Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Psychiatry

Family Aggregation of Schizophrenia: Heredity or Folie a Deux: About Two Cases

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DOI: https://doi.org/10.36347/sjmcr.2024.v12i08.029 | **Received:** 06.07.2024 | **Accepted:** 13.08.2024 | **Published:** 27.08.2024

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Abstract **Case Report**

Delusion is the predominant semiological entity in psychosis, which can, like many psychiatric or non-psychiatric pathologies, have a family character, assuming in the first place a genetic causal link, but authors have been able to individualize the transmission of delusion between subjects -who are not necessarily all psychotic- through promiscuity, and have called it "folie à deux". Folie à deux or shared psychotic disorder is a rare diagnosis that is subject to controversy concerning its phenomenology, its nosography, and its psychopathology, questioning the nature of delirium and its occurrence outside a psychotic structure as well as the question of the contagion of the symptom in psychiatry. We propose the semiological analysis of two intrafamilial cases of folie à deux, the first case in which the clinical particularity is the shared delusional symptoms without any other psychotic symptoms, and the second case is characterized by the shared delusional and non-delusional psychotic symptoms. From there, we underline the inadequacy of a purely descriptive approach and emphasize the possible link with other more frequent clinical situations with the common point of the transmission of psychic symptoms between two or more persons. Then, we propose a therapeutic reflection involving a non-pharmacological approach and a preventive strategy to avoid the contagion of the said delirium between biologically vulnerable subjects.

Keywords: Delusion, Family Aggregation, Schizophrenia, Phenomenology, Nosography, Psychopathology.

INTRODUCTION

Psychoses are a group of psychiatric disorders characterized by delusions, hallucinations, and other behavioral disturbances. They are complex, polymorphic, multifactorial mental disorders, sometimes with a familial aspect; typically, and classically explained by genetic relatedness and exposure to the same environmental factors [2]. However, in certain specific cases, researchers have identified another phenomenon that might explain this familial aggregation: the sharing of delusions between individuals who are not necessarily all psychotic, leading to the term "folie à deux" introduced in 1877 [1, 2].

METHOD

In this article on "folie à deux," we will analyze the cases of two pairs of patients diagnosed with "shared delusion." We will start with a clinical and semiological description of each patient and their inducing subjects, then discuss the etiopathogenic mechanisms and the impact of heredity in this pathology, and the different subtypes described in the literature. Finally, we will detail the management steps undertaken for these two cases and their evolution under treatment.

CLINICAL CASES

First Clinical Case

This involves Mr. M.E., a 46-year-old man with no prior psychiatric follow-up, who was brought by his elder brother to the emergency department for the management of behavioral disturbances including psychomotor agitation, restlessness, and insomnia, while both accused Mr. M.E.'s wife of poisoning him after allegedly killing their third brother.

Upon admission to our facility, the symptoms seemed to have started a few days prior with the abrupt onset of behavioral disturbances, including agitation with explosive outbursts, uttering obscenities and delusional statements questioning his wife's fidelity, accusing her of stealing his bank documents, poisoning his drinks, and even killing his brother (the brother who had previously exhibited psychotic-like symptoms but was never followed up, committed suicide in 2007 by hanging). Following this, Mr. M.E. fled to his elder

brother's house, who also believed in his sister-in-law's guilt. This brother started spying on her for evidence of adultery and went to the police to contest the circumstances of the deceased brother's suicide, hoping to implicate her in his alleged homicide.

It is noteworthy that Mr. M.E. had always had only his elder brother as his confidant, with whom he had long telephone conversations. This elder brother had a low opinion of his sister-in-law, doubted her integrity, and attempted to convince Mr. M.E. to separate from her, but these attempts were unsuccessful.

Once admitted to the psychiatry department and after stabilization on the motor level, Mr. M.E. began to express additional delusional ideas of persecution against his wife, with claims of being the son of a high-ranked and powerful person and intuitive and interpretive mechanisms reported with strong emotional charge. He was immediately placed on antipsychotic medication and was allowed to receive visits from his elder brother.

Since then, daily interviews noted a progressive distancing from the delusional beliefs of filiation, with the persistence of the delusion of persecution against his wife. The attending physician decided to consult with the elder brother and discovered that the persecutory elements were shared between the two brothers, that the elder brother had initiated legal proceedings against his sister-in-law accusing her of murder, adultery, and attempted murder, and that the main topic of their frequent meetings was the debriefing on the progress of this case.

Given these new elements, the physician banned visits from the "inducer" elder brother, and the evolution of the delusion of persecution against the wife was marked by a gradual distancing until criticism.

Second Clinical Case

Mr. M., a 30-year-old single male, an Army officer from Taza residing in Bouznika, was evacuated from his unit and admitted in March 2022 for incoherent speech and insomnia.

