



<sup>1</sup> Centre for Healthy Brain Ageing, University of New South Wales, Sydney, Australia

<sup>2</sup> Matilda Centre for Research in Mental Health and Substance Use, University of Sydney, Sydney, Australia

<sup>3</sup> Department of Old Age Psychiatry, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK

Correspondence to: L Mewton

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# Lifetime perspective on alcohol and brain health

## Harm prevention policies must take the long view

Louise Mewton,<sup>1</sup> Briana Lees,<sup>2</sup> Rahul Tony Rao<sup>3</sup>

The maintenance of brain health is central to health and wellbeing across the lifespan.<sup>1</sup> Evidence suggests three periods of dynamic brain changes that may be particularly sensitive to the neurotoxic effects of alcohol: gestation (from conception to birth), later adolescence (15-19 years), and older adulthood (over 65 years). Highly prevalent patterns of alcohol use may cause harm during these sensitive periods, including low level prenatal alcohol exposure, adolescent binge drinking, and low-to-moderate alcohol use in older adulthood.<sup>2</sup> Although these patterns of alcohol exposure may be associated with less harm to individuals than sustained heavy drinking, the overall burden of harm in populations is likely to be large.

From fetal development to later life, the human brain goes through several periods of dynamic change. The prenatal period is characterised by extensive production, migration, and differentiation of neurons, accompanied by substantial apoptosis.<sup>3</sup> Adolescence is characterised by synaptic pruning and increased axonal myelination.<sup>4</sup> Older adulthood is associated with brain atrophy, which accelerates after the age of 65 years, largely driven by decreases in neuron size and reductions in the number of dendritic spines and synapses.<sup>5</sup> Each of these changes in neurocircuitry could increase sensitivity to the effects of environmental exposures such as alcohol.<sup>6</sup>

### From cradle to grave

Globally, around 10% of pregnant women consume alcohol, with the rates considerably higher in European countries than the global average.<sup>7</sup> Heavy alcohol use during pregnancy can cause fetal alcohol spectrum disorder, associated with widespread reductions in brain volume and cognitive impairment. But recent evidence indicates that even low or moderate alcohol consumption during pregnancy is significantly associated with poorer psychological and behavioural outcomes in offspring, partially mediated by aberrant brain structure.<sup>8</sup>

More than 20% of 15-19 year olds in European and other high income countries report at least occasional binge drinking (defined as 60 g of ethanol in a single drinking occasion).<sup>9</sup> Longitudinal studies indicate that the transition to binge drinking in adolescence is associated with reduced neocortical volume and functional connectivity, attenuated white matter development, and small to moderate deficits in a wide range of cognitive functions.<sup>4,10</sup> In older people, alcohol use disorders were recently shown to be one of the strongest modifiable risk factors for all types of dementia (particularly early onset) compared with other established risk factors such as hypertension and smoking.<sup>11</sup>

Although alcohol use disorders are relatively rare in older adults, many older people frequently consume low to moderate amounts of alcohol.<sup>12</sup> Recently, even moderate drinking was shown to be associated with small but significant loss of brain volume in midlife,<sup>13</sup> supporting previous research indicating an association between low risk drinking and brain damage in older adults.<sup>2</sup> However, it is currently unclear whether these structural changes translate into functional cognitive impairment.

The evidence for the adverse effects of alcohol on brain health is compelling, but it is limited by the observational nature of the analyses. These findings require further replication, with a focus on more rigorous causal modelling.

### Demographic trends

Demographic trends may compound the effect of alcohol use on brain health. Women are now just as likely as men to drink alcohol and experience alcohol related harms.<sup>14</sup> In higher income countries, consumption has increased among older people<sup>15</sup> while in low and middle income countries, consumption and related harms have increased across the population. Global consumption is forecast to rise further in the next decade.<sup>16</sup> The effects of the covid-19 pandemic on alcohol use and related harms are unclear, but alcohol use increased in the long term after other major public health crises.<sup>16</sup>

A lifecourse perspective on brain health supports the formulation of policy and public health interventions to reduce alcohol use and misuse at all ages. This could increase longevity and quality of life by reducing the prevalence of fetal alcohol spectrum disorders, aberrant neurocognitive development in adolescence, and dementia in later life. An integrated approach to harm reduction across the lifespan is required in public health, mental health, primary care, social care, and voluntary sectors.<sup>17</sup>

Population based interventions such as guidelines on low risk drinking, alcohol pricing policies, and lower drink driving limits need to be accompanied by the development of training and care pathways that consider the human brain at risk throughout life. The effect of harm reduction strategies on maintaining brain health in both individuals and populations can then be more fully evaluated.

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