

Cuban Research in Current International Journals

The following selection—alphabetical by title—reflects Cuban publishing in international medical and population health journals over the last quarter on an array of topics.

A method for non-experts in assessing exposure to risk factors for work-related musculoskeletal disorders-ERIN.

Rodríguez Y, Viña S, Montero R. Ind Health. 2013 Dec 1;51(6):622–6.

A practical method for non-experts in assessing exposure to risk factors for work-related musculoskeletal disorders (WMSDs) is presented. Evaluación del Riesgo Individual (Individual Risk Assessment) (ERIN) is based on available ergonomic tools, epidemiological evidence and the joint IEA-WHO project for developing WMSDs risk management in developing countries. ERIN focuses primarily on the interaction of some physical workplace factors but also includes the workers' assessment. A scoring system has been proposed to indicate the level of intervention required to reduce the risk of injury. A worksheet has also been designed for increasing the usability of the method. Preliminary tests show that it is easy and quick to use, but further work is needed to establish its reliability and validity. The use of ERIN can contribute to the prevention of WMSDs in Cuba and other developing countries.

Active post-marketing surveillance of the intralesional administration of human recombinant epidermal growth factor in diabetic foot ulcers.

Yera-Alos IB, Alonso- Carbonell L, Valenzuela-Silva CM, Tuero-Iglesias AD, Moreira-Martínez M, Marrero-Rodríguez I, et al. BMC Pharmacol Toxicol. 2013 Sep 3;14(1):44.

Background After several exploratory and confirmatory clinical trials, the intralesional administration of human recombinant epidermal growth factor (hrEGF) has been approved for the treatment of advanced diabetic foot ulcers (DFU). The aim of this work was to evaluate the effectiveness and safety of this procedure in medical practice. **Methods** A prospective, post-marketing active pharmacosurveillance was conducted in 41 hospitals and 19 primary care polyclinics. Patients with DFU received hrEGF, 25 or 75 mug, intralesionally 3 times per week until complete granulation of the ulcer or 8 weeks maximum, adjuvant to standard wound care. Outcomes measured were complete granulation, amputations, and adverse events (AE) during treatment; complete lesion re-epithelialization and relapses in follow-up (median: 1.2; maximum 4.2 years). **Results** The study included 1788 patients with 1835 DFU (81% Wagner's grades 3 or 4; 43% ischemic) treated from May 2007 to April 2010. Complete granulation was observed in 76% of the ulcers in 5 weeks (median). Ulcer non-ischemic etiology (OR: 3.6; 95% CI: 2.8-4.7) and age (1.02; 1.01-1.03, for each younger year) were the main variables with influence on this outcome. During treatment, 220 (12%) amputations (171 major) were required in 214 patients, mostly in ischemic or Wagner's grade 3 to 5 ulcers. Re-epithelialization was documented in 61% of the 1659 followed-up cases; 5% relapsed per year. AE (4171) were reported in 47% of the subjects. Mild or moderate local pain and burning sensation, shivering and chills, were 87% of the events. Serious events, not related to treatment, occurred in 1.7% of the patients. **Conclusions** The favorable benefit/risk balance, confirms the beneficial clinical profile of intralesional hrEGF in the treatment of DFUs.

Challenges and Opportunities for Cancer Vaccines in the Current NSCLC Clinical Scenario.

Rodríguez PC, Sanchez B. Curr Top Med Chem. 2013;13(20):2551–61.

