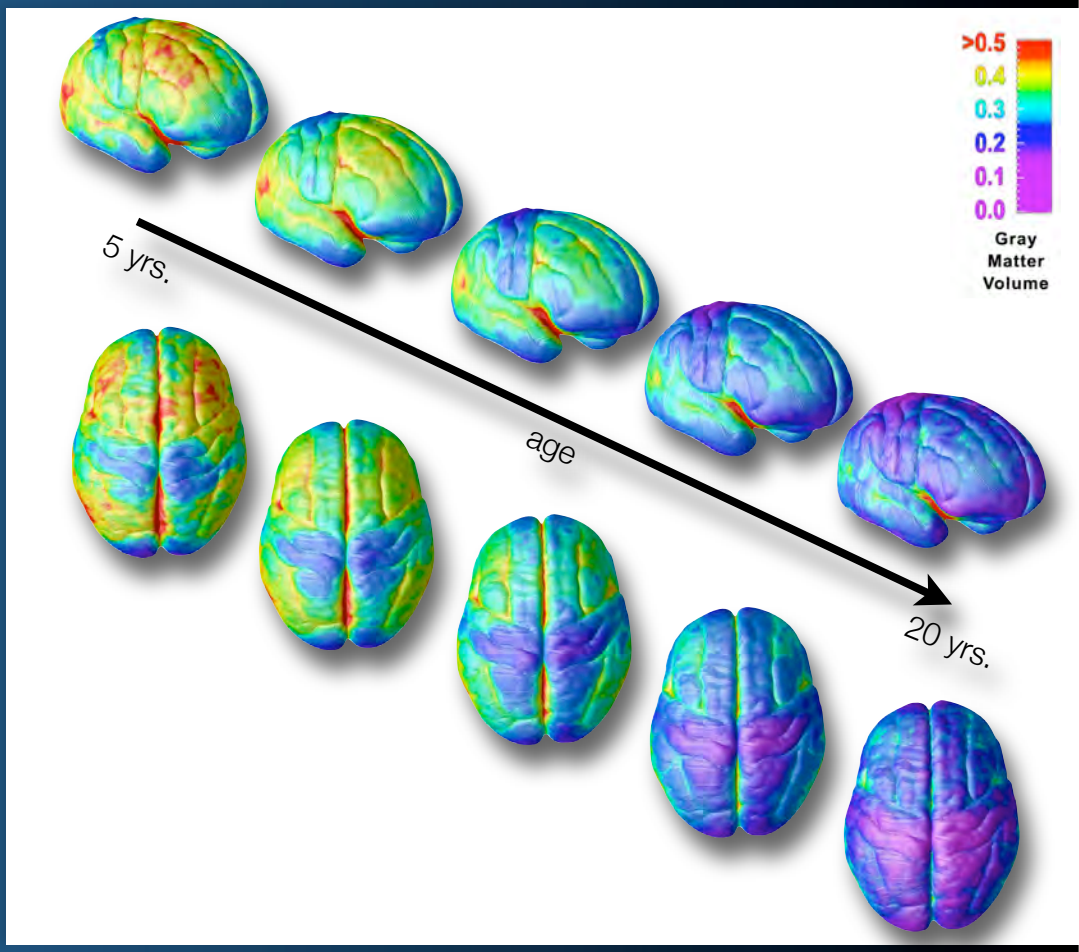

Alcohol and The Teenage Brain:
Safest to keep them apart

An Opinion Piece prepared by

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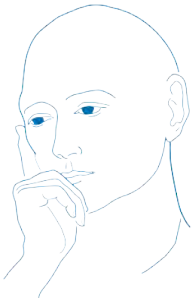

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Executive Summary

Traditionally, the major components of brain development were believed to occur before birth and in early childhood. Consequently, there has always been a strong view that exposure to alcohol and other substances that are toxic to brain cells should be minimized during these periods. The most recent NHMRC guidelines (2009) have recently significantly reinforced this perspective.

With the onset of puberty, most cultures have recognized that individuals move rapidly towards sexual maturity and associated adult responsibilities. Consistent with that major change in social roles, and its associated rites of passage, consumption of alcohol and other substances is encouraged or at least widely tolerated.

Following the discovery of new highly sensitive brain imaging techniques in the 1990s, as well as key findings about the ways in which nerve cell connections are radically reshaped in the post-pubertal period, these traditional views are now undergoing significant re-evaluation. At this time, it is rapidly becoming clearer that alcohol and the teenage brain don't mix and that exposure to alcohol should be postponed and preferably avoided at least until the late adolescent or early adult years.

Much of the clinical, neuroimaging and neuropsychological literature demonstrating the adverse effects of alcohol on the brain is based on adult rather than teenage subjects. The inferences concerning the likely toxic effects of alcohol on the adolescent brain also rely strongly on findings in developing animals rather direct observations in human studies. Those animal studies have tended to emphasise the long-term adverse cognitive and behavioural effects of alcohol and other drug exposures during the relevant "adolescent" periods of brain development.

Traditionally, the more conservative academic position has highlighted the lack of a large number of long-term human studies and, hence, concluded that the potential adverse effects of early exposure to alcohol amongst teenagers and young adults should not be overstated. While this perspective is understandable, it needs to be balanced first by the emerging findings in human neuropsychological and neuroimaging studies. On balance, the available studies suggest that the adolescent brain is particularly sensitive to the negative effects of excessive or prolonged alcohol exposure, including the adverse effects of binge drinking.

Additionally, one needs to consider the large body of evidence of the degree of direct harm due to injury (including significant head injuries) that results from excessive risk-taking in young people who consume alcohol. This degree of risk-taking while intoxicated is likely to reflect the combination of the disinhibitory effects of alcohol (which are present at all ages due to dampening down of frontal lobe function) and the relative lack of development of the frontal lobes in adolescents. From this perspective, the risk of accidental injury due to excessive risk-taking and poor impulse control is particularly likely to be evident in younger teenagers who use alcohol.

If one weighs up the available evidence concerning direct risks to brain development, short and long-term effects on cognitive and emotional development and risks of associated injury due to poor judgement and lack of inhibition, on balance, two conclusions now appear to be justified:

1. Alcohol should not be consumed by teenagers under the age of 18 years;

And,

2. Alcohol use is best postponed for as long as possible in the late teenage and early adult years.

The key emerging scientific issues that support this view are:

- The frontal lobes of the brain underpin those major adult functions related to complex thought and decision and inhibition of more child-like or impulsive behaviours. These parts of the brain undergo their final critical phase of development throughout adolescence and the early adult period. While there is considerable individual variation in this process, it appears to continue well into the third decade of life (age 22-25 years) and may be particularly prolonged in young men;
- Key parts of the temporal lobe, including the amygdala and hippocampus, continue to undergo development during the adolescent period. The amygdala underpins the normal fear response while the hippocampus is an essential part of normal memory function;

- The final phase of frontal lobe development occurs at the same time as the onset of all of the common and serious mental health problems. Seventy-five per cent of adult-type anxiety, depressive, psychotic and substance abuse related disorders commence before the age of 25 years;
- Alcohol has significant toxic effects on the cells of the central nervous system, and depending on dose and duration of exposure, is likely to result in serious short-term and long-term harm. Those harmful effects are most likely to be evident in areas in which the brain is still undergoing rapid development (i.e. frontal and temporal lobe structures);
- Alcohol, even in small doses, is associated with reduction in activity of the normal inhibitory brain processes. Given that such processes are less developed in teenagers and young adults, alcohol use is likely to be associated with greater levels of risk-taking behaviour than that seen in adults;
- Alcohol normally results in sedative effects as the level of consumption rises. It appears that teenagers and young adults are less sensitive to these sedating effects (due to higher levels of arousal) and are, therefore, likely to continue with risk-taking behaviours. As they also experience loss of control of fine motor skills, the chances of sustaining serious injuries (including head injuries) are increased;
- Exposure to significant levels of alcohol during the early and mid-adolescent period appears to be associated with increased rates of alcohol-related problems as an adult as well as a higher rate of common mental health problems such as anxiety and depression;
- Young people with first lifetime episodes of anxiety, depression or psychotic disorders who also consume significant amounts of alcohol are at increased risk of self-harm, attempted suicide, accidental injury as well as persistence or recurrence of their primary mental health problem.

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1.0 Adolescent Brain Development and Related Changes in Cognitive Function and Social Behaviour

1.1 Critical Changes in Brain Structure

When most scientists talk about brain development, they usually emphasise the importance of the fetal period and early childhood. This is understandable as the basic brain structure is laid out in utero and then the most intense period of growth in connections between brain cells occurs in early childhood (see Paus et al 2008; Bennett 2008). This process of basic wiring underpins the acquisition of simple motor and sensory functions and language, as well as those aspects of behavioural and emotional control that are central to normal development in the pre-pubertal years.

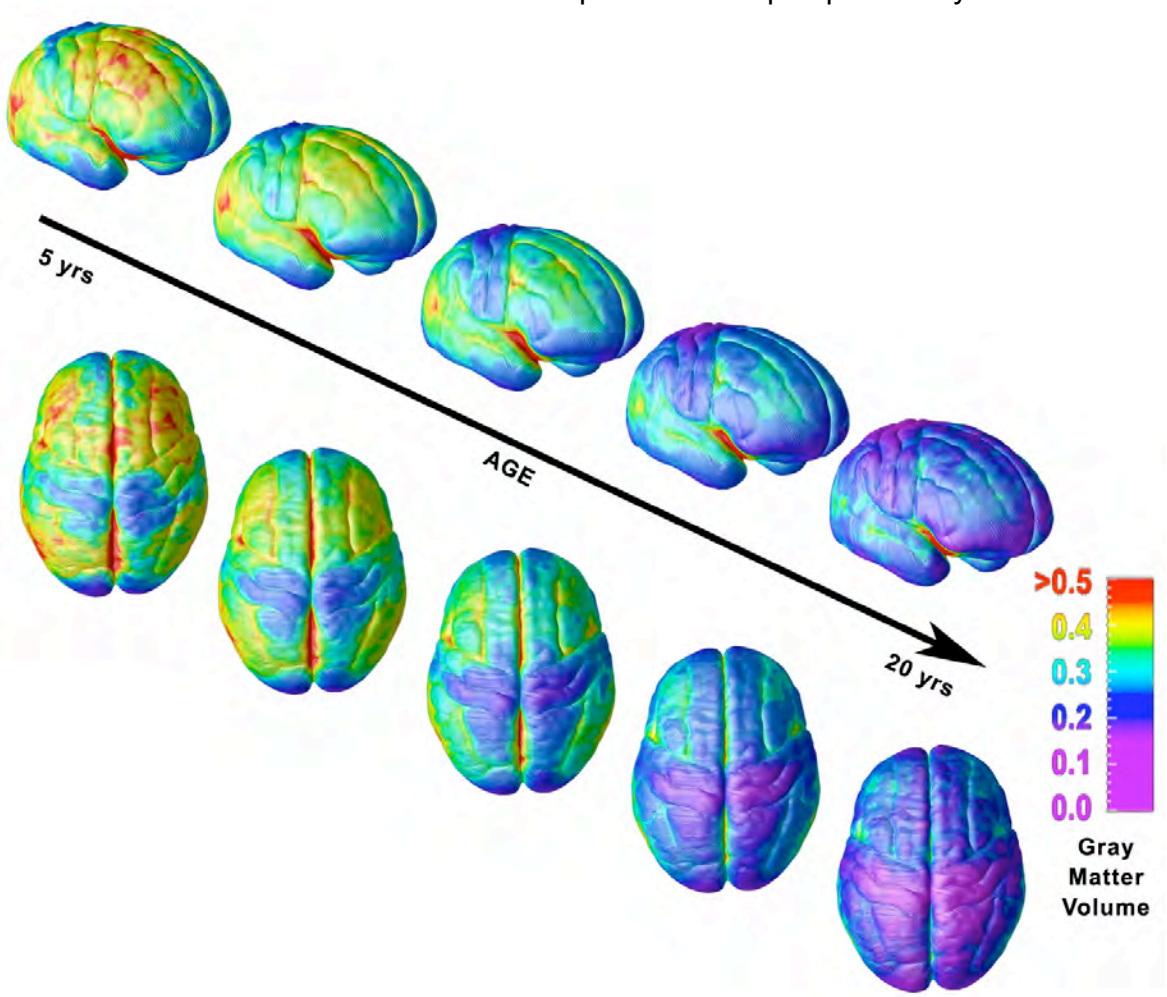


Figure: Gogtay, N. et al (2004). Dynamic mapping of human cortical development during childhood through early adulthood.

