

Human Neuropathies: Clues from Dolphins

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COLUMN ARTICLE

Stranded cetaceans, if adequately investigated, provide a unique opportunity for getting proper insight into their health as well as into that of their conspecifics and heterospecifics living in the open sea, both at an individual and at a population level, thereby allowing to obtain valuable and precious knowledge also on their increasingly threatened conservation status.

After almost 30 years spent investigating naturally occurring disease conditions in stranded cetaceans, I can affirm that several pathologies affecting them, of either infectious or non-infectious nature, parallel if not even “mirror” their human disease counterparts [1].

A remarkable example in this direction is represented by *Cetacean Morbillivirus* (CeMV) infections, which during the last three decades have been responsible for mass die-offs along the Eastern USA coast as well as in the Western Mediterranean Sea and in the Black Sea, with bottlenose dolphins (*Tursiops truncatus*) and striped dolphins (*Stenella coeruleoalba*) being dramatically affected by the aforementioned outbreaks along the Atlantic North American coastline and in the Mediterranean basin, respectively [2].

The lesions' spectrum exhibited by CeMV-infected dolphins mirrors that seen in *Measles Virus* (MeV)-infected humans and in other *Morbillivirus*-infected mammals, with affected cetaceans showing typical microscopic changes

consistent with their lymphotropism, epitheliotropism and neurotropism [3].

With special emphasis on its neurotropism, *Dolphin Morbillivirus* (DMV), the CeMV strain responsible for no less than 4 unusual mortality events among Mediterranean striped dolphins throughout the last 30 years, has been also the culprit (still in striped dolphins) of a peculiar neurologic disease, termed “*Brain-Only Form of DMV infection*” (BOFDI), which shares neuropathologic similarities with its human and canine counterparts, represented by “*Subacute Sclerosing Panencephalitis*” (SSPE) in (a very small subset of) MeV-infected patients and “*Old Dog Encephalitis*” (ODE) in *Canine Distemper Virus*-infected dogs [4]. In this respect, a recent study by our group has shown that brain astrocytes are marginally affected in BOFDI-affected striped dolphins, differently from what happens in ODE-affected canines [5]. We are currently investigating if the DMV isolates obtained from the cerebral parenchyma of BOFDI-affected striped dolphins bear “molecular genetic signatures” similar to/consistent with those reported in MeV strains recovered from SSPE-affected humans. Should this be the case, then BOFDI-affected striped dolphins could be regarded as “natural disease models” for the study of their SSPE human disease “analogue”.

Another relevant issue, still belonging to the challenging and intriguing field of “Comparative Neuropathology”, relates to Alzheimer's disease (AD), the most commonly occurring form of human dementia worldwide. As a matter of fact, the research team led by Professor Danielle Gunn-

Moore in Edinburgh has recently described the simultaneous presence, within the brain tissue from bottlenose and striped dolphins stranded along the Spanish coastline, of “amyloid-beta” aggregates and “tau protein” neurofibrillary tangles, the two pathological AD “hallmarks” [6]. Although these findings are of remarkable interest - provided that no natural nor experimental animal models capable of exhaustively “recapitulating” all the neuropathological AD features seem to exist-, we don’t know the precise biological, neuropathological and neuropathogenetic meaning of the aforementioned findings in dolphins’ brains. In other words, we don’t know whether dolphins may get either AD or any AD-like conditions.

The two examples reported above, hopefully “illuminating”, should be viewed as a sort of “window” on the far more numerous disease conditions, either neurologic or not in nature, for which dolphins and, more in general, cetaceans may serve as potentially useful “comparative pathology models” for the study of the human disease counterparts [1], far beyond the “iconic” essence of these marvellous and increasingly threatened inhabitants of the oceans and seas of our planet!

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