This review is aimed to focus on NSCLC as an emerging and promising model for active immunotherapy and the challenges for its inclusion in the current clinical scenario. Cancer vaccines for NSCLC have been focused as a therapeutic option based on the identification of a tumor hallmark and the active immunization with the related molecules that triggers cellular and/or humoral responses that consequently destroy or delay the rate of malignant progression. This therapeutic intervention in an established disease state has been aimed to impact into prolonging patient's survival with ethically accepted quality of life. Understanding of relationship between structure and function in cancer vaccines is essential to interpret their opportunities to impact into prolonging survival and increasing quality of life in cancer patients. It is widely accepted that the failure of the cancer vaccines in the NSCLC scenario is related with its introduction in the advanced disease stages and poor performance status of the patients due to the combination of the tumor induced immunosuppression with the immune senescence. Despite first, second and emerging third line of onco-specific treatments the life expectancy for NSCLC patients diagnosed at advanced stages is surrounding the 12 months of median survival and in facts the today real circumstances are extremely demanding for the success inclusion of cancer vaccines as therapeutic choice in the clinical scenario. The kinetics of the active immunizations encompasses a sequential cascade of clinical endpoints: starting by the activation of the immune system, followed by the antitumor response and finalizing with the consequential impact on patients' overall survival. Today this

cascade of clinical endpoints is the backbone for active immunization assessment and moreover the concept of cancer vaccines, applied in the NSCLC setting, is just evolving as a complex therapeutic strategy, in which the opportunities for cancer vaccines start from the selection of the target cancer hallmark, followed by the vaccine formulation and its platforms for immune potentiation, also cover the successful insertion in the standard of care, the chronic administration beyond progression disease, the personalization based on predictors of response and the potential combination with other targeted therapies.

Development of and institutional curriculum in ethics and public health.

Cañete R, Prior A, Brito K, Guilhem D, Novaes MR, Goodman KW. *Acta Bioethica*. 2013;19(2):251–7.

Bioethics teaching has traditionally focused on classroom activities, but there is a widely recognized need for professional development opportunities for people with active scientific, clinical or administrative duties. Moreover, there is a shortage of evaluations of ethics programs and curricula. In this cross-sectional study, we surveyed hygiene, epidemiology and microbiology professionals who attended 7 ethics courses in Matanzas province, Cuba. The curriculum consisted of 2 main themes: research ethics and public health ethics. The survey comprised pre- and post-test assessments and in-depth interviews of all participants 3 months after the end of each course. Most attendees (i) appeared to demonstrate increased of knowledge in research and public health ethics, including international guidelines, (ii) gave positive assessments of the courses and (iii) affirmed the importance and pertinence of such training activities. This small study is suggestive of the kinds of professional development opportunities available in limited resource settings.

Epicardial Fat Thickness Correlates With Carotid Intima-Media Thickness, Arterial Stiffness, and Cardiac Geometry in Children and Adolescents.

Cabrera JO, Iacobellis G, Castillo JA, Valiente J, Gendarilla JC, Marín SM. *Pediatr Cardiol*. 2013 Oct 2. [Epub ahead of print]

To determine the association between epicardial fat thickness and carotid arterial stiffness, carotid intima-media thickness (CIMT), left atrial (LA) volume, and left-ventricular (LV) geometry parameters in obese children and adolescents compared with controls. A case-control study was performed in 96 children and adolescents (obese $n = 66$, controls $n = 30$) age 9–16 years old (38 female and 58 male, mean age 11.7 ± 2.8 years) undergoing transthoracic echocardiography and carotid artery ultrasound. Clinical, anthropometric, and biochemical determinations were also recorded. Epicardial fat thickness (2.76 ± 1.2 vs. 1.36 ± 0.7 mm, $p < 0.001$), LA volume (35.7 ± 13.2 vs. 28.9 ± 9.8 mL, $p = 0.008$), LV mass (118.3 ± 38.6 vs. 96.4 ± 35.4 mL, $p = 0.008$), CIMT (0.48 ± 0.07 vs. 0.44 ± 0.05 mm, $p = 0.019$), and local pulse wave velocity (LPWV; 3.7 ± 0.5 vs. 3.2 ± 0.4 m/seg, $p = 0.007$) were significantly increased in obese children and adolescents compared with controls. Epicardial fat showed a significant and positive correlation with LA volume, LV mass, and LPWV as well as a significant and independent association with increased CIMT (odds ratio (OR) = $3.19 [1.88–7.99]$, $p = 0.005$) in the study population. Epicardial fat thickness is linked to obesity, carotid subclinical atherosclerosis, and cardiac geometry parameters and might be a useful tool for the cardiovascular risk stratification in children and adolescents.

