Low serotonergic tone and elevated risk for substance misuse†

David Nutt

Summary
Cox et al’s paper addresses an issue that has long been assumed to be a central aspect of brain function – the interplay of different neurotransmitters – but for which we have very little evidence so far. It is currently unclear whether these findings will have implications for the treatment of those with cocaine or other substance dependence.

Declaration of interest
None.

Implications for practice
Whether these new findings will contribute to the treatment options for cocaine or other stimulant dependence is less clear. In general, SSRIs have proved ineffective as anti-addiction agents except where they ameliorate primary anxiety or depressive disorders. The magnitude of the modulatory effect of 5-HT to limit dopamine release may be too little to offset the major impact of cocaine, which in preclinical studies can increase brain dopamine release up to ten-fold.

It also asks the question, to what extent might 5-HT regulate the effects of other drugs of addiction. Preclinical studies lead us to believe that 5-HT is central to the actions of MDMA (3,4-methylenedioxymethamphetamine) and psychedelics but this has been little explored in humans, and interactions with other drugs of misuse such a heroin and alcohol for which dopamine is less important might also repay investigation. In addition, future studies should consider the possible contribution of genetic variations in 5-HT functionality. Obvious targets are polymorphisms of the 5-HT reuptake site (‘ss’ or ‘ll’ variants) or those of tryptophan hydroxylase-2 (the main synthetic enzyme for 5-HT).

References

†See pp. 391–397, this issue.
The Last Vision of Angus McKay

Tom Pow

Angus McKay, Queen Victoria’s piper, went insane ‘over study of music’. He was admitted to the Crichton Royal from Bedlam in 1856 when he was 43 years old. ‘His most prominent delusion is that Her Majesty is his wife and that Prince Albert has defrauded him of his rights.’ (Crichton case notes)

Let it be noted (in copperplate), Angus McKay is a gentleman to watch. The stoutest furniture is firewood to him; a mattress, within a day, he’ll disembowel. He has been known to drink his own urine; to spit, shriek, howl and hoot like an owl:

though this last
does not appear
in his case notes from Bedlam –
“hooting and howling” in southern parts being thought not abnormal for a Scot.

Nevertheless, there is enough on his native ground to amaze and perplex his keepers.

F**k it! Angus McKay has done with them all.

He eases himself into the rivercold waters of the Nith across which lies Kirkconnell Wood and his freedom. At that moment

(to which the record is blind,
no body being found, never mind testament forthcoming)

something catches his eye – a sudden flurry and a bird with two necks interwined; one black, the other – bodiless – a shimmering Islay malt brown.

Angus McKay watches, mesmerised

as the cormorant lifts its white-cheeked head till its brassy twin – the eel – lifting with it, unwinds like a flailing clef and falls, bit by bit, into perfect darkness.

This, thinks Angus McKay, is how the bagpipe has devoured my life.

He lies on his back, drifting downstream, shadowing the black bag of a bird through flanges of light, past two gracefully disinterested swans. The eel rages still – the cormorant’s neck rising and falling in a helpless hiccup. Up ahead, the bird will calm, its neck settle again on its shoulders –

but there, the quicksand waits to welcome Angus McKay, sipping him, limb by limb, into its dark and clammy hold.

That evening, owls will keen – in Gaelic – from Kirkconnell Wood, where Angus McKay perches, pale and dripping.

Will a soul never find peace? he asks.
Oh, where has my plump little lover gone – and what’s become of that shit, Prince Albert?

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Chosen by Femi Oyebode.
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