Sometimes the 'mind' can be abandoned: A Bacchanal by Sebastiano Ricci (1659–1734)

All in the mind

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on the curious connections between Greek tragedy and neuroscience

At first glance the only relevance of Greek culture to neuroscience might seem to be to provide the analogy of the Hydra: as soon as you think you've solved one problem, seven more spring up. The moment we neuroscientists think we've solved a mystery of the brain we realize there are still deeper issues to probe – not least the essence of the human mind. And this is where Greek tragedy offers some interesting comparisons.

The evolution in characterization across the three great tragedians, from Aeschylus to Sophocles to Euripides, has a strong counterpart in neuroscience.

In the tragedies of Aeschylus, the dominant protagonist is arguably the Chorus rather than any single character who may be subject to forces, fates, acting beyond their control. A neuroscientist would view this determinism as comparable to the way some have considered genes: a biological Μοῖρα.

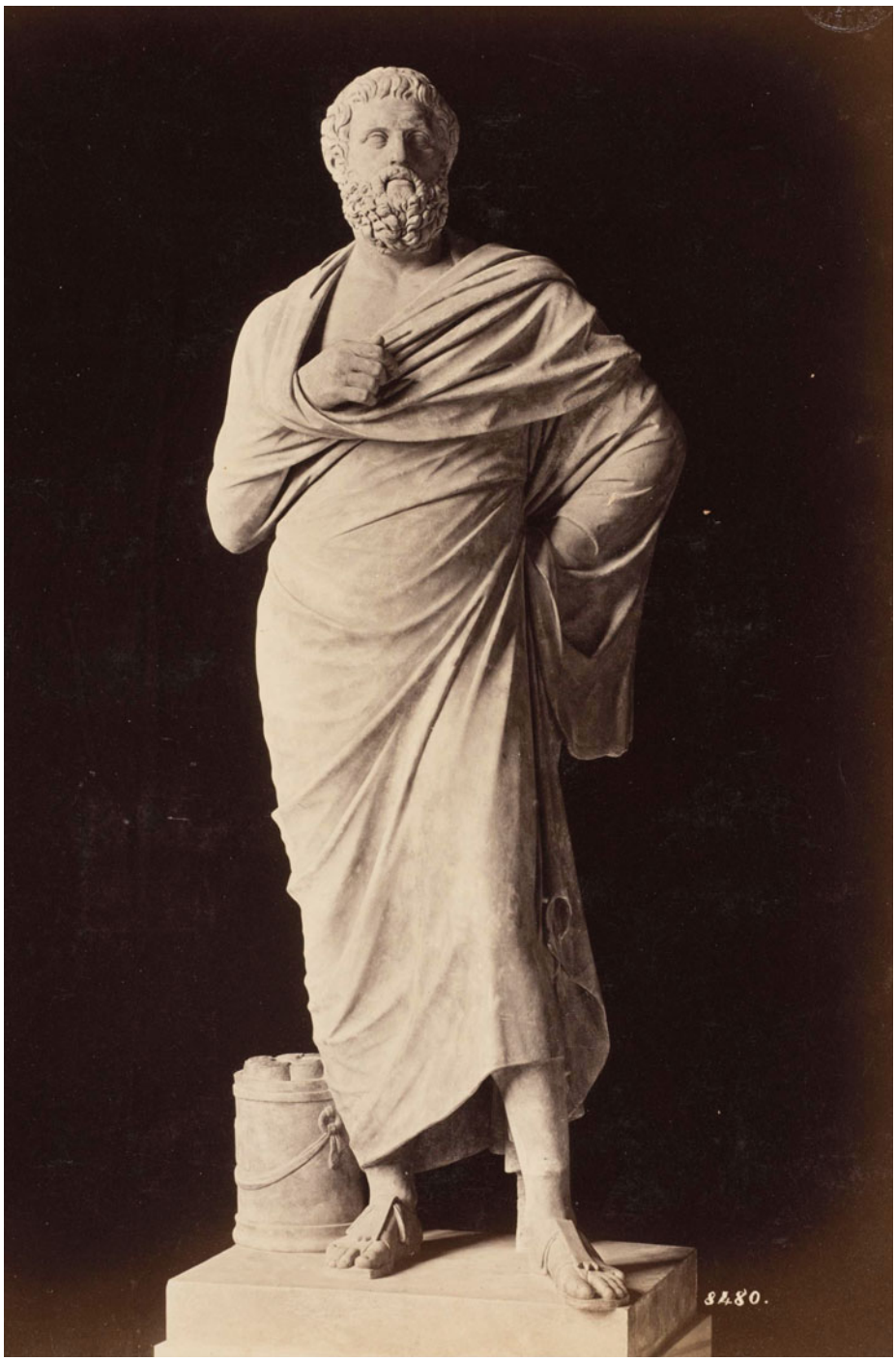
However, we now know that genes, whilst obviously necessary for brain function, are not sufficient in themselves; the environment plays an essential role. The best way to approach the question of how we might link DNA with complex mental traits would be to take an extreme example, one where very unusually a brain dysfunction does actually link to one single rogue gene. Normally, brain disorders such as schizophrenia, Alzheimer's or depression are very complex and