Brain development then undergoes a critical final phase after puberty. During this later phase, the brain shifts from simply acquiring new connections between nerve cells to 'pruning' those same connections. This occurs largely on the basis of learning and experience and leads to the establishment of the most efficient pathways for performing those more complex forms of thought and behaviour that characterize adulthood (see Gogtay et al. 2004). This process means that the thinking part of the brain (the grey matter) actually shrinks in size but increases its productivity.

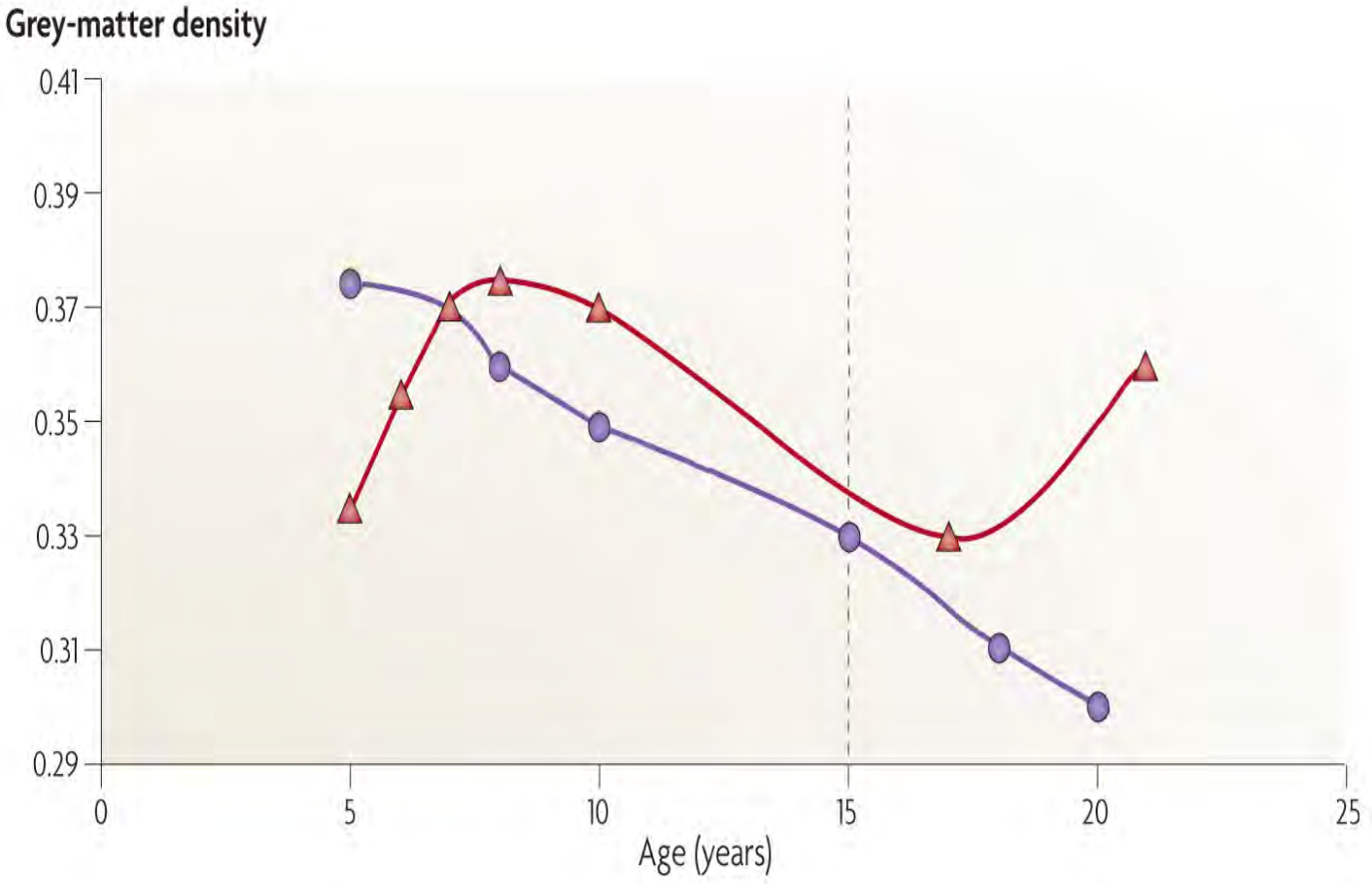


Figure: Paus T, et al (2008) Why do many psychiatric disorders emerge during adolescence?

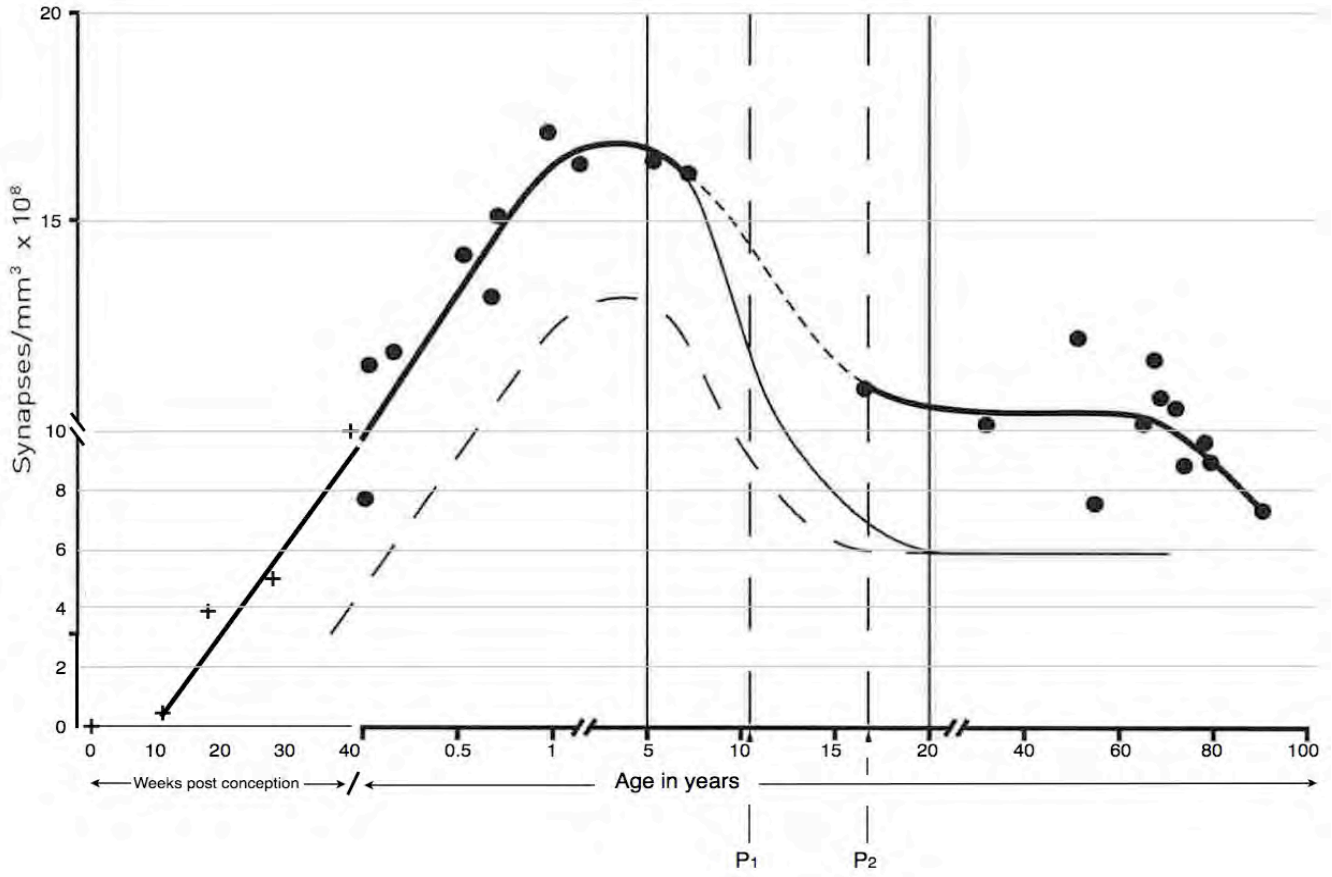


Figure: Bennett, M (2008) Dual constraints on synapse formation and regression in schizophrenia: neuregulin, neuroligin, dysbindin, DISC1, MuSK and agrin At week 20 all neurons in the foetal brain are present. For the remaining weeks of gestation the foetal brain develops synaptic connections at a rate of over 50 million connections per second. At birth this rate reduces to 1 million synapses per second.

As part of this process of improving the efficiency of the brain, the cabling system (the white matter) also undergoes its final phase of development (i.e. myelination). This results in enhanced communication between the key thinking regions of the cerebral cortex (see Fryer et al 2008). Of key relevance is the notion that better cabling is part of the way that the more adult parts of the brain (frontal and temporal lobes) increasingly exert their influence over the more primitive, instinctual or impulsive parts of the brain.

This last phase of brain development extends well beyond the early teenage years and is now known to continue into the third decade of life. This developmental period may start later (along with puberty) in boys and still be active into the mid-20s. Interestingly, we are sexually mature (i.e. able to reproduce) long before our brain reaches its fully mature state! While the whole brain is affected by these various grey and white matter processes, some regions are changing in more fundamental ways than others. Two critical areas – the frontal lobes and the temporal lobes (the latter includes the amygdala and hippocampus), are profoundly remodeled at this time (see Gogtay et al 2004.)

The frontal lobes of the brain underpin those major adult functions related to complex thought and decision-making. They are also critical to the progessive inhibition of more child-like or impulsive behaviours (see Table 2: Brown et al. 2009; Casey et al. 2008). Therefore, for humans to function in complex interpersonal or information-rich environments well-developed frontal lobes are essential. It is the size and sophistication of our frontal lobes that most differentiates humans from other primates.

Component	Behaviors
Goal-directedness	Establishing goal hierarchies, maintaining goals, organizing sequences, evaluating progress, using strategies
Initiation/inhibition	Initiating behavior independently, self-cueing, inhibiting inappropriate behavior, constraining actions with rules
Flexibility/perseveration	Generating novel possibilities, flexibly switching between guidelines, performing contingency-based revisions, strategizing
Abstract reasoning	Using rule-guided thinking, forming concepts, using hierarchical and temporal relationships
Reward appraisal	Evaluating reward likelihood, performing relative valuation, using reward appraisal to guide behavior
Social appraisal	Understanding social norms, apprehending social cues, incorporating social information into decision-making

Figure: Components of Executive functions and sample behaviours. From Brown S, et al (2008) A developmental perspective on alcohol and youths 16 to 20 years of age.

