



Did Blaise Pascal have autism spectrum disorder and a genetic predisposition for skull deformities?



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ABSTRACT

Many world-renowned scientists and artists had autism spectrum disorder (ASD). We suggest that the French mathematician and physicist Blaise Pascal (1623–1662) also had ASD. As a boy, he demonstrated his mastery of language, mathematics and science. He showed single-mindedness and obsessive interests in the pursuit of science in his younger years and later he pursued with religion with the same determination. Pascal neglected social interactions; he was cold and aloof and had an obsessive revulsion to any expression of emotional attachment. As shown by his funerary mask and the autopsy report Pascal had craniosynostosis (primary non-syndromic oxycephaly) with atrophy of the right half of the face. Congenital facial asymmetry due to craniosynostosis has a genetic basis. This suggests that Pascal's facial deformity may betray his propensity to suffer from genetically determined diseases including ASD. Despite the intrinsic limitations of a diagnosis based only on biographical information, we surmise that Pascal had the three key symptoms (obsessive interests, difficulty in social relationship and problems in communicating) that characterize ASD individuals.

Autism, also known as autism spectrum disorder (ASD), is a complex developmental syndrome with multiple non-genetic and genetic causes [1]. The wide spectrum of these developmental disorders is characterized by impairments in three behavioural domains: i. social interaction; ii. language, communication, and imaginative play; and iii. range of interests and activities [1].

The current diagnosis of ASD includes several conditions once diagnosed separately: autistic disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), and Asperger's syndrome. These conditions are classified under the broad umbrella of autism spectrum disorder in the DSM-V. According to estimates from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network [2] about 1 in 68 children have Autism Spectrum Disorder (ASD). ASD tends to occur more often in people who have genetic or chromosomal conditions. About 10% of children with autism also have Down syndrome, fragile X syndrome, tuberous sclerosis, or other associated genetic and

chromosomal disorders [2–4]. ASD commonly co-occurs also with other developmental, psychiatric and neurologic diagnoses [5]. The co-occurrence of one or more non-ASD developmental diagnoses is 83%. The co-occurrence of one or more psychiatric diagnoses is 10% [6].

The context

Progresses in neurosciences allow individuals with both primary and syndromic ASD (autism associated with a known cause) to be diagnosed in their early years [7]. However, it remains to be determined how many world-renowned scientists and artists were affected by these disorders [8–10]. Based on a perusal of their biographies, it has been proposed that scientists such as Isaac Newton, Albert Einstein, Henry Cavendish, and Irène Joliot-Curie had ASD [8,9]. Marie Curie, the theoretical physicist Paul Dirac, the painter J.M.W. Turner, the composer Bela Bartok and the philosopher Ludwig Wittgenstein may all

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Fig. 1. Portrait of Blaise Pascal (1623–1662), oil on canvas (70 cm × 56 cm) by an unknown artist (ca 1691), Palace of Versailles, France. Accessed from the Internet, https://commons.wikimedia.org/wiki/File:Blaise_Pascal_Versailles.JPG Sept. 15 2018.

have had ASD [8–10].

We propose that the French mathematician, physicist and mystic Blaise Pascal (1623–1662) (Fig. 1) had ASD and a genetic predisposition for skull deformities (oxycephaly) [11]. The son of Etienne Pascal and Antoinette Begon, a wealthy aristocratic family, Blaise was born on 19 June 1623 at Clermont-Ferrand (France) and had two sisters, Gilberte (1620) and Jacqueline (1625). His mother died prematurely when he was aged three. He was educated at home by his father and was taught grammar, linguistics and natural sciences and, later, Latin and Greek [12,13].

Obsessive interests and repetitive routine: science and religion

Blaise was a child prodigy who developed an early obsessive passion for the exact sciences. At the age of twelve, he had studied Euclid's geometry and had written a paper about sound waves [14]. He was not yet 16 when he published his first scientific essay (*Essai pour les Coniques*) [12,13].

A few years later, in 1642, while he was in Rouen with his father (who had been invited there by Cardinal Richelieu), he designed and built a calculator (which was presented to the public in 1652) [13,14]. Obsessed with science, he kept on working uninterruptedly on this project for four months going to bed around 2:00 AM [13].

At that time, Pascal was already severely ill. His health had deteriorated since the age of 18 and Gilberte -his sister- wrote: *from the age of 18 (1641), he would not have spent one day without pain* [12]. Headache was the principal symptom of his disease, which lasted twenty-one years until his premature death in 1662. Nevertheless, he never gave up his studies [13].

