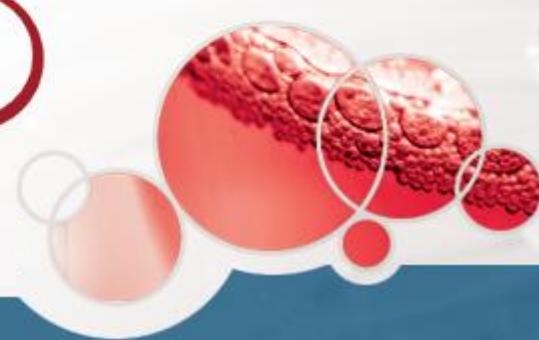




DUTCH
INSTITUTE FOR
ALCOHOL POLICY



*The effect of chronic binge drinking on
neurocognitive development:
A literature review*

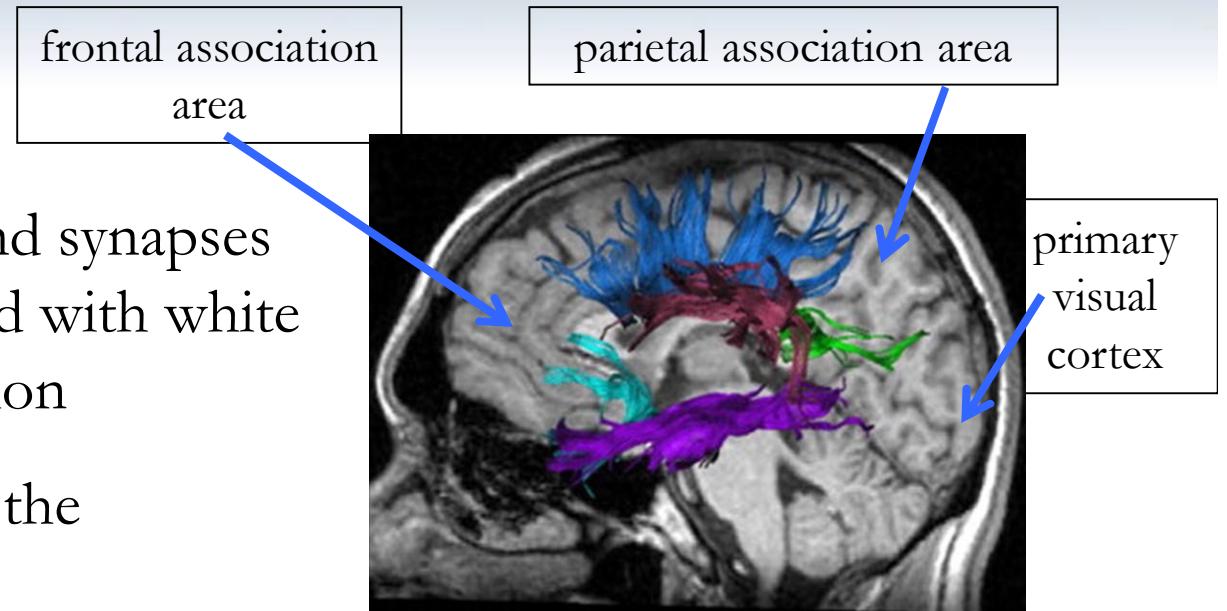
Background: youth drinking

- Binge drinking (BD) defined as consumption of ≥ 4.5 standard units (males: ≥ 5 , females: ≥ 4) within 2 hours, reaching a blood alcohol content (BAC) of 0.08 ($=0.8$ promille)
- By age 15, more than half of Dutch adolescents binge drink regularly (at least once a month) Verdurmen et al. (2011)
- BD remains prevalent in young adulthood (<30 yrs) Van Dijck & Knibbe, 2005
 - What happens in the brain during this period? Some neuroanatomy required

Background: A one slide crash course in neuroanatomy

” Brain consists of:
- ‘gray matter’; nerve cells and synapses
- ‘white matter’; fibers coated with white layer for rapid communication

” Cortex = outer layer of the brain:
- elementary processing occurs in ‘primary cortical areas’
- complex processing (attention; memory) in networks of ‘association areas’ that ‘associate’ info from primary areas