Feasibility of the superselective test with propofol for determining eloquent brain regions in the endovascular treatment of arteriovenous malformations.

González JA, Llibre JC, Prince JA, Vázquez F, Rodríguez RM, Ugarte JC, et al. *Interv Neuroradiol*. 2013 Sep;19(3):320–8.

The superselective test for determining eloquent brain areas, carried out prior to the embolization treatment for arteriovenous malformations (AVMs), is a tool contributing to increase the safety of endovascular procedures. Taking into account amobarbital unavailability, it was decided to carry out the present study to demonstrate the efficacy and safety of propofol as an alternative to amobarbital to perform this test. A group of 58 patients were treated in 91 embolization sessions for brain AVMs using endovascular surgery between February 2006 and February 2011. The superselective test was performed prior to embolization with Histoacryl, using the intra-arterial administration of 20 mg propofol through a microcatheter positioned near the AVM nidus. Ten (7.8%) of the 128 superselective tests were positive. Neurological deficits appeared immediately after propofol administration, lasted for one minute and disappeared after five minutes. Only one of the patients showing a negative test result developed neurological deficits after embolization, for 99.2% negative predictive value. Despite their positive test results, six patients were embolized and five developed post-embolization neurological deficits, for 83.3% positive predictive value. The test showed 83.3% sensitivity and 99.2% specificity. The use of propofol to perform the superselective test during brain AVM embolization is a safe and

effective alternative to amobarbital, and may predict the occurrence of post-embolization ischemic complications.

Molecular Epidemiology of Human Papillomavirus Infections in Cervical Samples from Cuban Women Older than 30 years.

Soto Y, Torres G, Kourí V, Limia CM, Goicoe A, Capó V, et al. G Low Genit Tract Dis. 2013 Nov 21. [Epub ahead of print]

Objective This study aimed to provide information about the molecular epidemiology of human papillomavirus (HPV) in a group of Cuban women. **Materials and Methods** DNA from cervical samples was analyzed using a quantitative real-time polymerase chain reaction (PCR), which detects 6 of the clinically most relevant high-risk HPV types. Furthermore, end point PCR and sequencing were performed. Three hundred twenty-two women (211 with positive and 111 with negative cytologic results) aged between 30 and 69 years were enrolled. Risk factors associated with HPV infections and premalignant lesions were also investigated. **Results** HPV DNA was detected in 76.1% (245/322) of the studied population, and 34 different genotypes were found. There was an association between HPV infection and low educational level, history of oral contraceptives, menopausal stage, as well as cigarette and/or alcohol consumption. Besides, in a multivariate analysis, previous positive Pap test result and positive colposcopy finding were both predictor variables for HPV infections and for premalignant lesions. Human papillomavirus infection was found in 94.3% of women (199/211) with positive cytologic result and in 41.4% (46/111) of those with negative results, being more likely that the first group was infected with any HPV (odds ratio = 23.43; 95% CI = 11.70-46.92; $p = .000$). The most common genotypes were HPV types 16, 18, 31, 58, 33, and 45. All the cases with HPV positive findings had at least 1 high-risk HPV genotype. **Conclusions** This is the first report of the molecular epidemiology of HPV in Cuban women, based on results from a DNA sequence and quantitative PCR. Most individuals were infected with high-risk HPV types. These findings support the inclusion of HPV vaccine in Cuba.

Potent Antihypertensive Action of Dietary Flaxseed in Hypertensive Patients.

Rodríguez D, Weighell W, Edel AL, Lavallee R, Dibrov E, Pinneker R, et al. Hypertension. 2013 Dec;62(6):1081-9.