indirect in their respective relationship, ultimately, with a provenance of many different types of genes. However, in the one case that formed the basis of a very insightful study some 20 years ago, this wasn't so. In this particular experiment, the scientists worked on a gene for Huntington's Disease (Chorea), a disease where, as its Greek root suggests, the patient presents with wild, involuntary flinging of the limbs in a grotesque form of dancing. Unlike almost all other brain dysfunctions, this disorder is attributable to just one gene. Accordingly, in this case, the experimenters were able to manipulate the genes of mice so that they had the mouse equivalent of Huntington's Chorea. Since no sophisticated cognitive process was at stake, it was a relatively easy task to evaluate the proficiency of the mice's objective movement by giving a score on a scale on various motor tasks.

The mice were divided into three groups: the inevitable 'controls', the benchmark group that did not have genetic modification, serving as the basis for comparison, and then two groups where the gene was deliberately manipulated so that the mice, as they aged, were destined to develop impairments in movement analogous to that in humans. However, the two groups differed in one important factor: environment. One group was kept in standard housing, the other in an 'enriched environment'. Since rodents are highly exploratory creatures, 'enrichment' for rats and mice consists of interaction with wheels, tubes, food hoppers and other three-dimensional, novel objects that they can explore.

Over 160 days, a fascinating and counterintuitive result emerged. The animals that did not have the modified gene for Huntington's Disease predictably moved just fine throughout the days of their lives. Those with the modified gene kept in standard housing lived out their very different genetic destiny and deteriorated in their movements as they aged, as would have been expected. But those animals with the enriched housing showed a marked difference: surprisingly, the age of onset was much later and the degree of impairment far more modest. So we can see that there is no one-to-one relationship between a single gene and a complex mental trait, even in the case of the simpler brains of mice and the exaggerated example of a single-gene disorder.

All a gene does is to trigger the production of a protein; to be exact, any one gene could cause some 30,000 different proteins to be manufactured. These proteins, like the genes themselves, do not have an agenda built into them but will have different effects depending on the context in which they are realised (i.e. their neuronal circuitry), and this in turn will constantly be changed by the environment. It is now, therefore, widely accepted that the old 'nature versus nurture' debate is actually a misleading dichotomy. We should think of the two as interactive but complementary – a kind of μέν and δε.



A statue of Sophocles in the Lateran Museum, Rome

Sophocles places more emphasis than Aeschylus does on individuals, albeit as hapless victims of their fate. Although his characters are special and not generic, it is arguable nonetheless as to whether they always have what we would call 'free will'. How might this be linked to individual identity? In the middle of the 20th century, one Paul MacLean conceived the idea of a 'Triune Brain'. MacLean's theory was the consequence of questioning the times in which he lived. Specifically, it was a response to the seemingly mindless behaviour of people attending the Nuremberg rallies. His reasoning ran that, anatomically, the brain could be regarded in three evolutionary stages: the reptilian brain, comprising the inner core basic part; layered on to which would be the mammalian brain, comprising areas such as the limbic system and hippocampus; and finally encompassing that would be the cortex, the outer layer of the brain, which is the monopoly of the neo-mammalian species. MacLean argued that these three layers represented increasing degrees of sophistication in mental processes. The reptilian brain underpinned very primitive urges, these being channelled into the appropriate context by virtue of having a mammalian brain; the neomammalian brain imposed further refinements and morality, or rules of how one might behave.