In mathematics, he has given his name to Pascal's triangle and is regarded as one of the mathematicians behind probability calculus [13]. In physics, he studied hydrodynamics and by using mercury and a glass tube, he showed that air can be weighed and that its weight varies with the height above the earth's surface (Rouen, autumn 1646–summer 1647). He proved that vacuum exists something previously deemed impossible [13–15].

In 1646 Pascal embraced the ideals of the Jansenists of Port-Royal des Champs (Paris) becoming faithful to their cause. Jansenism was a Catholic theological movement that emphasized sin, human depravity, the necessity of divine grace and predestination (only those chosen by God from the foundations of the world would be saved). Pascal shared their integral Augustinism [16–18] and their strictness fighting against Jesuits' laxness [12,13]. Pascal converted all of his family, especially Jacqueline (who joined the Port-Royal convent after their father's death in 1651) to this ideal, which obsessively dominated his thoughts until his death [13].

Difficulty in relationship with non-verbal communication problems and social impairment

After his father's death (September 1651), Blaise was alone and became depressed. Physicians recommended to renounce the self-imposed austerity and to go back into the world, which he did. He decided to live "the good life" (social life), but after three years (December 1654), he became disgusted with it (*une aversion extrême des folies et des amusements du monde; an extreme aversion against the good life –fun and entertainments of the world*) and retreated into a life of "quiet desperation", where he felt abandoned by God [12,13]. However, at the end of 1653, he had a second religious revelation (*la reconciliation totale et douce; the total and sweet reconciliation*) and went back to Port-Royal [13].

During the night between 23 and 24 November 1654, he had a mystical experience. The *God of Abraham, Isaac, and Jacob* spoke to him with words of resurrection and life. He secluded himself in the monastery of *Les Granges* where he peacefully lived for one year practising ascetic behaviours [12,13].

His period of rest was abruptly interrupted, when in 1655, he felt the need to defend the Jansenists from the attacks of the Jesuits [12,13]. He authored, under the pseudonym of Luc de Montalte, a series of eighteen *Lettres Provinciales*. In these letters, he defended the Jansenists and criticized the laxity of Jesuits [19].

In his mature years, Pascal exhibited signs of manic depression. Many details of his personal life reported by his sister Gilberte suggest a fundamentalist interpretation of religious belief. His sister wrote that Pascal had an obsessive repugnance to any expression of emotional attachment, which she attributed to his high regard for the virtue of modesty. She reported that *he could not even tolerate the caresses that I received from my own children* [12].

Pascal believed uncritically that God performed miracles. His faith was strengthened by the miraculous recovery (24 March 1656) of one of his nieces from a serious eye condition and the cure was attributed to what was believed to be a thorn from the passion of Christ [12,13]. In the meantime, a worsening of his health coupled with a growing sense of dissatisfaction and repugnance for the life he had lived so far and for the people surrounding him took place. A deep restlessness took hold of him. He had remorse because he thought he had been away from God, he felt that he had lost Him and he feared of being unable to meet Him again [12,13]. In 1658, Pascal became weaker and his life became a long process of sublimation with continuous efforts to reach the ideals of Christian perfection (*Imitatio Christi*) [20].

The final illness

At the end of 1658, his life became a long agony with few periods of recovery. Throughout this period, he continued with his ascetic behaviour (no comforts, poor eating habits, wearing an iron chain with thorns around his chest) even though his physical health had deteriorated [12,13]. In August 1660, he wrote to the mathematician Pierre Fermat that *I know that mathematics is the most valuable part of our intellect, but my ability to concentrate is now so poor that I can no longer deal with mathematics. I cannot walk without a stick and cannot remain sitting on a horse for long* [14].

In December 1661, Pascal had an epileptic seizure and from June 14, 1662, his condition further worsened. On July 2, 1662, he complained of abdominal pain, still treated, at the time, by a combination of laxative potions and emetic agents. His condition worsened further with major asthenia, loss of weight, and anorexia. On 14 August, his headaches increased to an almost unbearable pain. The doctors who were summoned noted that his pulse was distinct and regular, and therefore the prognosis was considered good. A combination of migraine and excess fluid was thought to be the reason for his headache [12]. On 17 August, around midnight, following an increase of his headaches, he had a violent seizure. He regained consciousness and pronounced his

last words. He had several more seizures, which lasted one day and died on August 19 at 1:00 AM [12,13].

The autopsy

The autopsy performed by Doctor Vallant and his assistants took place on August 21, 1662 shortly before Pascal's interment. The autopsy report is detailed in the writings of Pascal's sister, Gilberte [12]. Only the abdomen and the skull were examined. The stomach, the liver and the intestines were putrified. A strongly premature ossification of the bicoronal, lambdoid and metopic cranial sutures (craniosynostosis) was observed [12]. An enlarged, solid and dense brain was observed. Two impressions filled with blood clots were found in the ventricles and initial gangrene of the dura was present. The findings were probably thrombi located in the sinuses [12,21,22]. A diagnosis of Lhermitte-Duclos disease, which we fully support, was proposed by Laestedius [14].