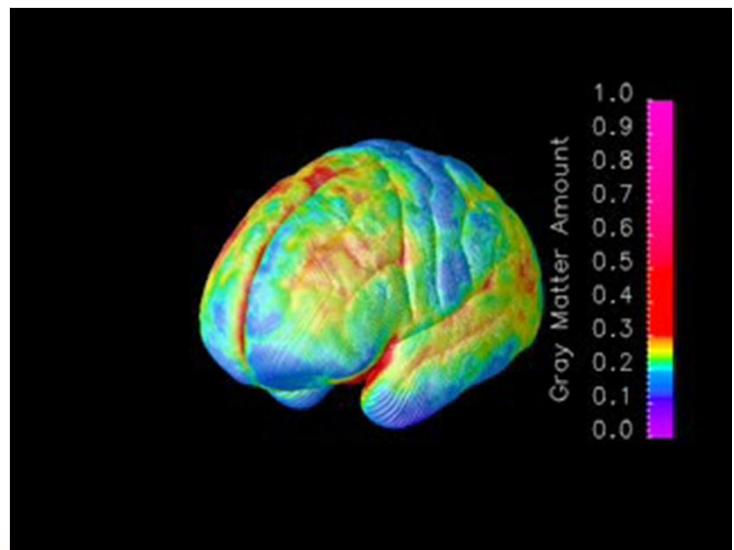


Medial view on MRI scan with rendered white matter tracts

Background: brain development

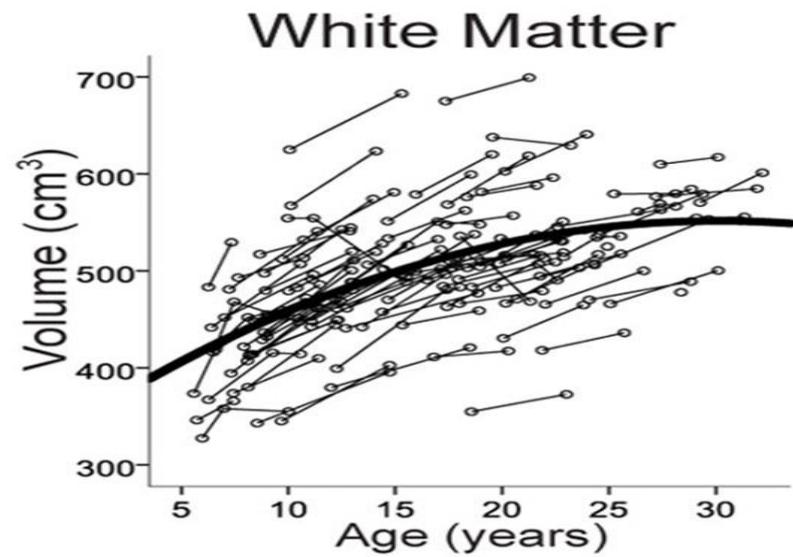
- There is significant brain development in the 15-30 year time window
- **Brain structure:** (1) reduction of gray matter ('pruning')^{Gogtay et al., 2004}

Cortical gray matter reduction from 4 to 21 (rendered MRI time series). Note that reduction starts in 'primary' areas and ends in 'association' areas (complex functions)



Background: brain development

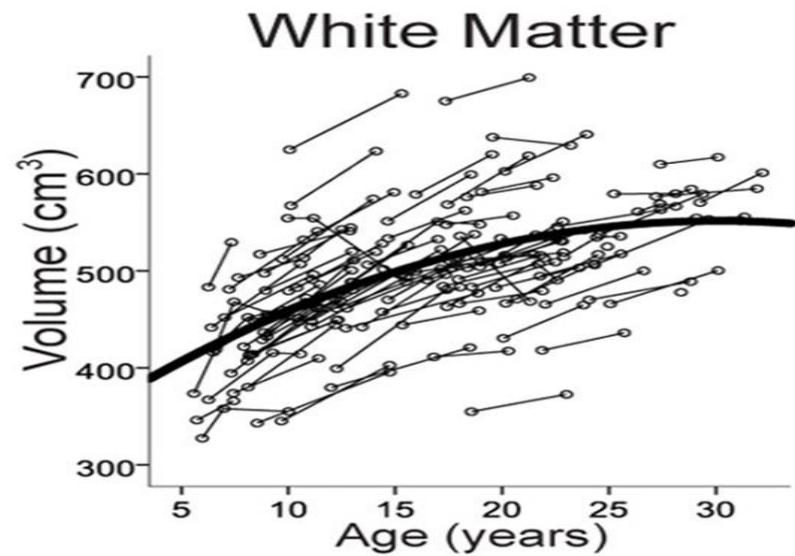
- (2) Increase in white matter volume^{Lebel et al., 2011}, reducing signal transduction time
 - remote areas (e.g. frontoparietal association network) benefits most
 - **Brain function:** more efficient information processing in networks of association areas, supporting complex cognitive functions (e.g., memory, attention). Luna et al., 2004



Adopted from Lebel et al.

