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TERTIARY SYPHILIS (GENERAL PARALYSIS OF THE INSANE) AND BIPOLAR DISORDER; THE ROLE OF THESE TWO DISORDERS IN THE LIFE OF FAMOUS COMPOSERS

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SUMMARY

Syphilis is a complex disease, which can lead to General Paralysis of the Insane if left untreated. Before antibiotics this was the natural progression of the disease, with many people being admitted to mental asylums with the diagnosis of GPI, and going on to die there. Diagnoses however, were difficult, as it was difficult to distinguish between GPI and other mental conditions such as bipolar disorder. We can use the works of the classical composers Beethoven, Schubert, Schumann and Smetana, who all suffered from mental illness, to gain an insight into what it is like to live with these conditions. All these are potential cases of GPI, highlighting how a sexually transmitted disease can end the life of such talented and influential people. With antibiotic resistance becoming a growing concern, it is key that we continue to recognise and treat syphilis in an appropriate manner, so as to limit the future of this disease.

Key words: *tertiary syphilis - general paralysis of the insane - bipolar disorder - classical composers*

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INTRODUCTION

Many famous composers were troubled with mental illness throughout their careers. There are many hypotheses as to the reason behind this, and two which stand out are tertiary syphilis (General Paralysis of the Insane) and Bipolar Disorder.

SYPHILIS

Syphilis is a disease that some believe dates back to 3000 BC, nonetheless, it has been recognised in Europe from the 13th century (Tampa 2014). This sexually transmitted disease is caused by the bacteria Treponema pallidum. The initial infection is characterised by open lesions, but these close as the infection enters its second phase – the multiplication of the organism in different tissues causing fever, malaise, and a mucocutaneous rash, and then its tertiary phase – inflammation due to high numbers of the organism causes tissue destruction, after a latent phase which may last 25 years. Inflammation of the parenchymatous parts of the brain leads to general paralysis of the insane (Radolf 1996).

In the 19th century, general paralysis of the insane became a very prominent issue in the world of psychiatry. Patients would be admitted to asylums for a wide variety of symptoms from grandiose to paranoid delusions, personality changes, insomnia and mania. Shivering and Argyll Robertson pupil were also observed. Throughout Europe, men in their late 30s and 40s were being admitted to asylums with the suspected diagnosis of GPI, however, at this time the cause of the disease was unknown and there was no cure. There were many hypotheses as to the cause of GPI from bereavement to excess alcohol and tobacco. Syphilis was suggested in 1857, but was not accepted until the discovery of Treponema pallidum (then called Spirochaeta pallida) in the brain of deceased patients in the 20th century. At this point, one fifth of male admissions to asylums were with the diagnosis of GPI and the prognosis for all those admitted was death. The seriousness of this disease affecting those expected to be at the peak of their life is thus clear (Davis 2012).

In the early 20th century, following unsuccessful treatments with heavy metals, a new treatment was developed in the hope to reduce deaths from syphilis; this method was to infect a patient with malaria in order to induce a fever to kill the Treponema pallidum, and then treat the patient with quinine to cure the malaria. Although this was more effective than previous treatments, the huge decline in syphilis in the mid 20th century, was due to the development of penicillin (Wallis 2012).

The availability of penicillin to treat syphilis meant that GPI all but disappeared in the UK, however, in 2015, there were 2811 new syphilis diagnoses in London, of which 39.5% were in the early latent phase (Public Health England 2016).Could this be due to antibiotic resistant strains of Treponema pallidum?

A point mutation has introduced macrolide resistance in some strains of T. pallidum found in areas of the United States, Canada, Europe and China, with use of these antibiotics thought to be adding selective pressure (Stamm 2009). Use of macrolides, therefore, in the treatment of syphilis must be done with caution under close clinical monitoring (Stamm 2009). Although this resistance should not be overlooked, it is

not itself critical in the future of syphilis treatment, as the first line drug remains penicillin (Stamm 2009). Penicillin is a β-lactam antibiotic which prevents cell wall synthesis and thus causes cell lysis. It is bactericidal for growing bacteria; however, many species are developing mechanisms of resistance. These include producing β-lactamase enzymes that destroy the critical β-lactam ring and the use of different transpeptidase enzymes, that have a lower affinity to the β-lactam ring (Stamm 2009). Neither of these, however, are yet to be found in T. pallidum (Stamm 2009). The thought behind this is that T. pallidum lacks plasmids, bacteriophage, or transposons, preventing horizontal transfer of genes; furthermore, development of genes to code for these new proteins would require multiple mutations in the DNA, compared to the single mutation required to confer macrolide resistance (Stamm 2009). This is not to say that resistance could occur at any point in the future (Stamm 2009).