On autism spectrum disorder and co-morbid genetic diseases

The autopsy report indicates that Pascal had oxycephaly, a form of isolated nonsyndromic craniosynostosis; this excludes conjunction with other anomalies in well-defined patterns resulting in clinically recognized syndromes [24]. The presence of nonsyndromic oxycephaly is confirmed by Pascal's funerary mask [11] (Fig. 2) in which the right half of the face is atrophic.

Nonsyndromic craniosynostoses, which have an autosomal inheritance pattern, show a genetic heterogeneity [25]. Isolated craniosynostosis-1 (CRS1) is caused by heterozygous mutation in the TWIST1 gene on chromosome 7p21 [25]. Craniosynostosis-2 (CRS2) is caused by mutation in the MSX2 gene on chromosome 5q [25]. Craniosynostosis-3 (CRS3) is caused by mutation in the TCF12 gene on chromosome

15q21 [25]. Craniosynostosis-4 (CRS4) is caused by mutation in the ERF gene on chromosome 19q13 [25]. Susceptibility to craniosynostosis-5 (CRS5) is conferred by variation in the ALX4 gene on chromosome 7p21 [25]. Craniosynostosis-6 (CRS6) is caused by mutation in the ZIC1 gene on chromosome 3q24 [25]. Susceptibility to craniosynostosis-7 (CRS7) is conferred by variation in the SMAD6 gene on chromosome 15q22 [25].

Research performed by Twigg et al. [3] has shown an association between ZIC1 mutation and autistic features in some patients. Congenital facial asymmetry due to craniosynostosis has also been noted in patients with Lhermitte-Duclos syndrome [23]. Based on Pascal's phenotype, we hypothesize that he may have had craniosynostosis-6 (CRS6), a bicoronal form associated with bony defects in the sagittal, metopic, or lambdoid sutures [25]. This suggests that Pascal's facial deformity may betray his propensity to suffer from genetically determined diseases including ASD.

From a perusal of Pascal's writing and biographies, it emerges that he had deficits in social-emotional reciprocity, in nonverbal communicative behaviors used for social interaction, and in developing and maintaining relationships. Moreover, he had an excessive adherence to routine, highly restricted and fixated interests, and a hypo-reactivity to sensory input from the environment.

These symptoms are consistent with the diagnosis of ASD. The differential diagnosis includes personality disorder, anxiety disorder and obsessive-compulsive disorder. However, individuals with ASDs may present psychiatric comorbidities, such as attention deficit, hyperactivity disorder, anxiety disorders and mood alterations [26]. We believe Pascal had ASD because of his single mindedness in the pursuit of science during his younger years and of religion in his later years with total neglect of social interactions. He had demonstrated his mastery of language, mathematics and science in common with other well-known scientists who had ASD. Despite the intrinsic limitations of a diagnosis based on biographical information and limited autopsy evidence, we surmise that Pascal had the three key symptoms – obsessive interests and repetitive routine, difficulty in relationship with non-verbal communication problems and social impairment – that characterized other renowned scientists diagnosed with ASD disorders.

Guarantors

I undersigned, Raffaella Bianucci, guarantor of the article declare that each co-author approved the final draft submitted.

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Competing interests

None.

Authors contribution

All authors equally contributed.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2018.11.020>.

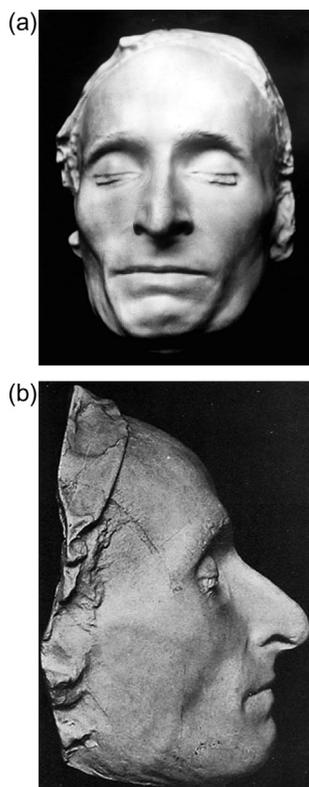


Fig. 2. Blaise Pascal's death mask, Library of the Port-Royal Society, Paris; a – Front view of Blaise Pascal's death mask; b – Lateral view. Accessed from the Internet https://en.wikipedia.org/wiki/Blaise_Pascal#/media/File:001Paskal.JPG Sept. 15 2018.

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