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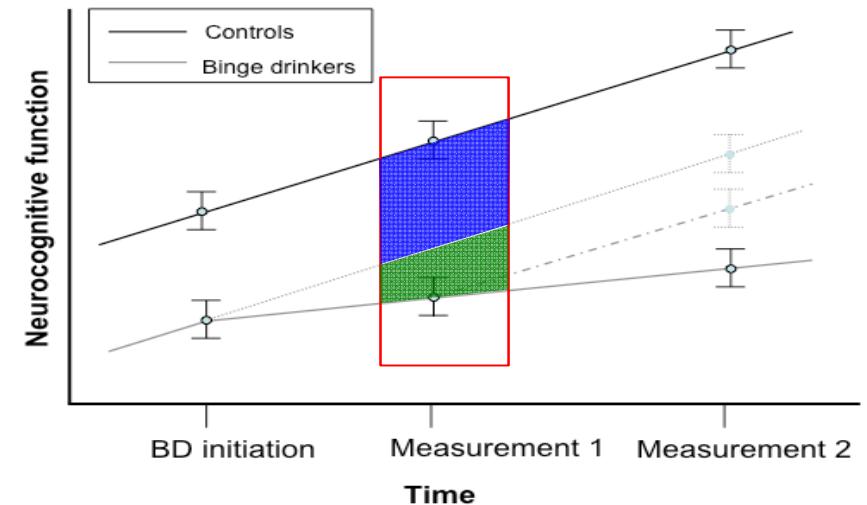
Adopted from Lebel et al.

Background: research question

- Developmental sensitivity hypothesis: developing brain is more prone to damage by external factors, such as alcohol ^{Crews et al., 2000}
- " If true, we would particularly expect an effect on:
 - " **Brain structure:** gray matter in the association areas, white matter development
 - " **Brain function:** networks of association areas
 - " **Cognitive functions:** complex (memory, attention)
- Before we can turn to the evidence we need to consider methodology

Methodological considerations

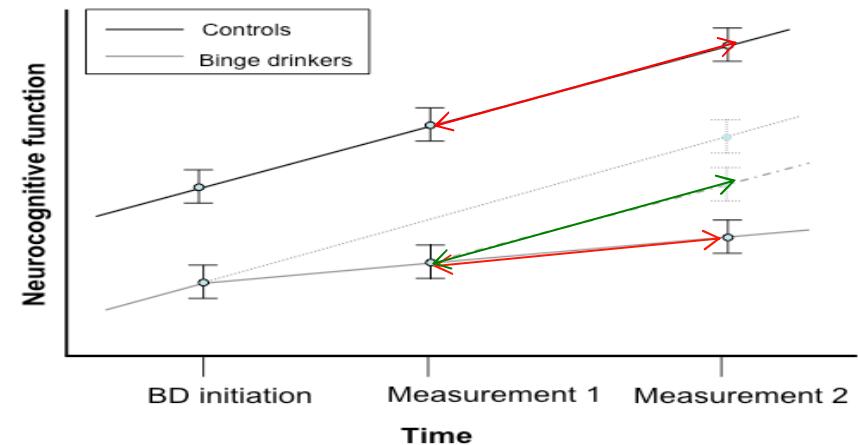
- Not only neurocognitive *consequences* of BD but also neurocognitive *risk factors* that predispose to BD, such as impulsivity E.g. Peeters et al., 2014
- If we compare a group of binge drinkers at 1 time point after BD onset with non BD controls
 - We cannot be sure to which extent neurocognitive deficit is *pre-existing* or *consequence* of BD



Methodological considerations

- Measure neurocognitive function twice (longitudinally) for both groups and look whether **change** in time differs (**non-parallel red lines**)

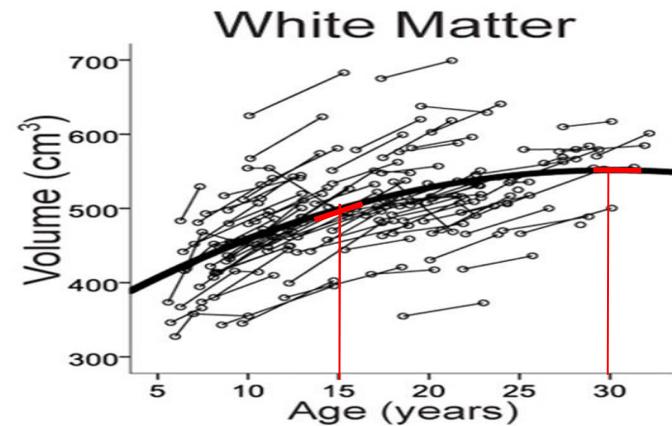
- If we do **not** find an effect and M1 is significantly later than BD onset, there still might be an effect that is masked by **adaptation**;



“ Change was affected before M1 resulting in deficit as compared to when BD group would not BD (dotted line), but rate has normalised by M1, preventing us from detecting it.

