These research projects, undertaken in partial fulfillment of the requirements for the MD degree at Sackler Faculty of Medicine, Tel Aviv University in 2009–2010, were considered the most outstanding of the graduating class

Representational neglect: comparison between the visual and tactile modalities

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Background: Unilateral spatial neglect (USN), a frequent sequel of stroke affecting the right cerebral hemisphere, is a compound neurological syndrome which is characterized by decreased efficiency in the processing of information arriving from the contralesional hemispace (most frequently the left hemispace). The Representational theory of Neglect (RN), introduced by Bisiach and Luzzatti in 1978 [13], claims that the basic fault in USN is a failure to create an exact representation of the outer world; thus, not only do patients fail to respond to left-sided stimuli but they also fail to recover left-sided details of spatial memory – e.g., a well-known place, such as the town square (the "piazza effect").

Objectives: To compare the characteristics of USN for spatially distributed perceived visual information and spatially reconstructed visual information presented serially in the midsagittal plane, and to compare the latter with spatially reconstructed tactile information.

Methods: Eleven right-hemisphere damaged stroke patients with left-side neglect and 8 healthy controls were presented with pairs of two-dimensional geometric shapes for same/different judgment in three testing conditions: a) 'visual static' (VS) – each object exposed in its entirety; b) 'visual dynamic' (VD) – objects moved horizontally (leftward/rightward) behind a central narrow slit exposing only part of the object at one time; and c) 'tactile dynamic' (TD) – a novel method where the blindfolded subject palpates the upper contour of objects similar in appearance to the visual objects, in both rightward and leftward directions, with the index finger of the healthy right hand. In tasks b and c the spatial representation has to be reconstructed mentally from partial, non-lateralized, sensory information. In order to quantify the spatial disturbance, we used a calculated laterality quotient to evaluate the difference between the correct performance on each side relative to the average level of performance ([R-L]*100/[R+L]).

Results: All patients demonstrated left-side disadvantage in at least two of the three tasks, six patients in all three tasks. The average calculated laterality quotients for correct performance was 54.4 for the VS task, and 14.4 and 20.1 for VD and TD tasks, respectively. Detection of left-side differences in VD and TD tasks improved when the left side of the object was presented last (recency effect).

Conclusions: Our novel method for the assessment of representational neglect is able to demonstrate clear contralesional disadvantage in both visual and tactile modalities. Patients who showed representational disturbance in one modality usually showed that also in the other modality, but dissociations occurred. Similar performance rates for the VS and TD tasks (for both groups) indicate the reliability of our novel method. The temporal order of the mental reconstruction process is important; the recency effect, though it does not withdraw from the presence of RN, which is prominent.

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Characterizing microRNA signature as a prognostic factor in diffuse large B cell lymphoma

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Background: Diffuse large B cell lymphoma (DLBCL) is a hematologic malignancy characterized by an acute manifestation with a rapid deterioration of the patient's condition if no treatment is given during the early stages of the disease. MicroRNA molecules are known to be involved in the development of different malignancies. Specific microRNA signatures are known to be related to the prognosis of patients with some of these malignancies

Objectives: To determine whether microRNA signature profiling can distinguish between DLBCL patients with a good prognosis and those with a bad prognosis

Methods: Two groups were defined: good prognosis group (complete remission without relapse of the disease in 5 years) – 40 patients, and bad prognosis group (lack of complete remission or relapse of the disease within 9 months of diagnosis) – 43 patients. We extracted microRNA from the biopsies obtained during diagnosis and compared the microRNA profiles of the two groups by using Rosetta Genomics microRNA chips.

Results: Our findings clearly show that combining hsa-miR-342-3p with hsa-miR-17 produced the best sensitivity (79%) and

specificity (73%) to predict the patient's prognosis, regardless of the disease stage or other clinical parameters.

Conclusions: It may be possible to predict the prognosis of patients with DLBCL, and perhaps change the treatment of patients according to the genetics of the tumor.

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Erythropoietin and cyclophosphamide combination treatment additively enhances immunoglobulin production in mice

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Background: Erythropoietin (EPO) is an important component in the treatment of cancer-related anemia, and it is usually combined with chemotherapy. Cyclophosphamide (CP) is a known cytotoxic alkylating agent used in cancer chemotherapy. The antineoplastic activity of CP at low doses is attributed to enhancement of cellular and humoral immunity. We have previously shown that EPO displays anti-neoplastic activity and that EPO treatment is associated with enhancement of both the humoral and cellular immune responses.

Objectives: To explore the humoral immunomodulatory effects of combining EPO and low dose CP, thus simulating clinical conditions.

Methods: We compared anti-dinitrophenyl (DNP) immunoglobulin (Ig) serum levels in DNP- keyhole limpet hemocyanin (KLH) injected C57BL mice that were treated with either EPO or CP, separately, or with EPO + CP combination. Diluent injection served as a control for CP and EPO treatment. The levels of IgG1, IgG2a and total Ig were measured using enzyme-linked immunosorbent assay in sera samples taken before, and 2 weeks after antigen injection.

Results: CP treatment alone resulted in increased anti-DNP IgG1 serum levels, 2 weeks following antigen administration. In contrast, EPO treatment alone significantly enhanced anti-DNP IgG2a levels. The combined treatment of EPO and CP increased both IgG1 and IgG2a, maintaining the effects of each treatment alone. While neither CP nor EPO alone significantly increased anti-DNP total Ig levels, the combined treatment additively led to their elevation.

Conclusions: Our findings emphasize a potential role for EPO as an immunomodulator, particularly when administered as a part of a combined treatment with CP.

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