

## **AN OBJECTIVE TEST FOR THE EVALUATION OF SEXUAL AROUSAL AND INTEREST**

Despite advances in the diagnosis and treatment of male and female sexual dysfunction, there is still no objective test to quantify the extent of sexual arousal and interest. Interest is a complex cognitive function. A common neurophysiological approach for the assessment of cognitive functions is based on event related potentials analysis, especially on the evoked component called P300. The P300 wave is a centroparietal positive deflection in human event related potentials which occurs about 300 ms after stimulus presentation and is known as the cognitive wave. Vardi et al (page 2736) from Haifa, Israel studied the potential application of event related potentials as a tool for objective assessment of psychological sexual arousal and sexual interest in normal subjects. A total of 30 healthy subjects were exposed to several blocks of auditory stimuli administered using an oddball paradigm. Baseline auditory P300 amplitudes were obtained, then the auditory stimuli were delivered while viewing visual clips with 3 types of content—sport, scenery and sex. Auditory P300 amplitude decreased during the viewing of all clips. Viewing the sexual content clips caused a maximal reduction of P300 amplitudes. In addition, a high correlation was found between the amplitude reduction and the scores of the sexual arousal questionnaire to the viewed clips. In addition, P300 amplitude reduction was significantly related to the sexual interest score. The change in auditory P300 amplitude during exposure to visual stimuli with sexual context seems to be an objective measure of subject sexual interest. This method might be applied for the assessment of therapeutic intervention and as a diagnostic tool for assessment of disorders involving impaired libido.

## **THE PIG STRIATED URETHRAL SPHINCTER MAY BE USEFUL TO EVALUATE SPHINCTER INSUFFICIENCY TREATMENTS**

New treatments for intrinsic sphincter insufficiency are currently under investigation. However, animal models for the study of resting urethral tone generated by the striated urethral sphincter are still lacking. Zini et al (page 2729) from Créteil, France, investigated the participation of the striated urethral sphincters in resting urethral tone to develop new tools for the evaluation of therapies for sphincter insufficiency. The participation of the pig striated urethral sphincter was assessed by analysis of the urethral pressure profilometry (maximum urethral closing pressure, functional urethral length

and area under the curve) before and after damage of the striated urethral sphincter. Serial urethral cross sections were immunostained for slow/fast myosin and digitalized for 3-dimensional reconstruction to determine the striated urethral sphincter volume. Endoscopic injury decreased maximum urethral closure pressure and functional urethral length. The striated urethral sphincter of the female pig displays the morphological and functional features of a tonic muscle. Methods of measurement of resting urethral tone generated by the striated urethral sphincter represent original tools for the evaluation of therapies for intrinsic sphincter insufficiency.

## **IMMUNOTHERAPEUTIC EFFECT OF CONCHOLEPAS HEMOCYANIN IN BLADDER CANCER**

Various nonspecific compounds such as bacillus Calmette-Guerin enhance the immune response and act as effective antitumor agents. In patients with bladder transitional cell carcinoma, subcutaneous stimulation with keyhole limpet hemocyanin significantly reduces the frequency of tumor recurrence. Although the biomedical interest in keyhole limpet hemocyanin goes back more than 30 years, it is not known whether hemocyanins from other mollusks might be equally or more efficient as an immunomodulatory agent.