The circuitry of the frontal part of the brain has major links to other regions (subcortical nuclei; temporal lobe structures) related to emotion, memory, complex motor behaviours and goal-directed learning (see Circuit refs). Our understanding of other behaviours linked to impulsivity, additive behaviours and other abnormal patterns of learning has advanced alongside the discovery of these critical circuits (see Crews & Boettiger, 2009; Balleine & O'Doherty, in press). Disruptions of these fronto-striatal circuits is likely to be critical to the onset and maintenance of addictive disorders.

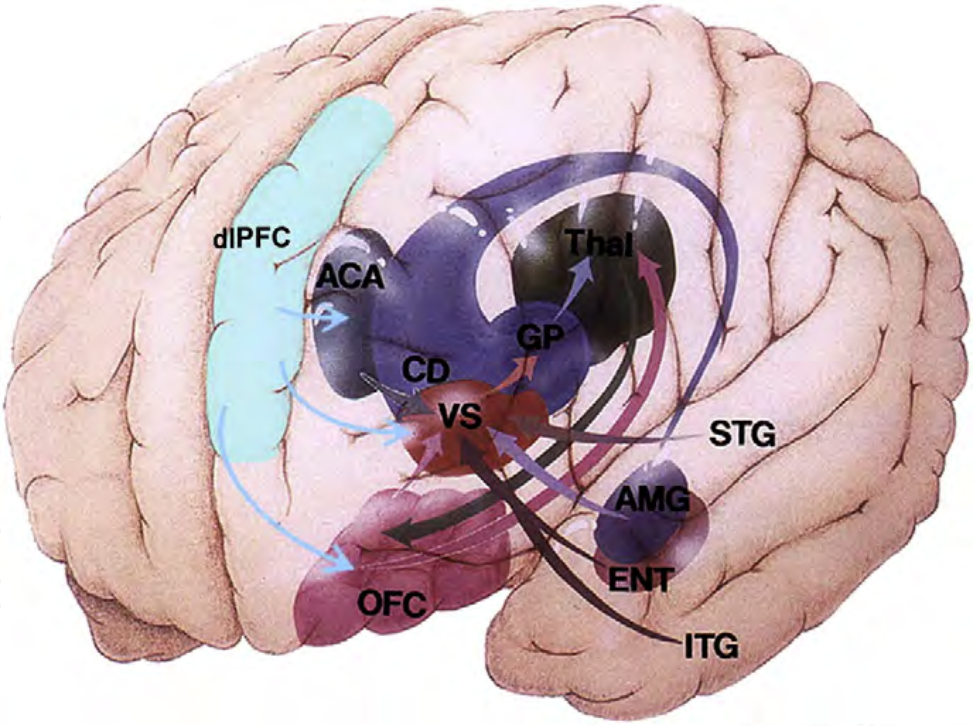


Figure: Crews F, Boettiger C (2009) Impulsivity, frontal lobes and risk for addiction.

Key parts of the temporal lobe, including the amygdala and hippocampus, continue to undergo development during the adolescent period. The amygdala underpins the normal fear response, while the hippocampus is an essential part of normal memory function. The hippocampus typically shrinks in size later life alongside illnesses like dementia (such as Alzheimer's disease) or late-life depression (see Hickie et al. 2005). It is also extremely sensitive to alcohol and is reduced in size in adults with established alcohol-related disorders.

1.2 Critical changes in Cognition and Social Behaviour

The teenage years are often seen to be very challenging from an emotional and behavioural perspective. In reality, the development of more adult-like moods, thought processes, identity and interpersonal relationships is a continuous process across the adolescent period. The general direction is from more immature and child-like thought processes, and relative lack of impulse control, to more mature, considered and thoughtful actions. This movement in behaviour is dependent on the continuing and active development of the underlying brain structures, particularly those in the frontal and temporal lobes (as described above).

There are, however, real challenges in behaviour to be considered. Immediately, following puberty more rapid changes in mood and more intense negative feelings may become apparent. Greater sensitivity to negative interactions with peers and a more fragile sense of self may be evident. Issues related to body image and other gender identity and sexual orientation issues may emerge. An individual's capacity to utilize new emotional and cognitive processes will be affected by a range of internal (rate of brain development, particularly frontal lobe development) and external processes (e.g. positive or negative social and educational experiences).

A key aspect of adolescent behaviour is the movement away from safe family environments and close kin relationships. The drive to greater novelty-seeking and a broader social network is a normal and desirable aspect of development. Experimenting with new environments, new relationships and first-ever sexual experiences all pose new challenges. While these challenges are associated with increased anxiety, they are also associated with an increased sense of mastery (when transacted successfully) and personal pleasure.

The key cognitive and behavioural challenges throughout this period are the capacity for thoughtful reflection, learning from experience and planning future events with a view to judging the likely consequences of new actions. In each case, weighing up the potential risks is critical. Taking time to integrate information relative to the desire to act impulsively is a key consideration.

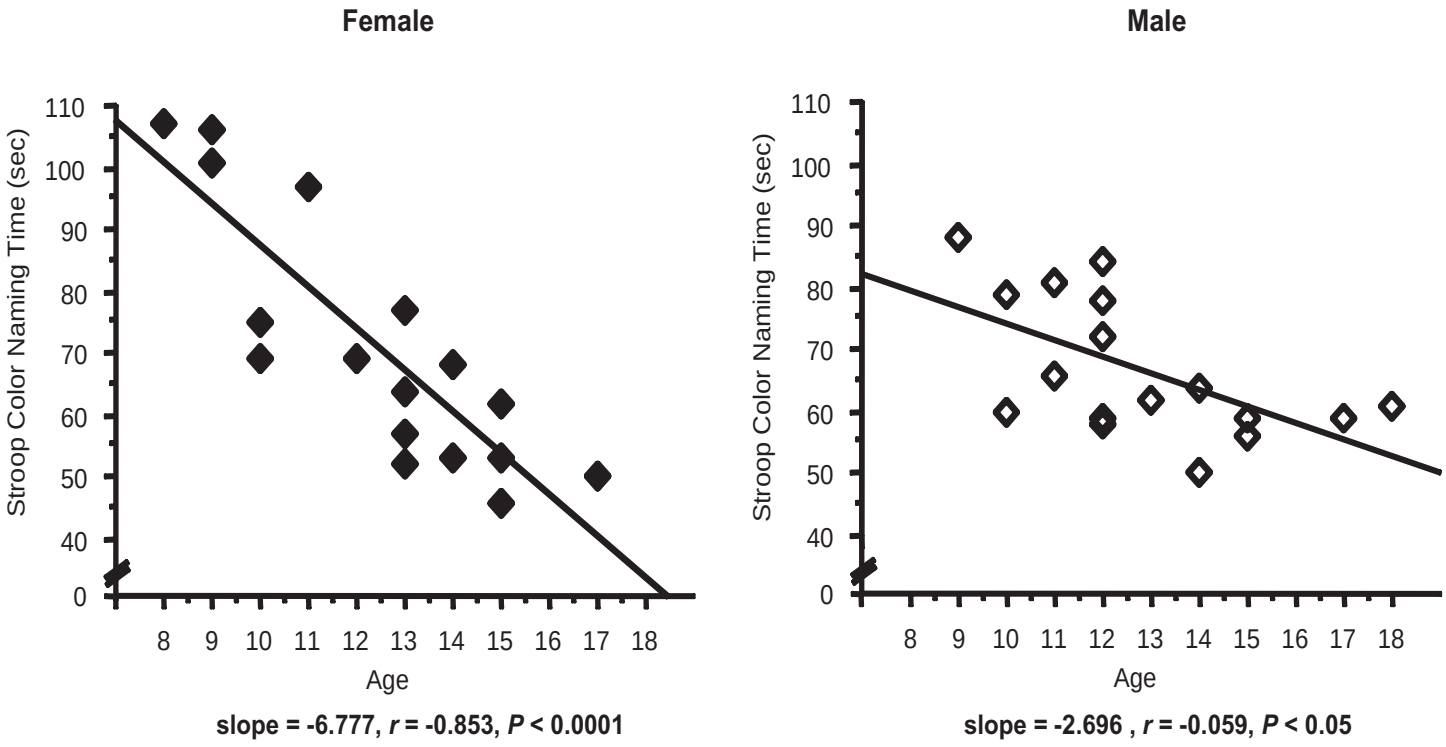


Figure: Silveri M,et al (2008) Relationship between white matter volume and cognitive performance during adolescence: effects of age, sex and risk for drug use.

Throughout the adolescent period, very specific advances in key cognitive functions affecting attention, working memory, visuospatial capacity, motor speed and coordination, abstract reasoning, decision-making, planning for the future and the capacity to make accurate social judgements become evident. However, these complex functions do not develop at the same rate in all people. There are also significant differences between young men and young women. Consequently, some of these very important adult capacities may be relatively underdeveloped in some individuals in their late teens or early 20s.

Other aspects of normal physiology, notably the 24-hour circadian cycle which determines the sleep-wake cycle, are strongly influenced by frontal lobe systems. During adolescence this system is shifted, resulting generally in increased wakefulness in the evening, delayed onset of sleep and later morning wakening. This increased alterness during the evening may offset the sedative effects of alcohol and other drugs.

1.3 A critical period of heightened vulnerability

Given the profound and sensitive nature of the processes related to brain, cognitive and emotional development taking place during adolescence, the human and animal research literature has begun to explore the concepts that:

- adolescence is a period of heightened vulnerability to any environmental insult; and
- brain insults during the adolescent period may have more profound long-term effects than insults that occur earlier in development or later in adult life.

The concept of heightened vulnerability rests primarily on the new biological evidence of the rapidity and extent of brain change taking place at this time. Therefore any injury (e.g. brain trauma or hypoxia) or other toxic insult (e.g. alcohol, other drugs, infection) at this time is likely to disrupt a wide range of key brain functions. The long-term ramifications of those changes are likely to be profound as some of the brains most important integrative functions may be permanently disrupted.