Methodological considerations

- Even with this ‘longitudinal’ design there are methodological pitfalls:
 - As neurocognitive development tends to be **non-linear**, the BD group and control group should not differ in age (or sex)
 - The groups should not differ in variables that might affect neurocognitive development and systematically covary with BD (such as psychiatry and use of other substances than alcohol)



Literature review: method

- Systematic search; effect chronic BD on neurocognitive development
 - Cognitive or neurobiological measure
 - BD group should BD at least once a month
 - Average group age = < 25 years

Result:

- 12 studies on brain structure: 2 longitudinal
- 16 studies on brain function: 5 longitudinal
- 14 studies on cognitive effects: 5 longitudinal
 - Will focus on longitudinal studies, as only these studies allow for causal inference!!

Effect of chronic BD on brain structure

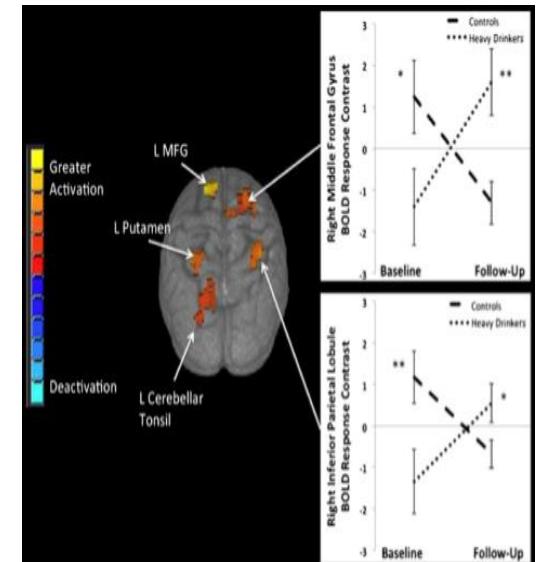
- (1) Bava et al. (2013): BD and cannabis use of adolescents (M=18 at M1) predicts decrease in integrity of long white matter tracts over 1.5 years.
 - (2) Jacobus et al. (2013): BD (and other drug use) of adolescents predicts decrease in white matter integrity over 3 years.
- *Conclusion:* initial evidence that chronic BD (and other drug use) causes disturbance of white matter development

Effect of chronic BD on brain function

- (1) Wetherill et al. (2013): BD associated with *increase* of frontal and parietal network activity over 3 years during a task,
while non BD controls show *decrease*.

No difference in task performance.

- (2) Squeglia et al. (2012): similar result for a
memory task



Effect of chronic BD on brain function

- (3) Maurage et al. (2009): initiation of BD over 9 month interval associated with slowing of electrical brain response while non BD controls show *faster* brain response. No differences at the behavioral level.
- (4) Caneda-Lopez et al (2009; 2013) claim similar results with level of electrical brain activity but fail to present the appropriate statistical test.



• *Conclusion:* initial evidence that BD causes slowing of the central nervous system response

Effect of chronic BD on cognitive function

- (1) Mota et al. (2013): Ceasing chronic BD over a 2 year interval is associated with increase in visual memory performance while performance development under continuation of BD is not different from controls (**adaptation?**)
- (2) Series of studies by the Tapert-group. Development of cognitive function for initially alcohol dependent BD adolescents as compared to non-BD initially alcohol dependent controls:
 - reduced development of attention/working memory over 4 years (Tapert 1999); medium to large effect size

Effect of chronic BD on cognitive function

- reduced development of attention and working memory over 8 years (Tapert 2002); effect size small to medium
- reduced development of verbal memory under continuation of chronic BD, but restoration of function when BD is ceased over 10 years (Hanson, 2011)
- reduced development of spatial memory over 3.5 years, but only for girls (Squeglia, 2009); effect size medium

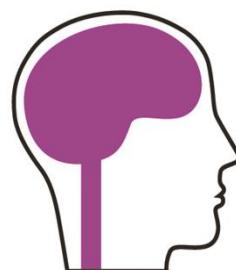
"Conclusion: chronic BD seems to impair cognitive development of attention and (working) memory. Ceasing chronic BD is associated with recovery of cognition.

Conclusion

- “ Research still is scarce but 12 longitudinal studies suggest chronic BD:
 - Brain structure:** disturbs white matter development
 - Brain function:** initially disturbs network of association areas without behavioral effect
 - **Cognitive function:** but cognitive defects apparent in (working) memory and attention with prolonged chronic BD
- “ Pattern of results in line with hypothesis of developmental sensitivity
 - “ Fortunately, *initial* evidence that cognitive function seems to recover when a chronic BD pattern is ceased

Thanks

Thanks to:



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