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Editorial

Vaccine hesitancy: is it a crazy stuff?

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Vaccine hesitancy is generally defined as a "behavioral pattern ranging from a delay in acceptance to a complete refusal of vaccine, in spite of vaccine availability" [1]. According to the World Health Organization, it is one of the 10 greatest threats to public health [2] .Vaccine acceptance is variably represented in different Countries, with the lowest rates in Kuwait (23.6%), Jordan (28.4%), Italy (53.7), Russia (54.9%), Poland (56.3%), US (56.9%), and France (58.9%) [3]. It is difficult to understand why such a relevant proportion of people is so reluctant to accept vaccination, taking into account the dramatic, individual and social consequences of the Pandemic and the fundamental role of vaccines for overcoming the infection. We acknowledge that the wide resistance toward vaccination cannot be seen per se as irrational or anti-scientific, reflecting sometimes legitimate concerns and/or doubts. However, we cannot ignore the important and very recent data from sociological research reporting that a wave of irrationality seems to be rising in our Country. This is what emerges from a series of beliefs shared by a relevant proportion of Italians such as the Earth is flat (5.8%), the man has never landed on the Moon (10%), the Covid does not exist (5.9%), the vaccines are useless and ineffective (10.9%), without also considering that 39.9% of Italians are embracing conspiracy beliefs [4]. These data has led to wonder if (and to what extent) psychopathological determinants may explain such positions, with particular reference to vaccine hesitancy. The latter has been associated until now to a series of demographic and individual factors, including psychological ones [5], with a substantial gap of knowledge existing as regard to the association with psychopathology. Anyway, in spite of the relative paucity of papers published so far on this issue, findings from the available literature show a not negligible contribution of psychopathology to vaccine hesitancy.

The first source information regarding this issue is represented by studies on non-clinical samples, usually defined as community surveys, which are conducted on samples drawn from general population. Some of these studies show that unspecific anxiety and/or depressive symptoms seem to be unrelated to vaccine acceptation/hesitancy [6], while other studies report that anxiety/depression symptoms are related to both a higher propensity for vaccination [7] and to a higher vaccine hesitancy [8,9], in particular among women [8]. These contradictory findings may be interpreted in light of other psychological factors mediating the behavioural response to emotional arousal, as we will see later. Other studies seem to indicate that vaccine hesitancy or acceptance may be related not so much to the anxiety dimension in general, but rather to specific types of anxiety. Indeed, fears of infection seem to be associated with vaccine acceptation while fears of social/economic consequences of the pandemics are more related to vaccine hesitancy [6]. Phobic anxiety, in terms of blood-injection-injury fears [10], is of particular interest, not only for its frequency (approx 10% of the sample studied) but also for being a potentially surmountable barrier to vaccination. On the whole, data from studies on community samples indicate that the higher the scores at anxiety/depression are, the higher the propensity both for vaccine hesitancy and acceptance will be, depending on the nature of anxiety,

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the concomitant presence of other related affects such as anger or depression and the mediating role of personality traits, generally considered as pathologic. However, in interpreting data emerging form non-clinical samples we should take into account the limitation constituted by the self-assessed evaluation of anxiety/depression according to the dimensional approach generally adopted in these studies, which may not be capable of discriminating between a clinically significant anxiety/depressive state and a unspecific condition of distress.