The patient reportedly expressed mystical-religious delusions after several months of intense religious involvement, which contrasted with his previous state. Upon hospitalization in our facility, it was found that the symptoms had started 6 months earlier with a progressive change in behavior including social withdrawal, isolation, and abulia, with an unusual deepening of his relationship with his younger brother, who had been treated for schizophrenia for a year. Mr. M. began praying regularly, significantly increasing the time devoted to prayer and reading the Quran while neglecting his professional duties and personal hygiene, with increased cannabis use, until he started verbalizing mystical-religious delusions with intuitive mechanisms and strong emotional charge and was promptly brought to our facility for adequate management.

During family visits, the attending physician noticed that the younger brother was occasionally agitated, appeared neglected, and expressed delusional statements with the same themes as the elder brother. It was finally discovered that the younger brother was on therapeutic leave due to several months of poor adherence to treatment.

The discussion with the patient's family revealed that the younger brother had been stabilized on Olanzapine. Based on the new data collected by the attending physician, the patient was also placed on Olanzapine and visits from the younger brother were prohibited due to the negative impact on his psychomotor state and thoughts. Psychoeducation was provided to the father to ensure the younger brother resumed treatment and, if necessary, to consider hospitalization in another psychiatric facility.

DISCUSSION

In our cases, the similarity in delusional content and mechanisms between the two pairs is striking, raising several questions about the genesis of delusions. Are they affected by the same schizophrenia spectrum disorder and developed the same delusions? Or is it a classic case of folie à deux? If so, who is the inducer and who is the recipient? Does the latter suffer from psychosis? If so, when did it start compared to the inducer's condition?

Family Aggregation of Psychosis

Similar to the clinical cases reported, all studies of family aggregation attest to the existence of familial concentration of schizophrenia as follows:

- The risk of developing the disease in a healthy family is 1%.
- The risk of developing the disease among siblings is 9%.
- The risk if one parent is schizophrenic is 13%.
- The risk if both parents are schizophrenic is 46% [2].

These findings, though enlightening, do not differentiate between genetic and environmental components. Twin studies have refined the characterization of the genetic component of schizophrenia [2]:

- Among monozygotic twin pairs where one is schizophrenic, concordance for the disease ranges from 40% to 70% [3].
- Among dizygotic twin pairs, concordance is much lower, at 15% [3].

Although concordance is high among monozygotic twins, it does not reach 100%, indicating that environmental factors modulate the effect of

genotype [3]. Adoption studies confirm the importance of genetic factors in the etiopathogenesis of schizophrenia. There is an increased risk of developing schizophrenia among biological relatives of schizophrenic patients compared to adoptive family members (healthy parents) [4].

On the other hand, geneticists have not yet managed to isolate a strongly implicated allele in the genesis of schizophrenia, leading to the emergence of more promising theories such as the association of vulnerable alleles that may interact with the environment, pre or perinatal infections associated with increased risk, or the microbiome theory [5].

Nevertheless, familial aggregation of schizophrenia cases is still explained by the overlap of environmental factors with genetic factors [4], as evidenced by Table 1 showing results from previous studies on the degree of involvement of environmental and genetic factors in psychotic disorders.

Gene Selection Strategy	Gene	Variant	Exposure	Outcome	Original report	Replication	
					Reference	Result	Reference
Candidate Gene	*BDNF*	rs6265	Childhood trauma	Psychotic symptoms	Alemany *et al.* (2011)	N	Ramsay *et al.* (2013)
						N*	de Castro-Catala *et al.* (2016)
	COMT	rs4680	Childhood trauma	Psychotic symptoms	Ramsay *et al.* (2013)	N*	Green *et al.* (2014)
		rs4680	Childhood abuse + cannabis use	Psychotic symptoms	Vinkers *et al.* (2013)	Y	Alemany *et al.* (2014)
		rs4680	Cannabis use	Psychotic symptoms	Caspi *et al.* (2005)	N	Zammit *et al.* (2011)
		rs4680	Stress (army induction)	Psychotic symptoms	Stefanis *et al.* (2007)	Y*	Collip *et al.* (2011)
	FKBP5	rs1360780	Childhood trauma	Psychotic symptoms	Collip *et al.* (2013)	Y	Alemany *et al.* (2016)
Function-informed systematic search	*AKT1*	rs2494732	Cannabis use	Psychotic disorder	van Winkel (2011)	Y	Di Forti *et al.* (2012)
						Y*	Morgan *et al.* (2016)
Genome-wide systematic search	*CTNNA3*	rs7902091	Cytomegalovirus *in utero*	Schizophrenia	Børglum *et al.* (2013)	Y	Avramopoulos *et al.* (2015)

Figure 1: Molecular gene-environment interaction in psychosis

Folie à Deux

In 1877, Lasègue and Falret first introduced the term "folie à deux" and proposed diagnostic criteria. Three criteria in particular condition the onset of a shared delusion between two individuals: the presence of an active element, superior intelligence, the existence of a sufficiently long and intimate cohabitation between the two individuals, and a "closed and isolated" environment [6, 7].

Folie à deux is a psychiatric condition characterized by a delusion shared by two or more people (one individual develops a delusion and a second adopts the same delusion) who maintain a close relationship. The incidence of shared delusional disorder is low, between 1.7% and 2.6% of psychiatric hospitalizations. The disorder is more common among genetically related individuals, particularly identical twins, and those who maintain a prolonged dependent relationship [7].