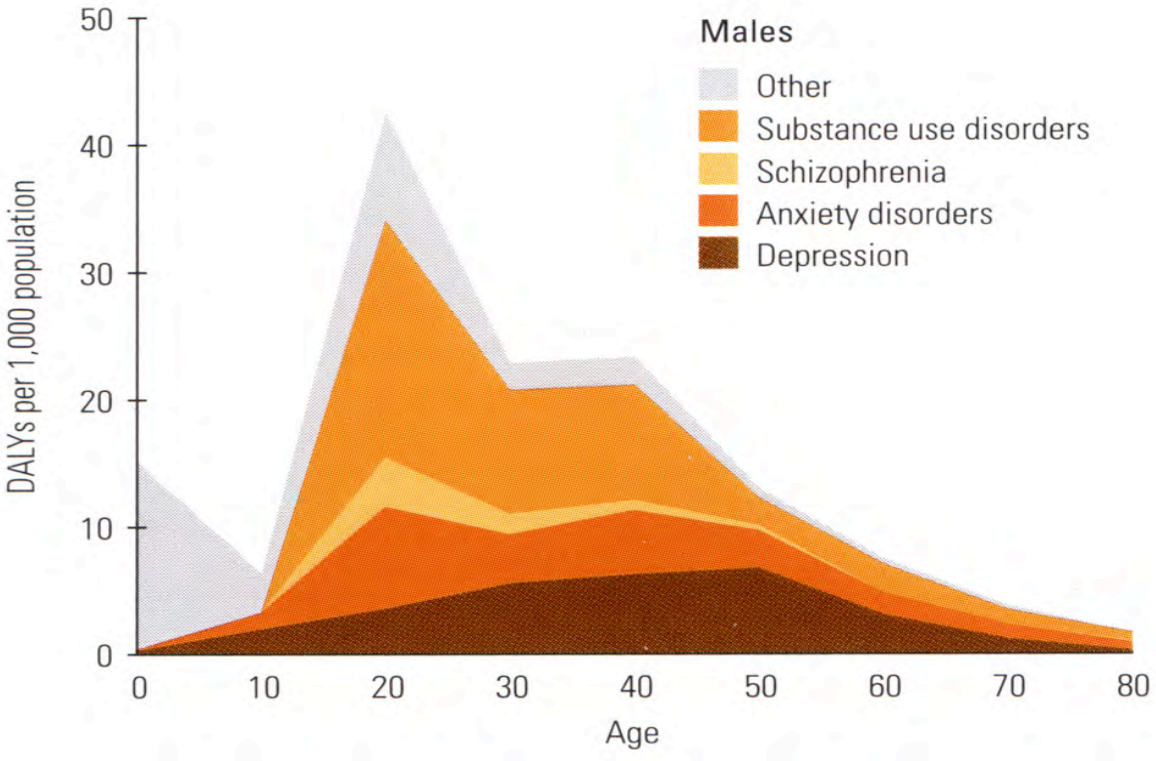
Further this view is also one that integrates new knowledge of the underlying biological processes with current evidence about the nature of the environmental risks that young people are likely to face. For example, as noted above, changes in sleep wake cycle during this period (i.e. being more awake at night) increases the chance that teenagers will ingest larger amounts of alcohol in the evening before becoming sleepy. Compared to adults, this interaction increases their chance of dose-dependent alcohol-related damage. Similarly, current patterns of binge drinking result in very high blood alcohol levels that appear (from comparable animal experiments) to be particularly likely to cause damage to sensitive regions of the brain (notably the hippocampus in the temporal lobe and the white matter connecting tracks).

In essence;

- ***The teenage years are those associated with the final critical period of normal brain development and, when transacted appropriately, result in the development of adult cognitive functions including mood-regulation, reduced impulsiveness, accurate social judgements and complex planning capacities;***
- ***From a behavioural perspective, an increase in novelty-seeking and social exploration outside prior family and kin relationships is expected but is also associated with a relative lack of development of impulse control, mood regulation and consideration of the long-term implications of risk-taking behaviour;***
- ***Given the scope and extent of reorganization of brain structure and functions during this period, the brain may be more sensitive to specific insults than at earlier childhood or later adult periods;***
- ***Damage to the brain during this critical development period appears to have long-lasting consequences on those higher order cognitive and emotional functions that are essential for maximum occupational and social function as an adult.***

2.0 Onset of mental health problems during the adolescent period

Seventy-five per cent of adult-type anxiety, depressive, psychotic and substance abuse related disorders commence before the age of 25 years. While prior to puberty a range of neurodevelopmental or other emotional problems are evident (childhood anxiety, conduct disorders, specific learning difficulties, attention-deficit and hyperactivity and autistic-spectrum disorders) the onset of adolescence is associated with a sharp increase in the rate of common forms of anxiety and depression (see Victorian Disease Burden Study; Paus et al 2008). Additionally, the more severe forms of psychotic disorder (first-episode psychosis, schizophrenia, bipolar disorder) often show their first signs during the mid and later adolescent periods. Those individuals who had developed child-onset disorders with associated social skill or educational difficulties also tend to face a new range of challenges as teenagers.



Victorian Burden of Disease Study: Incident YLD rates per 1000 population by mental disorder

Figure: Victorian Burden of Disease Study: Incident YLD rates per 1000 population by mental disorder

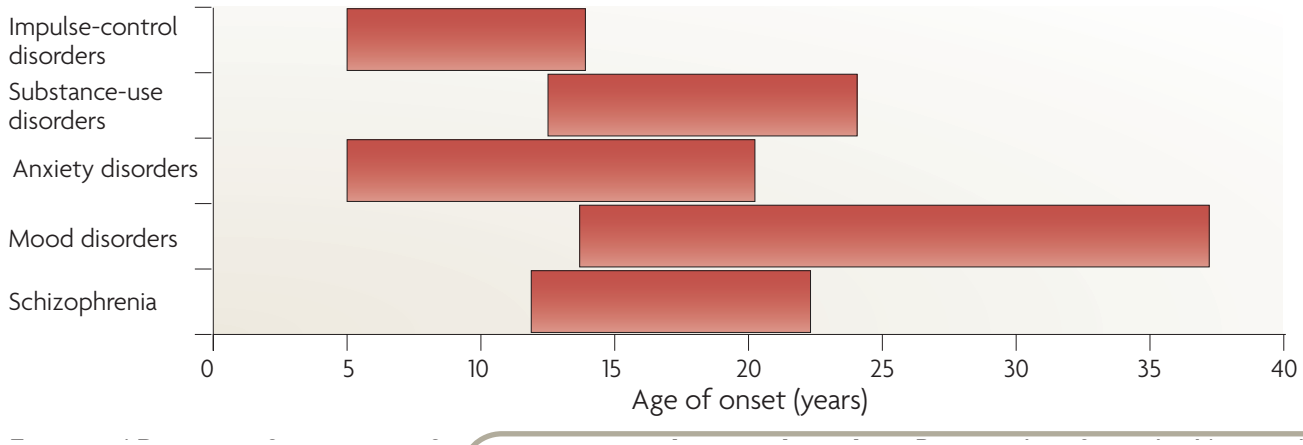


Figure: Paus T, Keshavan M, Giedd J (2008) Why do many psychiatric disorders emerge during adolescence?

Many of the more adult-like mood disorders emerge at the same time as the frontal and temporal lobes are progressing rapidly through their own program of reorganization (driven by synaptic pruning and myelination of white matter tracts). What has also become clear in recent years is that severe mood disorders and psychotic disorders also have the potential to cause damage to critical brain structures in those same frontal and temporal lobes (see Lorenzetti et al. 2009; Wood et al, 2009). Of particular note, is the reduction in hippocampal size in depression (see Hickie et al. 2005) and the changes in the frontal lobe regions that regulate mood. The hippocampus is located in the temporal lobe and is responsible for many aspects of short-term memory function. It is the structure which shrinks in dementias such as Alzheimer's disease and is known to be very sensitive to damage from high or persistent levels of alcohol in adults.

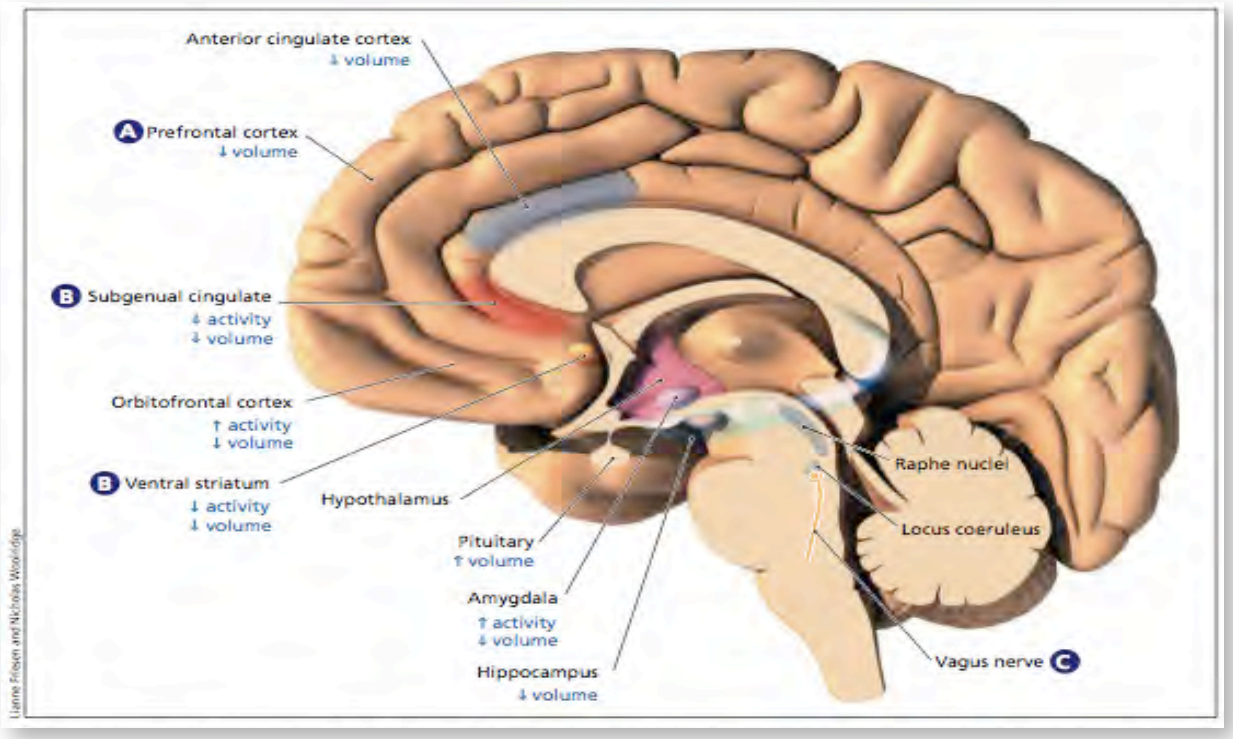


Figure: Brain structural abnormalities in major depression

The mechanisms underpinning such adverse effects are the subject of very active research and appear to include a reduction in nerve growth factors (particularly brain-derived neurotrophic factor [BDNF]) and possibly impaired neurogenesis (i.e. generation of new nerve cells, particularly in the hippocampus). The degree of damage appears to reflect both the severity and duration of the mental disorder as well as the length of time the disorder remains untreated. Many of the current medical treatments for depression and more severe psychotic illnesses actually result in increased levels of BDNF and may, therefore, reverse the loss of brain tissue seen in these illnesses (see Hickie et al. 2005).