As mentioned above, studies on non-clinical samples have also highlighted a series of pathologic personality traits which emerge as significant factors associated to vaccine hesitancy/acceptance, such as the tendency to conspiratorial and paranoid beliefs, the impulsivity in thinking style, and the emotional instability [3,11,12]. Conspiratorial beliefs emerge as of particular importance, in light of their correlation with psychopatology. Indeed, the US National Comorbidity Survey-Replication (NCS-R), where conspiracy attitudes were analysed in a community sample of 5,645 people, 1,618 of these (26.7%) endorsed a conspirational belief. Individuals endorsing this belief had lower levels of physical and psychological well-being, higher levels of suicidal ideation, weaker social networks, less secure attachment style, difficult childhood family experiences, and, above all, were more likely to meet criteria for a psychiatric disorder, with the conspiracy belief highly associated (odds ratio = 7.81) with paranoid beliefs [13]. Paranoia has been repeateldy related to cospiracy beliefs [14,15]. Several studies show as conspiratorial ideation may be also induced by a series of reasoning biases influencing individuals' likelihood of adopting epistemically-suspect alternatives to official versions of the facts, thus fostering paranoid thinking styles and distrust of the official sources of information, including scientists [16]. Other authors have shown as bias toward reduced data gathering during reasoning may cause paranoia, increasing the perceived dangerousness of vaccines and thereby reducing willingness to vaccinate [17]. The seemingly contradictory data regarding the role of anxiety in vaccine acceptance/hesitancy has been explained by other authors calling into question the mediating role of personality traits: indeed, fears of death and emotional distress related to the current pandemic has been shown related in a very complex way to paranoia, conspiracy theories, mistrust in science, and consequently to the propensity to accept or not vaccines [12].

The second source of information is constituted by studies on clinical samples. The majority of these studies were conducted in western countries and fundamentally indicate that vaccine hesitancy among people affected by mental disorders is as frequent as in the respective general population or even lower [18-21], although a study found that a specific disorders, namely Substance Use Disorder, is associated with higher vaccine hesitancy [22] and another study found a higher hesitancy respect to influenza vaccination among psychiatric patients [23]. Vaccine hesitancy seems to be related more to individual factors, which are substantially common to those of the population without mental disorders, than to the presence of psychopathology per se. In particular, the largest western study regarding psychiatric samples, conducted in USA, demonstrates that the higher prevalence of vaccine hesitancy which was found among patients with psychiatric disorders, was completely attenuated or disappeared when regression models of data analysis were applied, except than among subjects affected by substance use disorders and tobacco use, suggesting that the higher prevalence observed across conditions may be mostly related to the distribution of some socio-demographic characteristics associated to vaccine hesitancy [22]. Another limit of the above mentioned studies is that all western studies don't include people affected by psychotic disorders. The only exception is constituted by a study from Israel, which considered an in-patient sample of subjects with severe mental illnesses [21]. On the contrary, other studies, mainly conducted in eastern countries, report a higher rate of vaccine hesitancy, generally associated with low rates of vaccination, among psychiatric patients respect to general population [24-26]. Two of these studies, both conducted in China, examined specifically patients with severe mental disorders, including schizophrenia [25,26]. Vaccine hesitancy seems to be substantially independent from diagnosis both in western and eastern studies [21,24,25]. However we should consider that one of these studies [25] included specifically only severe mental illnesses (Major depression, Bipolar Disorders, Schizophrenia). Another large study found a vaccine uptake (i.e. the number of patients vaccinated) significantly lower among inpatients and patients with psychotic disorders; the latter were considered as less likely to take the vaccine due to their more frequent impairment of decisional capacity, whilst a lower vaccine acceptance (i.e. acceptance to be vaccinated) was found associated with having a lower insight, a factor considered as linked to a lower awareness of health-related needs [26].

In summary, data from studies on non-clinical samples indicate that affective psychopathology may have a role in contributing both to vaccine hesitancy and acceptance, partly in conjunction with pathological personality traits such as paranoia, which have seemingly a mediation role. Studies on clinical samples prevalently show that psychopathology linked to common mental disorders does not influence per se the attitudes toward vaccination, with the only exception of Substance Use Disorder and Phobias regarding injections, both associated to a higher vaccine hesitancy. On the contrary, a prevalent although not univocal association between severe mental disorders and vaccine hesitancy emerges from a limited number of studies published up to date. This means that further studies, possibly from different countries and regarding larger clinical samples with both in and outpatients, are needed to confirm this association. Unfortunately, no studies have been published so far regarding clinical samples of subjects affected by Personality Disorders. This represents

another significant gap in our knowledge of the relationship between psychopathology and vaccine hesitancy, considering the important role of pathological personality traits emerging from studies on non-clinical samples.

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