Genes for alcohol use turn up in drunk worms and *Cheapdate* flies

Kate Holden-Dye

General

Inebriated worms and drunken flies are helping researchers pick the genetic locks that drive some of us to drink. At Southampton University scientists are busy studying the wriggling of worms in alcohol. The worms in question aren't the familiar earth worms you dig up in the garden "they are natural soil dwellers like earth worms" says Prof Holden-Dye "but these worms are much smaller. They are only just visible to the naked eye". *C. elegans* are in fact just over 1 mm long. Somewhere way back on the path of evolution, they went their way and we went ours interestingly for researchers however these worms behave in much the same way as any of us after one too many. "What's been previously observed by other scientists is that worms initially become overexcited in alcohol, but then as the amount of alcohol increases they get sluggish", says Prof Holden-Dye, "we are following up on this work in our lab". Other researchers are using fruit flies instead of worms to demonstrate the same effects. Fruit flies positively love a drink it seems, perhaps not that surprising considering their fondness for rotting fruit. Scientists measure how unsteady on its feet a drunken fruit fly is by watching how quickly it tumbles through an aptly titled device, the "Inebriometer". The drunker the fly the more quickly it emerges out of the bottom.

So what is it exactly that scientists are hoping to learn by observing drunk worms and flies? "There is evidence that some worms are better at holding their drink than their others, essentially there is variation as to how quickly they get drunk," says Prof Holden-Dye, "other worms are good at building up tolerance to the effects of alcohol; worms that have become tolerant are more resistant to the effects of alcohol after more than one exposure". The same is seen in flies. It has been known for some time that these two factors, initial sensitivity to alcohol and tolerance might be linked to the development of alcohol abuse problems in the general population. "This definitely isn't the full story" says Prof Holden-Dye "but they are obviously important factors that we can look at in worms and other organisms like fruit flies and that might say something about how we deal with alcohol. We still don't really know that much about how alcohol acts on our brains". The Holy Grail is to find genes which are tied up with how the brain is affected by alcohol and those which may play a part in making some of us more likely than others to develop a dependency problem. The human brain is jaw-droppingly complex with billions of neurones, the specialised cells that comprise the brain and the nervous system and trillions of synapses, the junctions between neurones that act as communication gateways. It performs tasks of unimaginable complexity in the blink of an eye, frankly our brains stick two fingers up at even the most sophisticated of computers we have today. By comparison, *C. elegans* has a relatively reserved 302 neurones, each one of which has already been exquisitely mapped by scientists. These substantially more simple organisms are Nature's gift to those in the genetics business. In much the same way as it's advisable to learn your alphabet before you start on the great works of

Shakespeare; scientists are starting their search for interesting genes in worms and flies. So far this approach is proving fruitful. *Cheapdate* (does what it says on the tin, a Cheapdate fly gets drunk very quickly) and *Hangover* are two genes that have been identified in fruit flies and numerous others have wriggled their way into the spotlight in worms. Excitingly, some of these genes are also known to be at least partly responsible for governing how these organisms respond to certain stresses, adding credence to the long held belief that stress and drug and addiction behaviours are linked in all of us. The hard task now is to pin down exactly what these genes and others like them do, so we can begin to unravel how alcohol really works it magic or wreaks havoc on our brains.

Biography:
Kate Holden-Dye obtained a BSc in Biochemistry and is now finishing off a PhD at the University of Bristol in the School of Medical Sciences. Her PhD focuses on the stability of an integral membrane protein.

Sources: (Primary) Prof Lindy Holden-Dye Uni of Southampton (permission obtained)

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