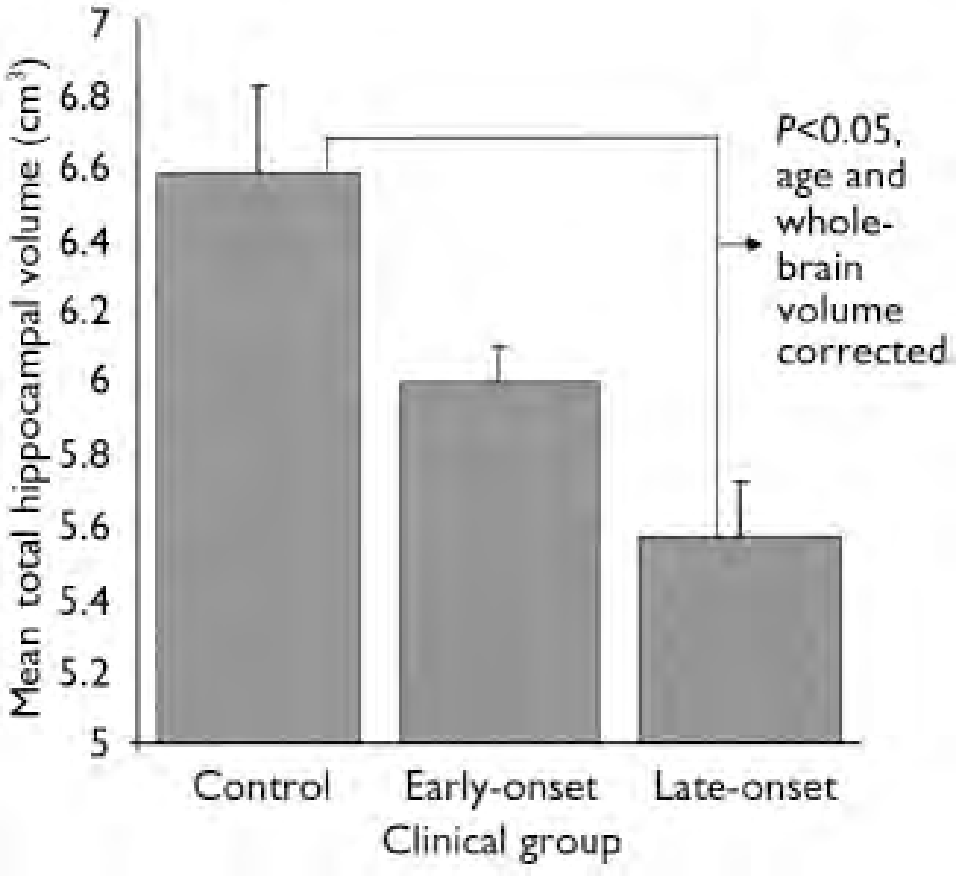
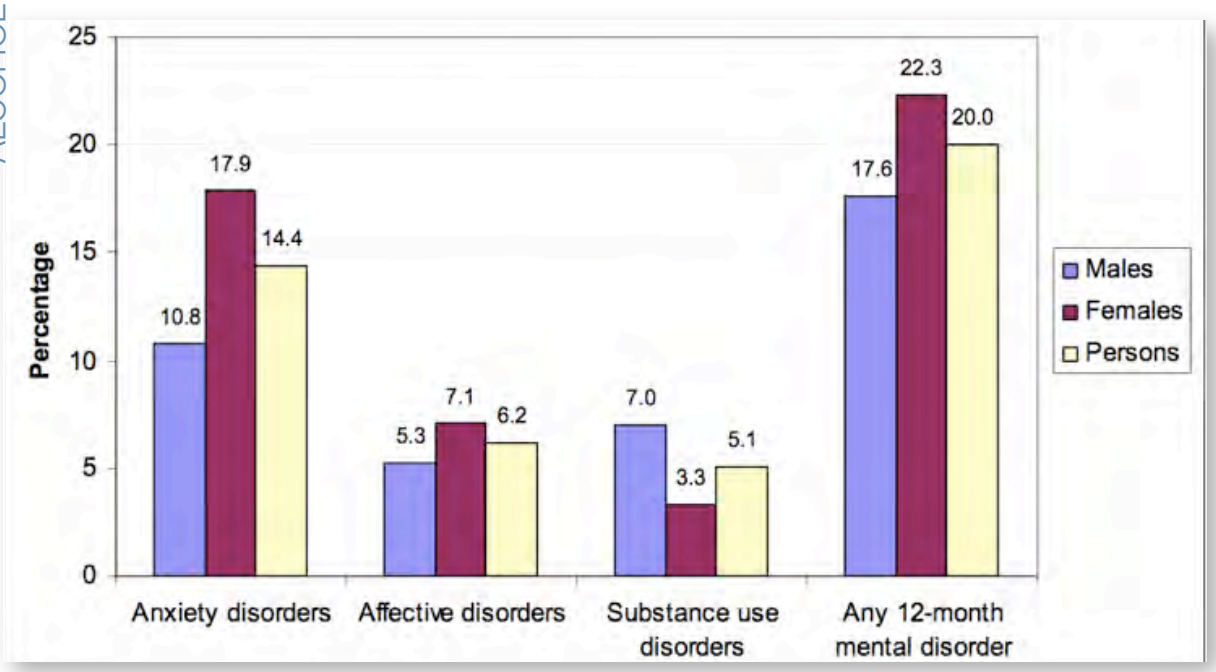


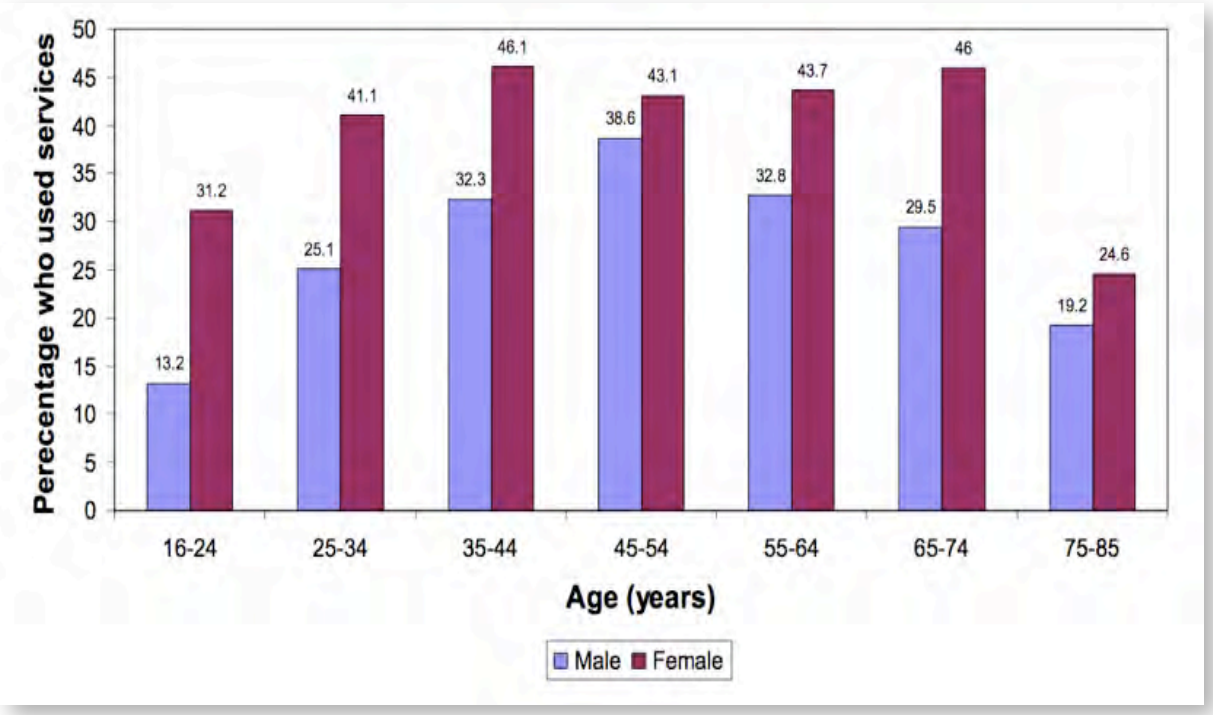
Figure: Hickie I.B. et al (2005) Reduced hippocampal volumes and memory loss in patients with early- and late-onset depression.

The early onset of alcohol and other substance misuse problems in the teenage years, before the onset of other anxiety or mood problems, appears to increase the chances that a young person will go onto develop another major mental health problem in the later adolescent or early adult period. This could be because they share common genetic or environmental risk factors or that the earlier use of substances is a direct cause of later difficulties. It is likely that use of brain-toxic substances early in the adolescent period has the potential to interfere with normal frontal and temporal lobe development and, thereby, put an individual at increased risk of later anxiety or mood-related mental health problems.

Unfortunately, use of formal health services for management of common mental health or alcohol or substance-abuse related problems by young people is unusual. Only 13% of young men and 30% of young women with mental health problems access mental health care in any 12 month period (Australian National Survey, 2007 – see table). When faced with tough times, it is evident that young people with mental health problems are more likely to use alcohol and other drugs as part of the way they cope with everyday problems. These maladaptive coping strategies not only increase the chance of poor outcomes including self-harm and injury but may increase the chances of causing further damage to critical brain structures during this critical developmental period.



Figures above & below: National survey of mental health and wellbeing: summary of results



In essence;

- ***Young people with first lifetime episodes of anxiety, depression or psychotic disorders who also consume significant amounts of alcohol are at increased risk of self-harm, attempted suicide, accidental injury as well as persistence or recurrence of their primary mental health problem;***
- ***Young people who consumer brain-toxic substances early in their teenage years are at increased risk of developing major mental health problems later in the later adolescent or early adult years; and,***
- ***Young people with major mental health problems and alcohol or other drug-related disorders have two sets of problems that are likely to have long-term adverse effects on their brain development.***

3.0 Damaging Effects of Alcohol on the Teenage Brain

3.1 Toxic effects of alcohol on the brain

The damaging effects of alcohol on brain structure and function have been studied for many years in humans and animals. The typical considerations include short-term effects of intoxication (which are strongly associated with changes in function but may not, in adults, be as strongly associated with changes in brain structure) as well as the longer-term damaging effects of alcohol on specific brain structures.

Short-term effects of intoxication

Alcohol has immediate effects on brain function soon after ingestion. With increasing dose, one will see predictable effects on arousal, motor coordination, impulsivity and judgement. These effects can be correlated with alcohol's known effects on key brain regions. Importantly, alcohol dampens down the inhibitory effects of the frontal lobes and the fear responses generated by the fronto-temporal lobe circuits. Consequently, with increasing levels of intoxication one will see increased impulsiveness and risk-taking. As blood alcohol rises increasingly poor judgement and lack of consideration for the likely consequences of one's actions become apparent.

Alcohol normal causes a predictable decrease in reaction time and motor coordination. As blood alcohol rises there is also an increase in the level of sedation. In adults, alcohol will tend to cause drowsiness with associated loss of attention and motor coordination. Higher levels of alcohol intoxication can lead to unconsciousness and depress even very basic physiological processes such as the drive to breathe.

Of particular relevance in the alcohol field, is the phenomenon of 'blackouts'. This is where a person cannot recall key aspects of their behaviour in the period immediately following a bout of intoxication. In essence, it indicates that the brain processes that code short-term memory (located in the hippocampus and related temporal lobe structures) were seriously disrupted when the person was intoxicated. It is believed that this phenomenon is indicative of at least short and, potentially, longer-term damage to the hippocampus.

Longer-term changes in brain structure and function

Human brain imaging and neuropsychological studies of adults with alcoholism have clearly shown that key brain structures are reduced in size and impaired in function (see NIAAA website for further information and images). The frontal lobes (controlling complex planning and impulse control), temporal lobes (regulating memory and fear responses) and the cerebellum (regulating motor coordination) are particularly sensitive to the adverse effects of alcohol.

Figure: Comparison of two female subjects who had volumetric MRIs created in a GE 1.5 Tesla MRI machine

In teenage and adult humans, it can be difficult to tease out those adverse effects directly related to alcohol from those related to other drugs, concurrent medical health problems, related nutritional deficiencies or earlier injuries. Consequently, animal experiments have been very important in demonstrating the direct toxic effects of alcohol. These toxic effects can be group as those that directly impact on: i) the integrity of brain cells - causing cell shrinkage or death – neurodegeneration; ii) brain cell connections, causing a direct reduction in synapses; and, iii) the normal regeneration of brain cells – leading to impaired neurogenesis.

