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*Letter to the Editor*

# Polyomaviruses and autism: more than simple association?

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Lintas *et al,* in a recent article published in the *Journal of Neurovirology,* report an association between autism and polyomavirus infection in post-mortem brains (Lintas *et al,* 2010), suggesting a possible role of this virus family in the genesis of autistic spectrum disorders. Because neuropathological studies of autistic brains document that the derangement of neurodevelopmental processes occurs during early pregnancy, the authors suggest that polyomaviruses might play a causative role in autism if transmitted from mother to child during the first months of pregnancy. Although this hypothesis is intriguing, there are open problems that need to be addressed. Firstly, whether autistic patients enrolled in the study acquired polyomavirus infection before, during, or after delivery remains unknown. Although polyomaviruses may be reactivated during pregnancy, transplacental transmission is unlikely (Boldorini *et al,* 2008; Kalvatchev *et al,* 2008; Zheng *et al,* 2004). An exception may be represented by the rare cases of primary infection of the mother, as suggested by experimental animal models (McCance and Mims, 1977). Thus, to comply with the study hypothesis, it should be assumed that vertical transmission in early pregnancy may occur, though rarely, and contribute to the genesis of autism; it should also be assumed that autism would not develop in case of later transmission, which occurs in the large majority of cases polyomavirus infection.

The study was based on autoptic brain samples from cases and controls who died at different ages. The lack of age matching may introduce biases in the results if the risk of being infected varies across different age classes (i.e., infection prevalence may increase with age and the risk of brain tissues invasion may differ in unknown ways).

Combining three different members of the polyomavirus species in the analysis of the association with autistic disorders may be questionable, unless it is assumed that there is no specific effect of one of the three viruses on the genesis of the disorder and a common mechanism is implicated. Actually, when considering JC virus (JCV), which was most frequently identified virus, sequences were detected in six patients with autism and only in three controls (odds ratio: 2.2), but the difference was not statistically significant. Because a significant association may be found only summing all virus sequences detected in cases and in controls, a plausible biological explanation should be provided in order to interpret the association. To this regard, it should be mentioned that JCV is a known neurotropic virus, whereas BK virus has a tropism for kidneys and simian virus 40 (SV40) is a simian virus whose role in human beings is still matter of intense debate (Shah, 2004; White *et al,* 2005). Moreover, multiple infections with viruses such as JCV might be the consequence of immunosuppression or tissue susceptibility rather than being the cause of a specific disorder.

In conclusion, the association between autism and polyomavirus is an interesting hypothesis that should be further tested by evaluating the role of single agents on larger population samples. Follow-up studies of newborns would be useful to evaluate timing of polyomavirus infection and the risk of developing autistic disorders.

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## References

Boldorini R, Veggiani C, Amoruso E, *et al.* (2008). Latent human polyomavirus infection in pregnancy: investigation of possible transplacental transmission. *Pathology* **40:**72–77.

Kalvatchev Z, Slavov S, Shtereva M, Savova S (2008). Reactivation of *Polyomavirus hominis* 1 (BKV) during pregnancy and the risk of mother-to-child transmission. *J Clin Virol* **43:**328–329.

Lintas C, Altieri L, Lombardi F, Sacco R, Persico AM (2010). Association of autism with polyomavirus infection in postmortem brain. *J NeuroVirol* **16:**141–149.

McCance DJ, Mims CA (1977). Transplacental transmission of polyomavirus in mice. *Infect Immune* **18:**196–202.

Shah KV (2004). Simian virus 40 and human disease. *J Infect Dis* **190:**2061–2064.

White MK, Gordon J, Reiss K, *et al.* (2005). Human polyomaviruses and brain tumors. *Brain Res Rev* **50:**69–85.

Zheng H-Y, Kitamura T, Takasaka T, Chen Q, Yogo Y (2004). Unambiguous identification of JC polyomavirus strains transmitted from parents to children. *Arch Virol* **149:**261–273.

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