Four subtypes have been described:

- **Folie Imposée**: An individual with psychosis transfers the delusion to an individual without psychosis.

- **Folie Simultanée:**

Two individuals develop psychosis simultaneously, which fits the circumstances of the delusional ideas emerging in the second clinical case.

- **Folie Communiquée:**

The recipient experiences the delusion after a period of prolonged resistance and continues despite separation from the inducer.

- **Folie Induite:**

An individual with a preexisting psychosis adopts additional delusions under the influence of another psychotic individual [7, 8], which is similar to our first clinical case.

It is noteworthy that the most frequently encountered themes in folie à deux are grandeur and

persecution. The etiology of this disorder remains poorly understood; however, genetic susceptibility and family history are considered important factors, along with female gender, low IQ, histrionic behavior, social isolation, and life events, as evidenced by studies on folie à deux on figure 2.

	Lasègue and Falret [1]	Gralnick [15]	Silveira and Seeman [22]	Arnone et al. [23]
Searched period, number	Period not described, *N* = 7	1879–1942, *N* = 103	1942–1993, *N* = 75	1993–2005, *N* = 64
Definition or way to identify cases	Delusions of psychotic individual transferred to a mentally sound one who has been in close association with the first one. Separation causes recipient to abandon the delusions	Shown in text	*DSM III-R* or *DSM IV*	Database (eg, MEDLINE) search with keywords "induced delusional disorder," "shared delusional disorder," or "*folie à deux*" (there is variability of diagnostic criteria)
Sex	Females more often affected than males, both as inducer and as recipient	Female more often affected than males, both as inducer and as recipient	Females more affected than males in inducer group; females and males equally affected in recipient group	Females and males are equally affected both as inducer and as recipient
Age	Recipient younger than inducer	Recipient younger than inducer	Age difference between inducer and recipient not significant	Age difference between inducer and recipient not significant
Relationships	Limited information due to very small sample size	2 sisters (most common), husband and wife, mother and child, 2 brothers, brother and sister, pairs of friends, entire families	Incidence in married or common law couples equal to that in siblings (sisters more common than brothers)	Married or common law couples, sisters (50% twin)
Dominance and submission	Inducer is more active, older, and more intelligent than recipient	Not found	Not found	Not described
Comorbidity of recipient	Not clearly described (but in some cases, slight mental retardation seems to be suspected)	More than one half of recipients affect "*dementia praecox*, paranoid" (paranoid type schizophrenia)	Comorbidity described in 62.8% of cases; relatively high frequencies of depression, dementia, and mental retardation	Comorbidity described in 28.6% of recipients: schizophrenia (14.3%), depression (7.1%), bipolar disorder (4.8%)
Treatment	Separation effective, especially in recipient	Same therapeutic measures as in psychoses in general, and separation	Effective treatment of recipient requires neuroleptics and separation from inducer	Separation by itself insufficient; effective treatment of secondary requires neuroleptics and separation from primary

Figure 2: Demographic characteristics of some studies on folie à deux [9]

Therapeutic Approach

As with any psychiatric condition, schizophrenia is no exception and remains bio-psycho-social. From a pharmacological perspective, treatment primarily involves antipsychotics [8]. With a range of antipsychotic medications available, the choice of treatment initially depends on various parameters including clinical presentation, background, comorbidities, socio-economic level (as some treatments are excessively costly), and possible side effects. The clinician retains the right to switch from one antipsychotic to another based on therapeutic efficacy, clinical progression, and side effect tolerance.

In cases of familial aggregation, it is also important to have arguments about the familial nature of the treatment response. In schizophrenia, similar to what was reported in the second clinical case where both brothers were stabilized on the same antipsychotic, some studies describe concordance in response to clozapine or olanzapine among monozygotic twins with schizophrenia. Family studies have also shown intra-family concordance for adverse events such as abnormal movements, tardive dyskinesias, or weight gain under antipsychotic treatment.

The importance of genetic factors in schizophrenia, as previously described, is well demonstrated by epidemiological studies comparing concordance within families, among monozygotic and dizygotic twins. These studies have shown that heritability (weight of genetic factors) in schizophrenia can reach approximately 85% [3].

Obviously, in cases of shared delusions among siblings, individual management of each patient is crucial, with an additional goal of understanding the relationship between the co-delusional individuals and the "utility" of their shared delusion, which often attempts to preserve a threatened dyadic fusion relationship. This understanding allows for coherent management, provides the necessary tools to discuss the need for physical separation of co-delusional individuals, which can be crucial in most cases as done for the two cases reported in our study, and guides psychotherapeutic work aimed at achieving psychic separation [10, 11].

CONCLUSION

The clinical, epidemiological, and biomolecular data collected on schizophrenia and its genesis, rooted in both genetic capital and environmental elements, can

help manage the patient holistically with satisfactory results. They can also aid in developing psychotherapeutic strategies for the close entourage, which often constitutes a vulnerable ground for preventing "contagion" of the delusion.

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