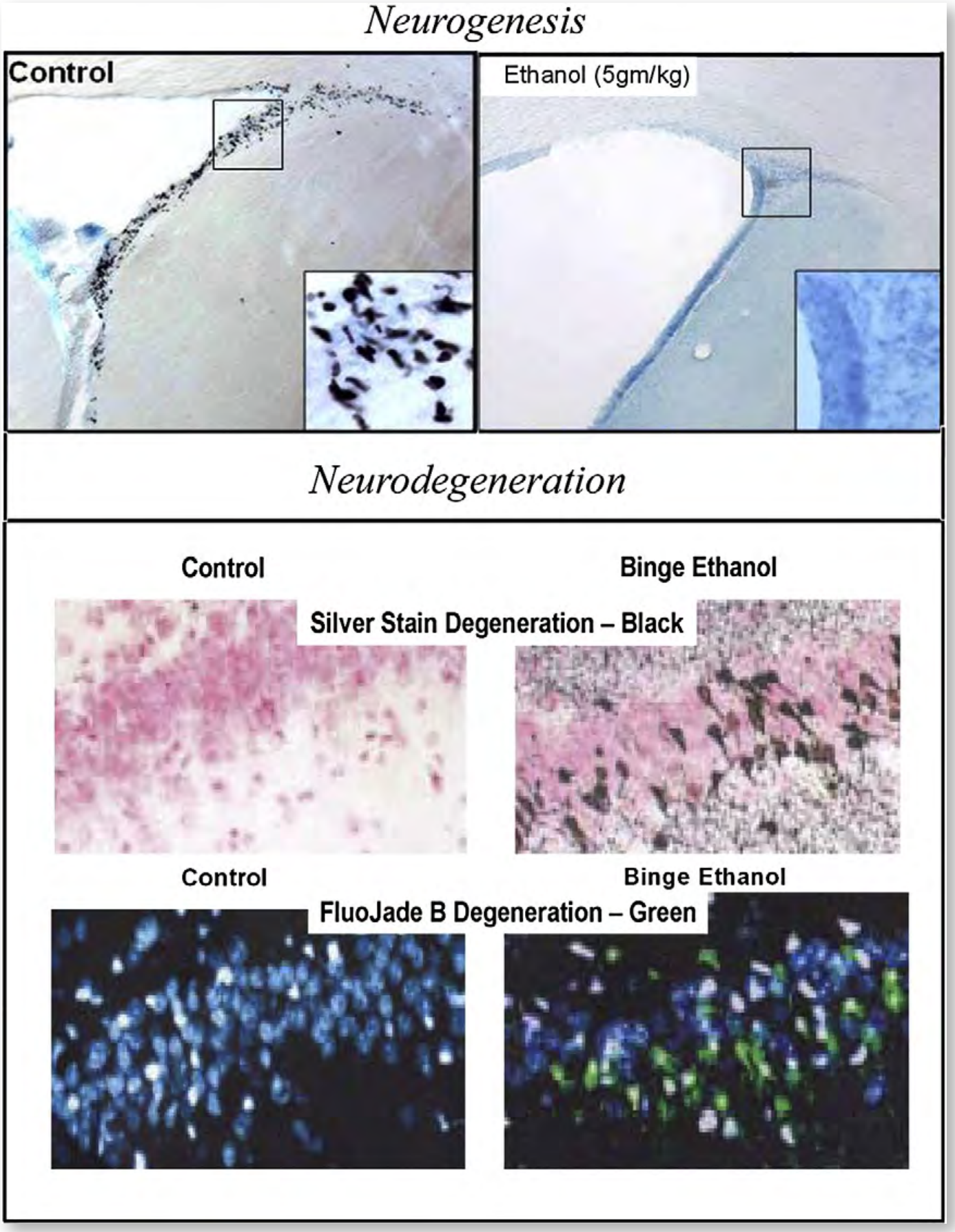


Figure: Ethanol induced brain damage and inhibition of neurogenesis. Crews F. & Boettiger C.

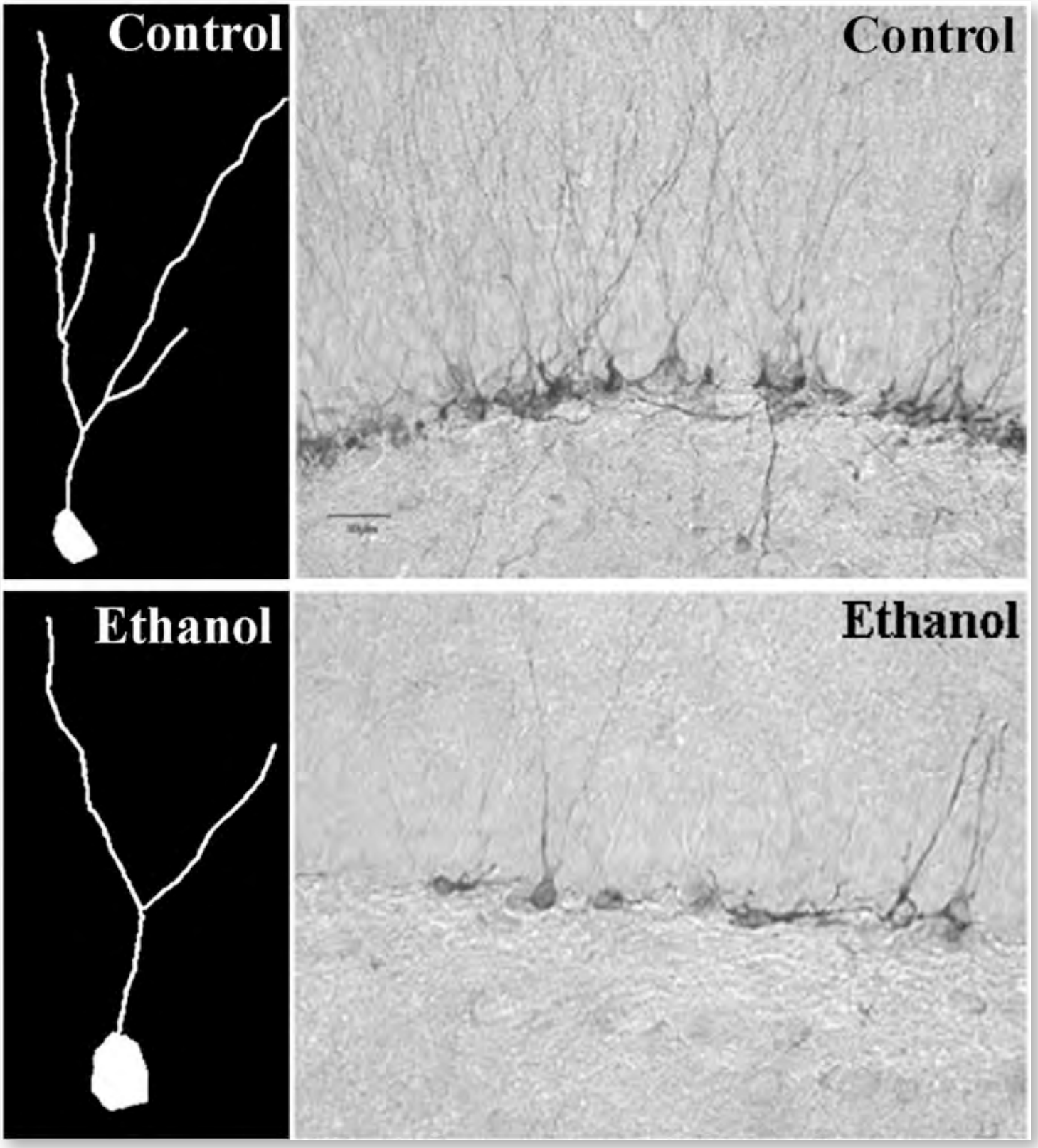


Figure: Alcohol reduces new neuron dendritic growth.
Crews F. & Boettiger C.

3.2 Alcohol exposure during the teenage period

When one considers the normal physiological effects of alcohol on the brain, some additional perspectives need to be considered with regard to alcohol use during the teenage years. Given that the frontal lobes, and related inhibitory responses are relatively underdeveloped in adolescents, smaller amounts of alcohol may be expected to result in greater degrees of disinhibited, impulsive and risk-taking behaviour. Further, given the shift in the sleep-wake cycle, alcohol consumed in the evenings may be less likely to lead to sedation than in older adults.

Young people typically reach their peak in motor skills (e.g. reaction time, motor coordination) in the late adolescent and early adult period. Consequently, they perceive that they are able to continue to perform a range of motor tasks well despite the adverse effects of increasing blood alcohol levels. This relative lack of perception of decrement in performance may be associated with increased risk of injury.

Young people who continue to drink at high levels over short periods (i.e. binge drink) may be at increased risk of experiencing 'blackouts'. Binge drinking among young people is underpinned by both cultural and biological determinants. The cultural issues relate to social norms, peer expectations and availability (reflecting low price and easy access) of alcohol. The biological factors relate to the capacity to continue to consume alcohol due to relative preservation of wakefulness and motor co-ordination.

Neither of these phenomena, however, protects the temporal lobe structures (that underpin short-term memory function) from the immediate or longer-term adverse effects of high blood alcohol. Repeated 'blackouts', which are common among young people who frequently binge drink, are likely to be associated with serious short and long-term damage to these temporal lobe structures. It is also likely that key white matter connections are significantly disrupted during periods of acute intoxication (see McQueeny et al. 2009).

A reasonable number of studies have been conducted of the effects of excessive and or persistent alcohol use during adolescence on cognitive function (see Squeglia et al 2009). Those cognitive functions which would be expected to be continuing to improve throughout this period –memory, attention, speed of information processing, future planning and abstract reasoning strategies – have all been shown to be affected (see Squeglia et al 2009). The longer term educational and vocational effects of these changes are likely to be decrements in performance and achievement compared with peers.

In recent years there has also been a concerted effort to use new brain imaging technologies to investigate the longer-term structural effects of alcohol during the teenage years. The technologies make use of Magnetic Resonance Imaging (MRI) techniques which have an exquisite capacity to

examine the volumes of grey matter (cortical and subcortical nuclei) and white matter integrity (through diffusion tensor imaging). The volumetric studies focus on key regions such as the prefrontal cortex and the hippocampus, while the white matter studies look at the big connecting cabling systems such as the corpus callosum (see Silveri et al. 2008; Squeglia et al 2009; McQueeny et al 2009).

While this is a relatively new area of research, to date, the results are highlighting:

- there are likely to be significant adverse effects of alcohol on both the developing white matter tracts and cortical grey matter that are undergoing rapid change; and
- those at risk of developing alcohol and other related substance abuse disorders may already have evidence of abnormal brain development prior to their exposure to these substances. These abnormalities may help to explain, at least in part, why some teenagers are more impulsive as well why they are more likely to develop substance-related misuse or dependence disorders (see McNamee et al. 2008; Hill et al. 2009).