BIPOLAR DISORDER

Another condition with potentially similar symptoms to tertiary syphilis is bipolar disorder (APA 2013, WHO 1994). This is characterised by periods of depression, followed by periods of mania. Interactions between a collection of genes and environmental and social factors making a person more likely to develop the condition (Craddock 2005, nhs.uk 2016). Both the depressive and manic states of bipolar disorder may feature hallucinations and delusions.

Bipolar disorder was not recognised until the 19th century, when Jean-Pierre Falret described 'la folie circulaire' – circular insanity. He documented the change in patients from depression to mania, and how this condition tended to run in families (Mason 2016).

In the early 20th century, the distinction between bipolar disorder and schizophrenia was noted by Emil Kraepelin. Although neither term was yet coined, 'dementia praecox' (schizophrenia) showed positive (e.g. hallucinations) and negative (e.g. anhedonia) symptoms in the setting of a 'chronic mental disorder in which a person loses touch with reality (psychosis)'; this contrasts to the distinct periods of mania and depression seen in bipolar disorder (Krans 2018).

DISCUSSION

On admission to an asylum, or when diagnosing retrospectively, the presence of grandiose delusions applies to both the manic phase of bipolar disorder and to GPI (Mason 2016). Before the introduction of serological tests, it is understandable that the diagnosis of GPI as a result of tertiary syphilis may be delayed as other possible disorders were excluded.

Ludwig von Beethoven (1770-1827)

It is well known that Beethoven was completely deaf for the final 9 years of his life; his post mortem revealed vestibulocochlear nerve atrophy (Franzen 2008). In addition to this, he suffered from ascites, hepatic failure, chronic alternating constipation and diarrhoea, and uveitis. Tertiary syphilis could explain the atrophy of the eighth cranial nerve, due to meningeal irritation, which could also be responsible for the uveitis. Untreated tertiary syphilis may also cause gummas of the liver, leading to cirrhosis, and hence the ascites and liver failure. Syphilis however, does not give a reasonable explanation of the bowel symptoms.

The most likely explanation for the bowel symptoms is irritable bowel syndrome, although Crohn's disease and ulcerative colitis are other possibilities. Whipple's disease is also a possible cause of Beethoven's symptoms; however, it is extremely rare (Donnenberg 2000).

With regards to Beethoven's compositions, the most interesting symptom is inevitably his deafness. Other than syphilis, it has been proposed that this could be due to low-dose chronic exposure to heavy metals, such as lead in wine. This explanation is favoured by some as his hearing loss was slow over years; an autoimmune hearing loss would develop in months (Stevens 2013).

Franz Schubert (1797-1828)

Schubert received his diagnosis of syphilis aged 25 after experiencing mood changes, depression, headaches and dizziness. He was treated with mercury inhalation which had many side effects including hair loss (Franzen 2008). The effect of his condition on his work is very obvious, in a way that Beethoven's is not. This may be because he was diagnosed with syphilis, whereas Beethoven's infection is a retrospective postulation; or perhaps it is because he had more neurological (at least documented neurological) symptoms than Beethoven.

Upon diagnosis, Schubert decided to not complete his *Unfinished Symphony*, leaving it as a two-movements-symphony, not the traditional four, perhaps a reminder of mortality? His sense of hopelessness is also reflected in other compositions including *Der Tod und das Mädchen* (Death and the maiden), really enforcing his fear of approaching death.

