

tipping the mind

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Talk about the other side of the coin. There is growing evidence that creativity may well go hand in hand with psychosis. Intuitively, it does not seem so far-fetched a notion. Just think of Salvador Dali, for example. Or Peter Sellers. Mental illness has been around for as long as humans, so why does evolution bother to preserve it? Precisely because of the advantages of a creative mind. Researchers are not suggesting that someone suffering from a mental disorder is inevitably a potential artist. Or vice versa. At least not quite... But what they are slowly demonstrating is that there seems to be a genetic predisposition for creativity and psychosis. And that this predisposition has exactly the same origin for both traits. More specifically, a protein known as neuregulin-1 may have the capacity – given the environment – to tip a mind into mental illness or genius.



by Frédéric Aeby

Courtesy of the artist

The term “schizophrenia” was coined by the Swiss psychiatrist Eugene Bleuler, in 1911. Until the very end of the 19th century, psychiatric disorders had certainly been diagnosed but it was only in 1887 that the German psychiatrist Emil Kraepelin tried to classify them. In so doing, he suggested “dementia praecox” – or premature dementia – to sum up the symptoms of what is now defined as schizophrenia. Eugene Bleuler changed the name because Kraepelin’s

designation suggested a gradual mental deterioration, which is not necessarily the case.

Centuries ago, the causes of mental disorders were believed to be the doings of evil spirits that had taken possession of a body. The treatment proved to be as naïve as the times were in medical knowledge, and patients could be subjected to extreme treatments, such as the drilling of holes into their skulls through which the demons were released. Alternative and less drastic treatments also existed, one of which was the exposure of patients to certain types of music – a therapy that is not far-removed from a current alternative therapy known as the Tomatis Method, in which music is used to help alleviate mental disorders such as autism or depression for instance. Until relatively recently, people suffering from psychosis spent a great part – if not all – of their adult life in asylums. Thankfully, during the second half 20th century, great advances were made in the field of psychiatry and many patients suffering from mental disorders are now able to live an independent – albeit marginal – life.

Such advances include the medical treatment of schizophrenia, which affects as much as 1% of the general population... Running thoughts, delusions, hallucinations, social withdrawal, lack of affect and deficits in executive function are only a few of the disturbances characteristic of someone suffering from this particular form of psychosis – a number of which may even appear before the onset of the illness. This is why the recent discovery of neuregulin-1 and its probable involvement in

schizophrenia is encouraging. But what, exactly, has been discovered?

Neuregulin-1 is a signalling protein that mediates cell-cell interactions and plays a critical role in organ development. There are four isoforms. Isoform type IV is particular to the nervous system, and is greatly expressed in the foetal brain – and to a lesser degree in the adult brain – where it is thought to be at the heart of neurogenesis, neuronal migration, synaptic plasticity and the regulation of neurotransmitter function. It is hardly surprising, then, that the deregulation of neuregulin-1 can bring about psychiatric disorders. A mutation within the promoter region of the neuregulin-1 type IV gene is believed to be the culprit. This mutation causes the protein to be expressed differently and lays the foundations, very early on in life, of a psychiatric fragility whose symptoms usually first appear during the later years of adolescence – given the unfortunate circumstances.

Neuregulin-1 is expressed in neurons and secreted at the synaptic cleft, where it binds to a receptor known as ErbB4 situated on the postsynaptic membrane. This action sparks off a signal which is relayed further, ultimately fuelling a variety of pathways all involved in brain development. One hypothesis could explain the onset of schizophrenia:

the effects of neuregulin-1 on synaptic plasticity via glutamatergic transmission. Abnormalities in plasticity may explain cognitive drawbacks characteristic of schizophrenia, such as deficits in memory, attention and executive function. As for neuregulin's role in creativity, all scientists have observed to date is that out of a sample of 200 particularly talented people – judged by their creative achievements and creative thinking – the great majority carried the neuregulin-1 isoform specific to schizophrenia.

One surprising discovery is that the neuregulin-1 isoform which predisposes to schizophrenia also seems to protect carriers from cancer. Why? No-one knows. As no one can say in what way neuregulin-1 is able to galvanise creativity. Naturally, there is no way that one sole protein could have such intimidating power. Brain development is hugely complex and involves myriads of intricate biological pathways. However, this particular brain-specific neuregulin-1 may well prove to be precious for the design of drugs which would not have the violent side effects current medication has on patients. And is it not intriguing – not to mention somewhat daunting – to realise that psychiatric fragility and creativity are, perhaps, not only related but may also be inheritable?

Cross-references to UniProt

Neuregulin-1, *Homo sapiens* (Human) : Q02297

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