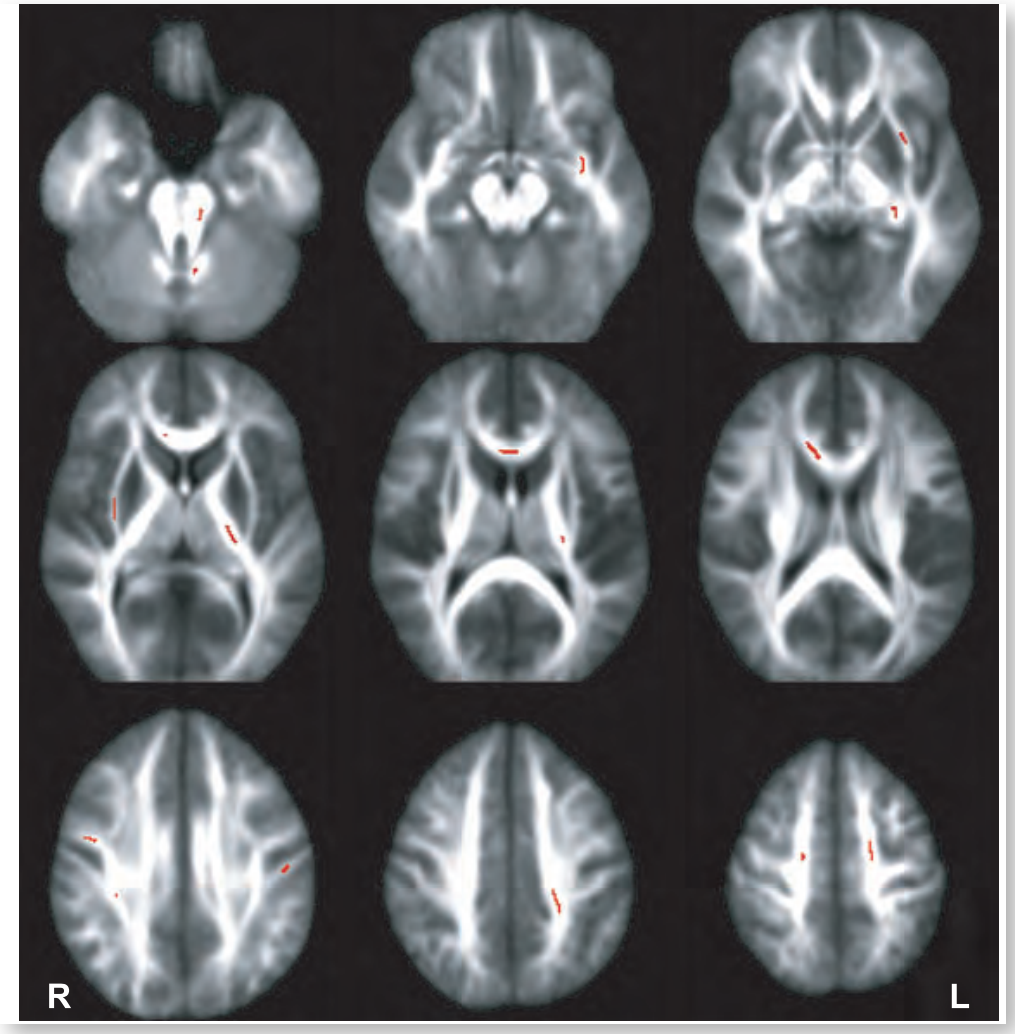


Figure: Clusters (darkened areas) overlaid on average fractional anisotropy mask highlight where binge drinking adolescents had lower fractional anisotropy than controls. McQueeny T, et al

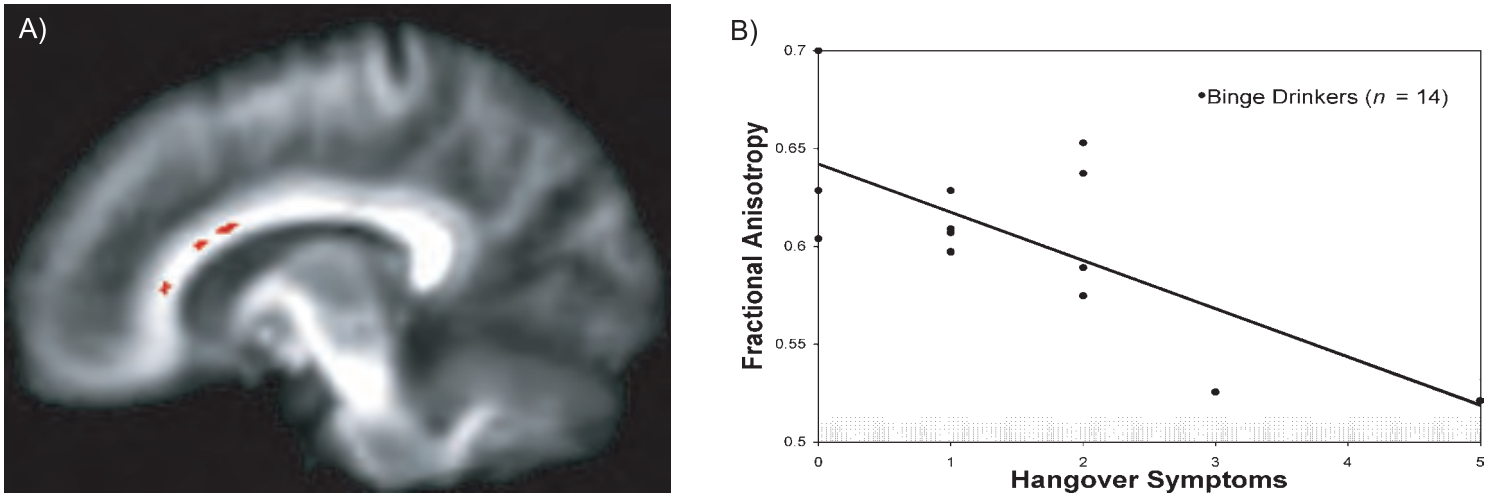


Figure: (A) Clusters (darkened area along callosal fibers) and (B) bivariate scatterplot indicate where lower fractional anisotropy was significantly linked to more hangover symptoms in the body and genu of the corpus callosum. McQueeny T, et al

Although there are only small series of direct studies at this time, it would appear that excessive teenage drinking is associated with reduction in the size of the hippocampus in the temporal lobe. (see Nagel et al. 2005; DeBellis et al 2000; Medina et al 2007). The hippocampus is essential to short-term memory function and, in animals, is one of the few areas of the brain in which new nerve cells are generated in adulthood. In a similar fashion, it appears that the prefrontal cortex is reduced in volume in heavy teenage drinkers (DeBellis et al. 2005).

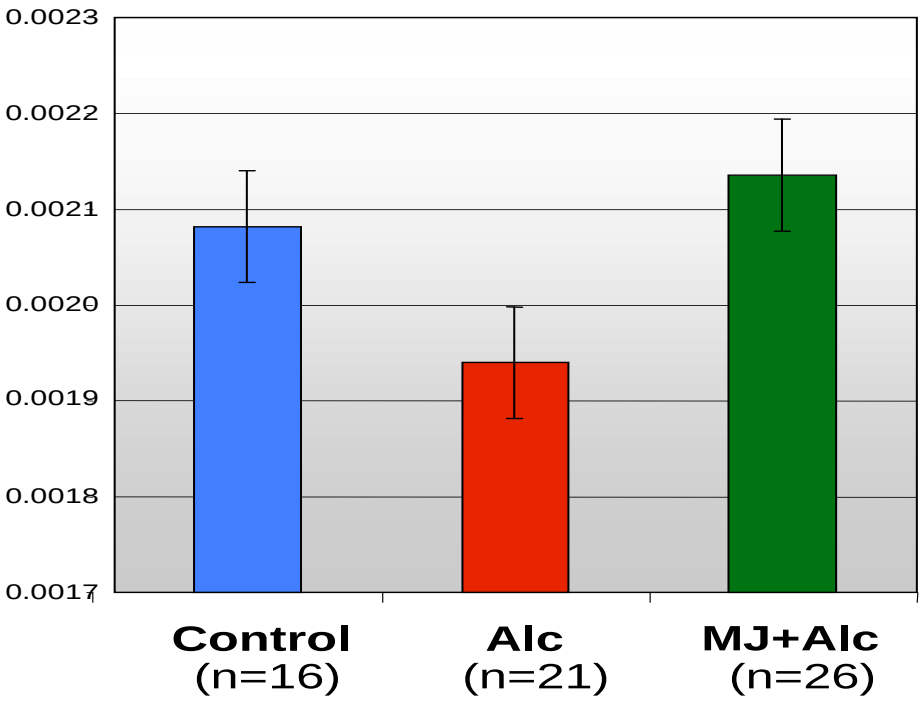


Figure: Hippocampal volume for adolescents with different substance use patterns. Squeglia L et al

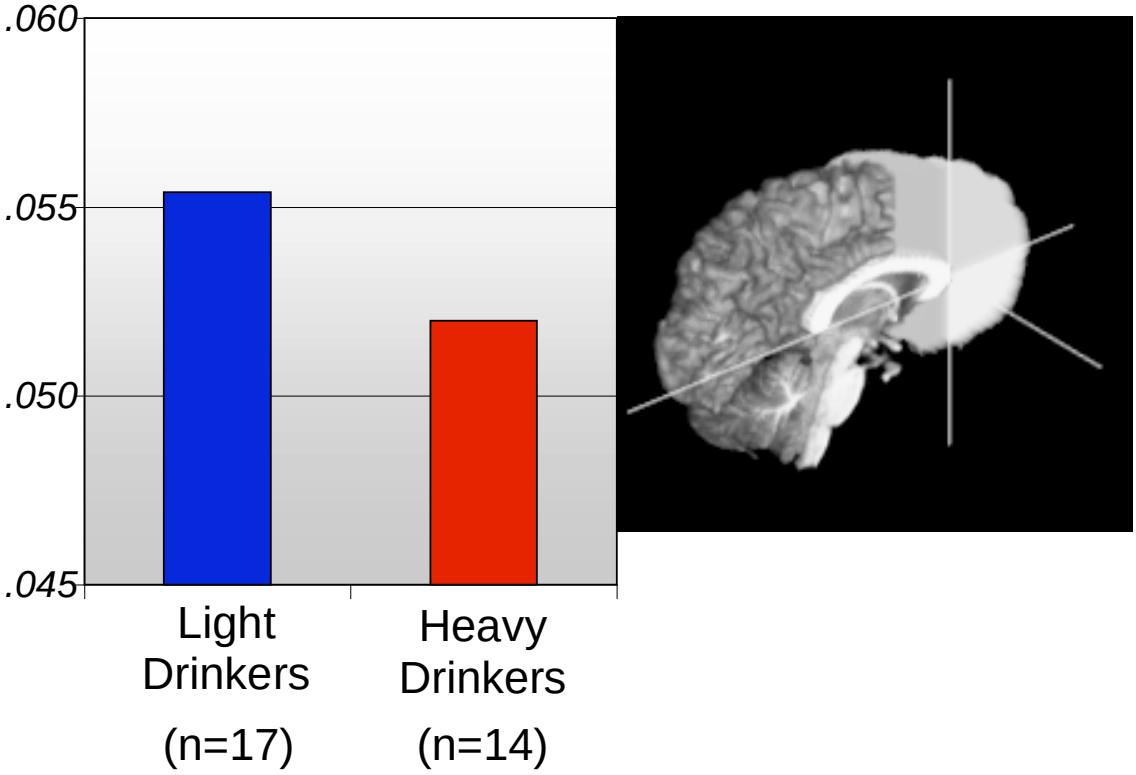


Figure: Ventral prefrontal volume in adolescents with minimal and heavy drinking histories; ventral prefrontal region is highlight in white in the figure to the right. Squeglia L et al

