Science, medicine and Golgi

To the editor — In 1993 on the 150th anniversary of Camillo Golgi's birth a historiographic research study highlighted his contribution to modern biomedical sciences. An unrecognized aspect of Golgi's life was his interest in neuropsychiatry. From 1866 to 1868 he attended the Clinic for Nervous and Mental Disease in Pavia directed by Cesare Lombroso, the founder of modern criminology. During this period Golgi was involved in research on the aetiology of psychiatric ailments. He criticized heavily the nosological system proposed by his academic mentor as "lacking an experimental basis"[1]. This discontent pushed him to search for a more rational method for studying brain functions and diseases. He embraced the scientific thought of his age and started his seminal work on the fine structures of the central nervous system (CNS) for which he was awarded the Nobel Prize in 1906.

In spite of his anatomical-based approach to the CNS, he maintained a curiosity for the phenomenology of functional and organic mental disorders. Occasionally he was able to relate clinical observations to neuropathological findings. An outstanding example of this is the case of B.A., an active, upper-class, 48-year-old woman ("Nobildonna") with a slowly changing personality and reducing cognitive and social skills: "B. A. became childish and capricious, irreverent and foul-mouthed, unable to sustain attention in the execution of even simple tasks, incapable of abstract thinking, and devoid of concern and interest"[2]. Golgi attended this patient for over three years providing a paradigmatic description of the frontal lobe syndrome, only one year after the famous case of Phineus Gage, described by Harlow[3]. B.A. died falling from a the balcony in 1869 and the autopsy, performed by Golgi himself, revealed the presence of a "an orange-sized fungoid mass arising from the arachnoid layer of the meninges and severely compressing, without invading the left frontal lobe"[2]. The histology sample, an original specimen of which was found in 1993 in a cabinet at the historical laboratories of the University of Pavia, revealed a psammomatous meningioma. Golgi observed that the characteristic formation of whorls in which the meningial cells are closely wrapped around one another precedes the formation of psammoma bodies, which were first described in this case. They consisted of concentric laminae of calcium salts laid down in the degenerating cells. Golgi's original drawing of the meningioma recognized the main histological findings: the external capsules (a); connective trabeculae (b); tunour alveoli occupied by psammoma bodies (c); and arteriosus vessel penetrating the tumour following the traebecular system (d).

Golgi's original observations represented the first contribution towards understanding the pathphysiological development of psammoma bodies and to the histological typing of brain meningiomas. Camillo Golgi left us an early example of the integration of disciplines.

Acknowledgements

We thank the C. Golgi Foundation, Brescia, Italy for financial support and L. Santamaria and V. Vanini for the original specimens preserved at the C. Golgi Istituto di Patologia Generale, University of Pavia School of Medicine, Pavia, Italy.

1. Golgi, C. Sull'eziologia delle alienazioni mentali. Annali Universali di Medicina, 1869. Reported in: C. Golgi Opera Omnia, Vol. III, Chapter 31. Milan: Hoepli, 1903: 763-785.
2. Golgi, C. Sulla struttura e sullo sviluppo degli psammomi. Rendiconti Istituto Lombardo,1869. Reported in: C. Golgi Opera Omnia, Vol. III, Chapter 32. Milan: Hoepli, 1903: 786-809.
3. Harlow, J.M. Recovery from the passage of an iron bar through the head. Mass Med Soc Pub 2 327-346 (1868).

PAOLO LIBERINI
PIERFRANCO SPANO
Division of Pharmacology and Experimental Therapeutics
European School of Molecular Medicine
University of Brescia
Via Valsabbina 19, Brescia, Italy

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

Golgi's original drawing of the meningioma. From C. Golgi Opera Omnia, Vol III, Table 43; preserved in Medical Library, Spedali Civili of Brescia, Italy.

Apoptosis and HIV disease

To the editor — In a recent *in situ* study of lymph nodes from HIV-infected children[1], Finkel *et al.* observed that DNA fragmentation is rarely detected in productively infected cells, whereas HIV is rarely detected in apoptotic cells. They conclude that apoptosis occurs predominantly in bystander (uninfected) cells rather than in the productively infected cells themselves (implying a resistance of infected cells to apoptosis). We think that several points need to be clarified before their conclusion can be justified.

Two recent studies[2,3] on HIV-infected patients treated with three antiretroviral agents provided estimates of a minimum $CD4^+$ T-cell turnover rate of $\sim 2 \times 10^9$ cells per day and a minimum HIV turnover rate of $\sim 10^9$ virions per day. Given that a single $CD4^+$ T blast cell produces around 10^4 virions before dying (deduced from replication kinetics of 66 primary isolates[4]), a daily turnover of 10^9 virions corresponds to a daily turnover of 10^5 productively infected $CD4^+$ T cells. This suggests that approximately 2×10^9 (-10^5) $CD4^+$ T cells should be destroyed every day by other 'bystander' mechanisms rather than by viro-cytopathy.

Since Finkel *et al.* have observed that the number of predominantly uninfected cells undergoing apoptosis is positively correlated with the number of a productively infected cells[1], it is possible that thousands of viral antigens released by produtively infected cell bind to thousands of uninfected $CD4^+$ T cells which then undergo apoptosis via as-yet-undefined 'bystander' mechanisms. This is in keeping with our recent findings from 44 HIV-infected individuals treated with prednisolone (a potent anti-apoptotic agent[5]), demonstrating a rapid $CD4^+$ T cell increase without significant modification of viral production[6], which supports also a bystander mechanism.

On the other hand, the data from Finkel *et al.* do not necessarily imply 'a resistance of infected cells to apoptosis'. Although HIV RNA is constantly detectable in productively infected cells, DNA fragmentation in productively infected $CD4^+$ T cells cannot be detected until 48 hours postinfection (the time required for optimal membrane expression of viral envelope glycoproteins). Given that apoptotic cells are removed within 0.5–2 hours after DNA