## What do puberty blockers do?

Blockers suppress the vertical cascade of hormones, from hypothalamus to pituitary to gonads and then to body, that bring about the changes of puberty, neutralising sexualisation. If stopped, the process may resume, giving partial justification for the word 'reversible'. Problems, however, lie in the associated blocking of the broader, say horizontal, functions of Gonadotropin Releasing Hormone (GnRH), as it is named, whose receptors are found throughout the brain, in regions involving cognition, emotion, memory, reward and sexuality<sup>123</sup>. Extensions of the nerve cells producing GnRH in the hypothalamus actually extend horizontally into the limbic system while distribution of their product to other regions may occur through cerebro-spinal fluid<sup>4</sup>

International research refutes the claim of 'reversibility'. For example, researchers in Glasgow and Oslo universities, have long demonstrated sustained, deleterious effects of blockers on peri-pubertal sheep (whose lengthy period of puberty is relevant for human comparison). Blockers invoke pathological enlargement of components of the limbic system, associated with interruption of the function of many genes in the amygdala and hippocampus whose role should be the preservation of the integrity of neuronal cells. In consequence, there is lasting reduction in spatial memory and increased emotional lability, reducing performance in mazes. Male sheep become more 'gung ho', females more fearful in their confusion.

Recently, from New York, researchers report 'behavioural and neurological' effects of blockers on mice. Admittedly, the sexual behaviour of rodents might seem esoteric but the authors explain the model 'has the potential to isolate the biological effects of GnRH...on brain function and behaviour from the dysphoria and psychological distress associated with incongruence between gender identity and natal sex'.

In females, blockers resulted in 'profound effects on...behaviours', interpreted as depression (despair-like behaviour), and on the neural activity in the hippocampus, 'a brain region crucially involved in stress processing, depression and cognition'. Blocked males exhibited 'pronounced differences in locomotion (they were hyperactive. Ed) and social preference (they preferred the company of males, and showed none of the usual interest in the opposite sex. Ed), and increases in neuroendocrine responses to stress'.

In humans, given blockers to reduce the provocative effect of sex hormones in such diseases as endometriosis and prostate cancer, research has long reported unwanted effects on cognition, emotions and executive function, though conclusions are rendered difficult by confounding effects of age, disease and other treatment<sup>11121314151617</sup>.

Studies on the developing brain of adolescence are very limited but should temper claims of reversibility. In one transgendering adolescent, two years of blockers prevented expected brain development, and were associated with some reduction in operational memory. The authors speculated on disruption of the synchronic development of the brain.<sup>18</sup>

Outside the brain, biopsies, investigating the increased incidence of intestinal symptoms in women receiving blockers for endometriosis, have revealed marked reduction in the nerve cells directing peristalsis<sup>19</sup>, adding clinical weight to laboratory contention that GnRH has a widespread role in maintenance of neuronal integrity<sup>2021</sup>

Thus, there is no evidential support for the fulsome assurance of 'reversibility'. To the contrary, there is evidence and strong suggestion of damage.

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