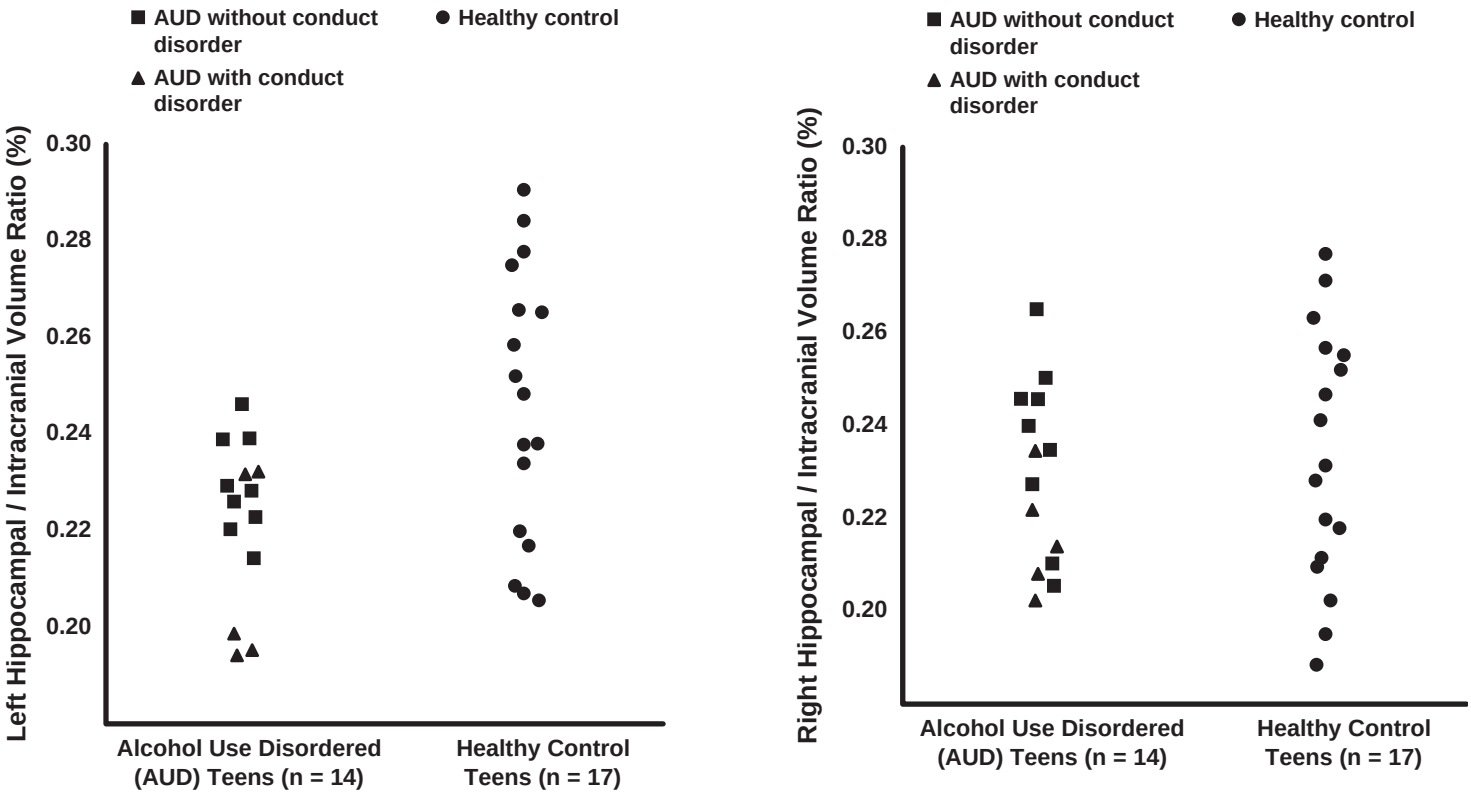


Figure: Left & right hippocampal volumes expressed as a ratio to overall intracranial volumes in AUD and healthy control teens. Nagel B, et al

3.3 Longer-term brain effects of teenage alcohol exposure

Of increasing relevance in these areas of research has been the use of specifically designed animal studies to look at the direct effects of binge drinking (as distinct from chronic alcoholism) as well as exposure to alcohol alone (or in combination with other drugs) during the comparable teenage period of development. The animal experiments have tended to reinforce the notion that indeed the teenage years are a period of sensitivity to the adverse effects of alcohol and that alcohol-related changes in cognitive capacities and behaviour are likely to persist into adulthood (see Schulteis et al 2008; Sircar et al 2008; Hargreaves et al. 2009; Zou et al. 2009; Criado et al. 2008). Of key interest is the notion that the fundamental biochemical systems that are linked to addictive behaviours may themselves be altered by repeated exposure to alcohol during the adolescent period (see Pascual et al 2009).

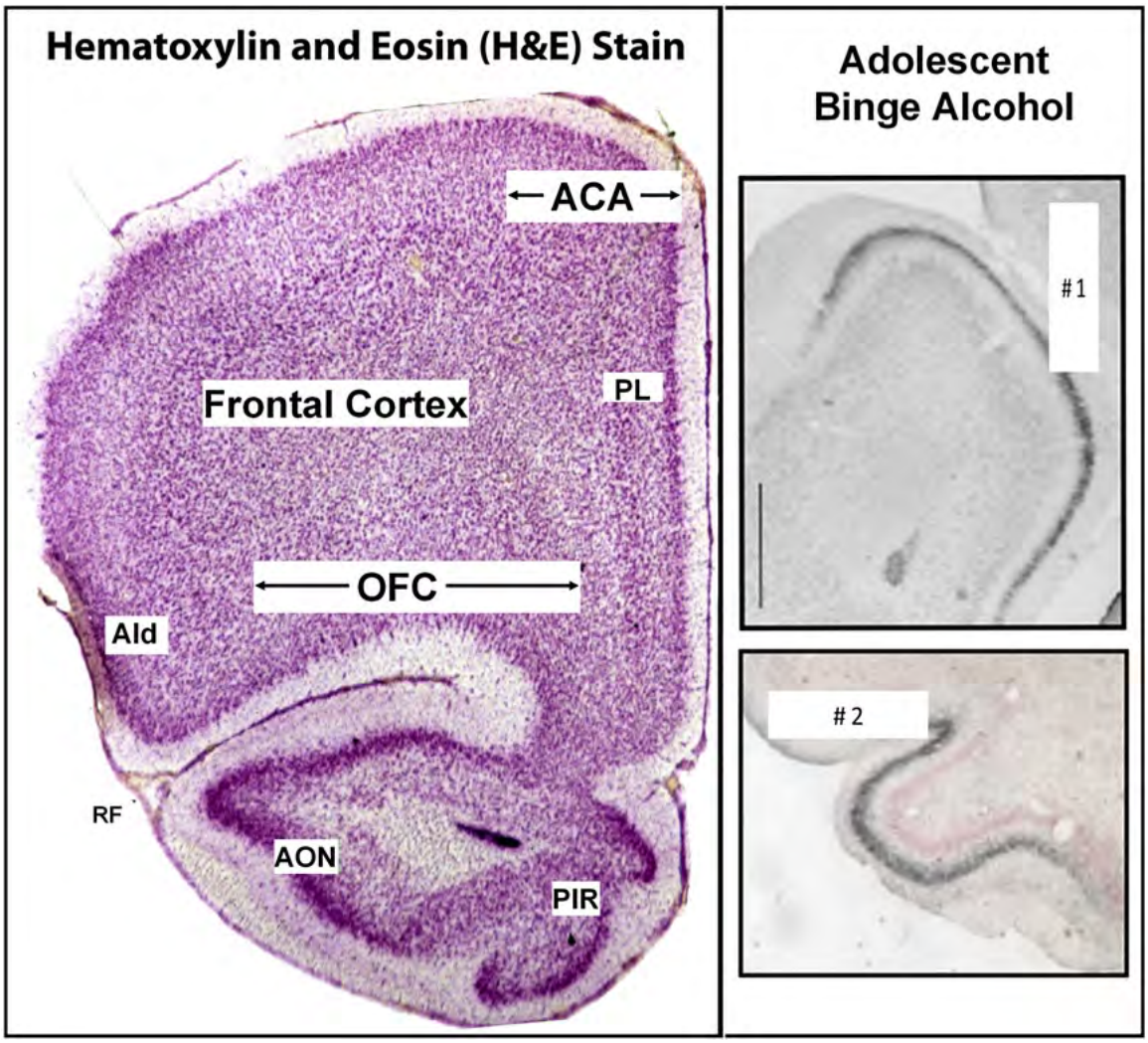


Figure: Binge drinking in adolescent rats damages frontal brain regions. Crews F, Boettiger C

To date, there are insufficient long-term studies of the adverse effects of alcohol exposure on teenagers and young adults. However, given that high levels of alcohol exposure (in binge drinking periods or chronically) have particularly severe effects on frontal and temporal lobe structures, as well as white matter tracts, researchers have suggested that exposure during the adolescent period would be expected to result in:

- long-term reduction in the normal inhibitory capacities of the frontal lobes. This would lead to long-term increases in impulsivity with a resulting long-term increased risk of developing life-long alcohol and other substance use related disorders as well as accident or injury (see Crews & Boettiger, 2009);
- long-term impacts on those memory functions underpinned by hippocampal and other temporal lobe structures; and,
- long-term impacts on those functions subserved by functionally-efficient white matter tracts, including the key cortical and subcortical circuits that are abnormal in adults with a range of mental disorders (particularly mood disorders) and also those with substance dependence.

3.4 Avoidance of Alcohol following overuse

An interesting new line of evidence related to the effects of alcohol on the brain relates to the potential benefits of periods of abstinence following significant alcohol exposure. At least in animal models, there is evidence that periods of abstinence may result in bursts of growth of new nerve cells (Crews & Nixon, 2009). Human work with older subjects is consistent with this view (Wobrock et al. 2009).

In essence;

- ***Alcohol has significant toxic effects on the cells of the central nervous system, and depending on dose and duration of exposure, is likely to result in serious short-term and long-term harm. Those harmful effects are most likely to be evident in areas in which the brain is still undergoing rapid development and/or those areas which are particularly sensitive to the toxic effects of alcohols (i.e. frontal and temporal lobe structures);***
- ***Animal experiments confirm that the toxicity of alcohol independent of other substances and that exposure during the teenage period may be particularly likely to have long-term cognitive and behavioural consequences;***

- ***Alcohol, even in small doses, is associated with reduction in activity of the normal inhibitory brain processes. Given that such processes are less developed in teenagers and young adults, alcohol use is likely to be associated with greater levels of risk-taking behaviour than that seen in adults;***
- ***Alcohol normally results in sedative effects as the level of consumption rises. It appears that teenagers and young adults are less sensitive to these sedating effects (due to higher levels of arousal and delayed sleep onset) and are, therefore, likely to continue with risk-taking behaviours. As they also experience loss of control of fine motor skills, the chances of sustaining serious injuries (including head injuries) are increased;***

4.0 Behavioural effects of early alcohol exposure

The common cultural assumption in many societies is that early exposure to alcohol use in the teen years is unlikely to impart any increased risk of alcohol or other substance use disorders, or other mental disorders such as anxiety or depression, in the longer term.

By contrast, accumulating epidemiological evidence suggests that exposure to significant levels of alcohol during the early and mid-adolescent period is associated with increased rates of alcohol-related problems as an adult as well as a higher rate of common mental health problems such as anxiety and depression. The combination of mental health problems and alcohol and other substance use related disorders in adolescence is particularly likely to be linked to intentional self-harm and injury (see Windle 2004).

Certain types of mental health problems that emerge in adolescence are particularly likely to lead to alcohol misuse. Social anxiety, which is particularly common in adolescent males, is frequently linked with alcohol misuse (see Thomas et al. 2003). Depressive symptoms commonly co-occur with alcohol misuse and, in men, the severity of depression is typically linked with increasing likelihood of having an alcohol-related disorder.

Recent Australian data looked at the ten-year outcome of those who drank at various levels during adolescence. All levels of teenage alcohol consumption, including low levels were associated with increased rates of alcohol related difficulties as adults (see Moore et al 2009). Dramatically, the authors concluded that “any drinking, even at the low-risk level, may not be appropriate in adolescence”.

The co-association between alcohol and other substance use disorders and common mental health problems now attracts considerable academic research and health policy attention (see Lubman and Yucel, 2008; Hall et al 2009). Better understanding of these complex relationships may enhance primary and secondary prevention programs.

In essence;

- ***There is increasing reason to believe that early exposure to alcohol in the teenage years increases the risk of later alcohol-related difficulties and mental health problems; and***
- ***Reduction in alcohol, substance use and mental health problems, and their adverse health and social consequences in adulthood, may well be enhanced by delaying exposure to alcohol during the teenage years.***

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