Schubert's life seems to be clouded with depression, but also auditory and visual hallucinations which also suggests bipolar disorder. It is very difficult to know for certain, what exactly ailed him, as a diagnosis of syphilis was highly stigmatised in the 19th century and so medical records were destroyed or doctored to keep the diagnosis from friends and family. This is thought to be an explanation for the rather unexplained typhus of Schubert (Rempelakos 2014).

Robert Schumann (1810-1856)

At age 23 Schumann first displayed signs of a mental disorder, with alternating depressive and manic episodes. Consistent with his history of frequently changing sexual partners, it is thought that Schumann contracted syphilis aged 20, which quickly progressed to the tertiary stage. He suffered serious decline in mental stability and in 1854 he attempted suicide by jumping in the Rhine. Following his rescue, he was admitted to a mental asylum where he died two years later (Franzen 2008).

Schumann's exact diagnosis is argued with possibilities, other than tertiary syphilis, including bipolar disorder and schizophrenia. Regardless, his mental condition is very apparent throughout his compositions. A marking of 'lively but not too fast' in the third movement of *Violin Concerto in D minor* led to 'awkward music flow'; the explanation for this marking being that Schumann heard music at different speeds to others. Furthermore, a single sounding note in *Ghost Variations for piano*, his last published work, could indicate tinnitus (Rempelakos 2014).

Bedrich Smetana (1824-1884)

Smetana first developed symptoms of tertiary syphilis aged 38, when he experienced auditory hallucinations, followed by tinnitus, and by aged 50, he was completely deaf. This however, did not halt his composing. In 1876 he composed *'Aus meinem Leben'*, a string quartet in e minor (Franzen 2008).

This composition depicts his journey with his illness, with, in the last movement, a poignant harmonic high E from the first violin, over a low tremolo chord by the lower three instruments. This reflects the tinnitus from which he suffered throughout his deafness.

Due to severe neurological decline, Smetana was admitted to an asylum following violent behaviour, memory loss and writing letters to imaginary friends. He died in this asylum (Rempelakos 2014).

In 1987, his body was exhumed, and the tissues tested for syphilis, all with a positive result. This provided a full explanation for all his symptoms and ceased different hypotheses as to their origin. For instance, it had been suggested that his hearing loss was related to a gunpowder accident that happened when he was 11 and resulted in osteomyelitis. High levels of mercury were also found in his body, suggesting that they suspected at the time that he had syphilis (Höschl 2012).

CONCLUSIONS

Life for these composers became very bleak through the course of their illness. The diagnosis could never be certain, as appropriate tests had not been developed yet; and even if a confident diagnosis was made, the treatment with mercury most probably contributed to their mental deterioration.

Now that we have the appropriate treatment, the key is to establish the presence of syphilis as soon as possible, to kill the bacteria before it causes irreversible damage. Available now are serum analysis for syphilis with non-specific lipoidal tests (venereal disease research laboratory tests) and treponemal-specific tests (fluorescent treponemal antibody absorption) (Wlodarczyk 2017). These tests used to be routine on admission to a mental hospital but were stopped as incidence decreased. Perhaps, however, they should be brought back and awareness of syphilis increased, as this disease is returning (Wlodarczyk 2017).

We have also now developed tests to look at the affect that neurosyphilis has on the brain. By looking at the apparent diffusion coefficient (ADC) of water under MRI, one can look for white matter atrophy; unimpeded diffusion indicates white matter disintegration (Czarnowska-Cuba 2017). This imaging may suggest neurosyphilis before a person becomes symptomatic and so could prove invaluable in the future of syphilis screening.

Whether or not Beethoven had syphilis, we will most likely never find out, although we can be fairly certain that Schubert, Schumann and Smetana were all infected. Again, a diagnosis of bipolar disorder is also hard to determine, as at this time, this condition was not recognised, and the limited literature available does not provide sufficient detail. We can, however, learn a lot about what it can be like living with these conditions through the interpretation of their compositions. This should act as a reminder that syphilis must be recognised as a serious disease, which, if diagnosed in the primary stage, is entirely treatable.

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Contribution of individual authors:

Isabelle K. McGill carried out the literature search and drafted the text.

Mark Agius corrected and commented on the text and supervised the project.

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