MacLean's idea was that the behaviours of those at the Nuremberg rallies represented an unleashing of the reptilian brain by a suppression of the more sophisticated outer layers. The problem with this idea is that the behaviour of those who may seem otherwise to have 'lost their minds' is not comparable to that seen in crimes of passion. It is, rather, emotion channelled into a narrative, a story. For example, people who attend football matches today, like their more sinister counterparts at rallies in Nazi Germany, are very mindful of who the enemy is and who they themselves are. They are living out not unbridled emotion, but a story. Interestingly enough, this story is frequently a David-and-Goliath narrative, with those who are exhibiting the collective rage being the David character, the small, much-wronged helpless and weaker party, as opposed to the all-pervasive enemy, be it an international conspiracy or a large and powerful country like America. So what could be the biological basis for the narrative that each of us regards as our unique life story?

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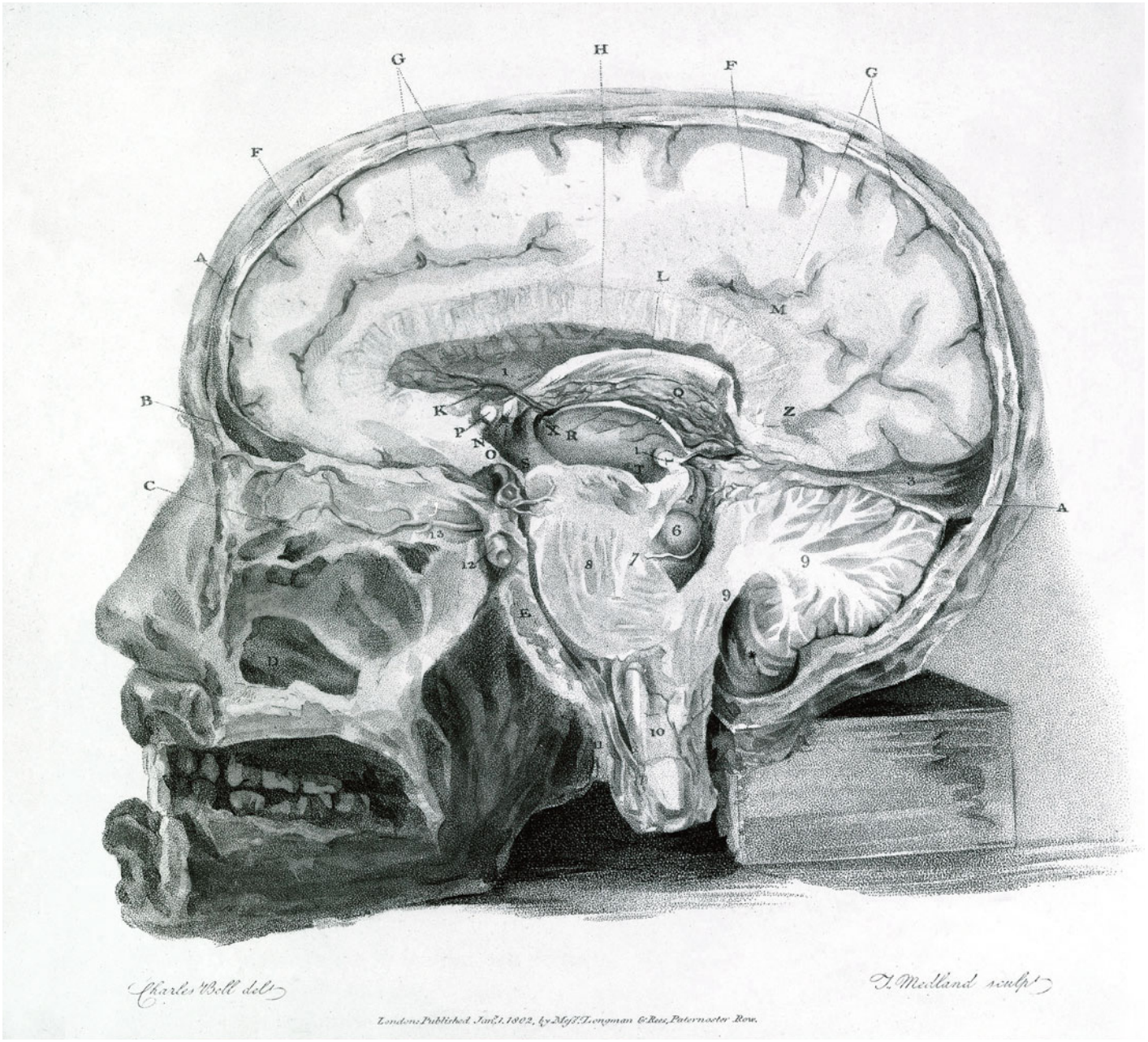
Of the three great tragedians, Euripides places most emphasis on individuals and their inner conflicts. A character may know his own mind, but this 'mind' may also be abandoned. In the *Bacchae,* for example, the prophet Teiresias warns the repressive King Pentheus that there are two forces at work within humans, that of wine and that of bread. Both are needed for true balance. One needs a mind that is logical (bread) but offset by moments of abandonment or loss of mind (wine).