The antitumor properties of the hemocyanin obtained from the Chilean gastropod *Concholepas concholepas* were investigated by Moltedo et al (page 2690), from Santiago, Chile. They determined if *Concholepas concholepas*, in spite of the structural differences from keyhole limpet hemocyanin has an immunotherapeutic value as an antitumor agent. Mice were primed with *Concholepas concholepas* before the subcutaneous implantation of MBT-2 cells. Treatment consisted of a subcutaneous dose of *Concholepas concholepas* at various intervals after implantation. Keyhole limpet hemocyanin or phosphate buffered saline was used as positive and negative control. Mice treated with *Concholepas concholepas* showed a significant antitumor effect as demonstrated by decreased tumor growth and incidence, prolonged survival, and lack of toxic effects. These results were similar to those obtained with keyhole limpet hemocyanin. Analyses of sera from treated mice showed an increase of interferon- $\gamma$  and low interleukin-4 levels that correlated with antibody isotypes, confirming that hemocyanins induce a Th1 cytokine profile. These results are the first to show an antitumor effect of a hemocyanin other than keyhole limpet hemocyanin. *Concholepas concholepas* may be an alternative candidate for providing safe and effective immunotherapy for human superficial bladder cancer.

## **RADIATION INDUCED LATE BLADDER DAMAGE TO THE BARRIER FUNCTION OF SMALL BLOOD VESSELS**

In clinical radiotherapy inclusion of a substantial amount of normal tissue in the treatment volume is inevitable, with a potential consequence of side effects. The early side effect phase usually starts during treatment and resolves within a few weeks after the end of radiotherapy. After a dose-dependent, symptom-free latent time of several months to many years, a progressive and irreversible late response occurs. The symptoms in both response phases are alike, comprising dysuria, nocturia, urgency and increased micturition frequency. The symptoms in both phases are similarly based on a decrease in bladder storage capacity. Early reactions are mainly based on inflammatory changes. The late phase is dominated by irreversible changes in collagen metabolism. Morphologically, irradiation results in pronounced fibrosis that is mainly seen around blood vessels, thus indirectly indicating contribution of the vasculature. However, the precise role of blood vessels in the pathogenesis of radiation induced late damage to the bladder currently remains unclear.

Jaal et al (page 2696) from Dresden, Germany identified the changes in vascular barrier function in relation to collagen deposition during the late radiation response of mouse bladder. Albumin leakage was assessed as a marker of blood vessel barrier disruption. Mice were irradiated with a single dose of 20 Gy and sacrificed up to 360 days later. The fractional area of subepithelial tissue with extravascular albumin signal was defined. Moreover, the amount of collagen was determined after Masson's trichrome staining. Irradiation of the bladder resulted in late damage to the barrier function of small subepithelial blood vessels, causing pronounced albumin leakage at the early steps of the chronic radiation reaction, clearly preceding excessive collagen deposition in the bladder wall. These data suggest a vascular compo-

nent in the development of late radiation induced changes in the bladder.

## **BLADDER OUTLET OBSTRUCTION ABOLISHES PROTEIN KINASE C CONTRACTION**

Despite the acute onset partial bladder outlet obstruction in the rabbit induces detrusor remodeling similar to that seen in men with benign prostatic hyperplasia in terms of the impact on structural and functional alternations in the smooth muscle. Stanton et al (page 2716) from Philadelphia, Pennsylvania determined whether partial bladder outlet obstruction induced remodeling alters the protein kinase C signaling pathway that leads to contraction. Smooth muscle samples from control animals and those subjected to 2 weeks of partial bladder outlet obstruction were analyzed. Smooth muscle strips from animals subjected to partial bladder outlet obstruction exhibited little to no increase in stress in response to phorbol dibutyrate and no increase in myosin light chain phosphorylation levels. Muscle strips from control animals produced a robust contraction with concomitant increases in myosin light chain phosphorylation. Inhibition of protein kinase C by bisindolylmaleimide-1 significantly depressed carbachol induced contractions of muscle strips from control animals but had no effect on carbachol induced contractions of muscle strips from outlet obstructed animals. Phorbol dibutyrate increased phospho-adducin levels in muscle strips from both animal sources, suggesting that protein kinase C could be activated. The authors propose that partial bladder outlet obstruction does not alter activation of protein kinase C but abolishes or uncouples the pathway(s) downstream of protein kinase C leading to contraction. Loss of this pathway may contribute to the loss of normal voiding behaviors and the resultant decompensated state.

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