Goddess Demeter is one – she's the earth …
and she feeds mortal people cereal grains.
The other one … born of Semele –
he brought with him liquor from the grape,
something to match the bread from Demeter.

There may well be a neuroscience counterpart to this distinction if we look further at what makes us so special, both as humans and as individuals, by comparing our brains to those of our nearest relatives: the chimpanzees. When we compare the human and chimp brains, one area in particular needs special mention, the 'prefrontal cortex', which, as its name suggests, sits at the front of the brain, behind the forehead. Whilst we do not possess a qualitatively unique brain area that makes us human, the prefrontal cortex is the key brain region that shows a huge quantitative difference between our species and the rest of the animal kingdom, lionising 33% of the adult human brain but only 17% of that of chimps, our nearest relatives. Moreover, we can see that human individual development, 'ontogeny', does indeed reflect 'phylogeny', evolution, in that the human prefrontal cortex only becomes fully matured and functional in the late teenage years and early 20s.

Interestingly enough, however, even when we are adults, the prefrontal cortex can be temporarily put out of action by one particular chemical messenger, the transmitter dopamine. If you are highly excited or aroused, feeling rewarded or indeed if you are addicted to drugs, this same single transmitter would somehow be playing a key part in these different subjective experiences. In all these cases, the chemical messenger dopamine is playing a pivotal role by being released like a fountain from the primitive region at the top of the spine (brainstem) outwards and upwards throughout the brain, where it then changes the responsiveness of neurons in many different areas, including the prefrontal cortex. When dopamine reaches the prefrontal cortex, it inhibits the activity of the neurons there, and so recapitulates in some ways the immature brain state of the child: remember that this area of the brain is only fully active in late teenage years. Just as children are highly emotional and excitable, so adults in this condition are also more reactive to the outside world and to sensations rather than inner 'cognitive' thought processes.

Since schizophrenics resemble children in many ways, not least in their hyper-reactivity to the outside world, it should come as no surprise that schizophrenia can be characterized by an underactive prefrontal



Section of the brain by Sir Charles Bell, 1802

cortex and, among many other changes, by excessive levels of functional dopamine. This highly emotional state mediated by dopamine appears to be the final common conduit of all psychotropic drugs, regardless of their primary site and mode of action. Small wonder, then, that this dopamine system has also been linked to processes in the brain linked to feelings of reward. When we talk of having a 'sensational' time, 'letting ourselves go' and, indeed, 'blowing the mind', we have surely contrived situations – typically 'wine, women and song' or the more modern equivalent of 'drugs, sex and rock'n'roll' – where the senses are being maximally stimulated, dopamine is released and the prefrontal cortex is disabled.

We can think of the normal human condition as comprising two basic modes. In the first, there is strong prefrontal cortex activation, where thinking dominates. Here, normal levels of dopamine prevail and we are mindful of consequences. We have a past, a present and a future – a narrative. In the other, we can revert to the world of the small child, where one is completely in the here-and-now present, reacting to the external sensory input of an atomized moment that is independent of preceding events, of future consequences and hence of 'meaning': a state once described by the musician John Cage as 'no purpose, just sound'. These modes, and indeed the balance that we normally achieve between them, relate very closely to the distinction in the *Bacchae* between the 'bread' and 'wine' forces: the rational, individual adult mind as opposed to the 'loss' of mind.

In the search for who we are and who we may become, the ancient tragedians have much to teach us. We may not have obvious answers, but if neuroscience can now point to counterparts in the physical brain of ideas originally conceived two and a half millennia ago, then we can appreciate even more the profundity of the goal to 'know thyself', γνῶθι σεαυτόν.