Flaxseed contains ω -3 fatty acids, lignans, and fiber that together may provide benefits to patients with cardiovascular disease. Animal work identified that patients with peripheral artery disease may particularly benefit from dietary supplementation with flaxseed. Hypertension is commonly associated with peripheral artery disease. The purpose of the study was to examine the effects of daily ingestion of flaxseed on systolic (SBP) and diastolic blood pressure (DBP) in peripheral artery disease patients. In this prospective, double-blinded, placebo-controlled, randomized trial, patients (110 in total) ingested a variety of foods that contained 30 g of milled flaxseed or placebo each day over 6 months. Plasma levels of the ω -3 fatty acid α -linolenic acid and enterolignans increased 2- to 50-fold in the flaxseed-fed group but did not increase significantly in the placebo group. Patient body weights were not significantly different between the 2 groups at any time. SBP was \approx 10 mm Hg lower, and DBP was \approx 7 mm Hg lower in the flaxseed group compared with placebo after 6 months. Patients who entered the trial with a SBP \geq 140 mm Hg at baseline obtained a significant reduction of 15 mm Hg in SBP and 7 mm Hg in DBP from flaxseed ingestion. The antihypertensive effect was achieved selectively in hypertensive patients. Circulating α -linolenic acid levels correlated with SBP and DBP, and lignan levels correlated with changes in DBP. In summary, flaxseed induced one of the most potent antihypertensive effects achieved by a dietary intervention.

Prevalence and Genotype Distribution of *Pneumocystis jirovecii* in Cuban Infants and Toddlers with Whooping Cough.

Monroy EX, Armas YD, Illnait MT, Toraño G, Díaz R, Vega D, et al. J Clin Microbiol. 2013 Oct 16. [Epub ahead of print]

This study describes the prevalence and genotype distribution of *Pneumocystis jirovecii* obtained from nasopharyngeal (NP) swabs of immunocompetent Cuban infants and toddlers with whooping cough (WC). One hundred sixty three NP swabs from 163 Cuban young children with WC and admitted to the respiratory care units at two pediatric centers, were studied. The prevalence was determined by a quantitative PCR (qPCR) assay targeting the *P. jirovecii* mitochondrial large subunit (mtLSU) rRNA gene. Genotypes were identified by direct sequencing of mtLSU rDNA and restriction fragment-length polymorphism analysis of the dihydropteroate synthase (DHPS) gene amplicons. qPCR detected *P. jirovecii* DNA in 48/163 (29.4%) samples. mtLSU rDNA sequence analysis revealed the presence of three different genotypes in the population. Genotype 2 was most common (48%) followed in prevalence by genotype 1 (23%) and 3 (19%); mixed genotype infection was seen in 10% of the cases. RFLP analysis of DHPS PCR products revealed four

genotypes, 18% of which were associated to sulfa drugs resistance. Only contact to coughers (prevalence ratio (PR) 3.51, 95% CI: 1.79-6.87, P=0.000) and exposure to tobacco smoke (PR 1.82, 95% CI: 1.14-2.92, P=0.009) were statistically associated with being colonized by *P. jirovecii*. The prevalence of *P. jirovecii* in infants and toddlers with WC and the genotyping results provide evidence that this population represents a potential reservoir and transmission source of *P. jirovecii*.

QEEG Spectral and Coherence Assessment of Autistic Children in Three Different Experimental Conditions.

Machado C, Estévez M, Leisman G, Melillo R, Rodríguez R, Defina P, et al. J Autism Dev Disord. 2013 Sep 19. [Epub ahead of print]

We studied autistics by quantitative EEG spectral and coherence analysis during three experimental conditions: basal, watching a cartoon with audio (V-A), and with muted audio band (VwA). Significant reductions were found for the absolute power spectral density (PSD) in the central region for delta and theta, and in the posterior region for sigma and beta bands, lateralized to the right hemisphere. When comparing VwA versus the V-A in the midline regions, we found significant decrements of absolute PSD for delta, theta and alpha, and increments for the beta and gamma bands. In autistics, VwA versus V-A tended to show lower coherence values in the right hemisphere. An impairment of visual and auditory sensory integration in autistics might explain our results.

Recessive Spinocerebellar Ataxia with Paroxysmal Cough Attacks: A Report of Five Cases.

Velázquez L, González R, Rodríguez R, Aguilera R, Galicia L, Vázquez Y, et al. Cerebellum. 2013 Oct 6. [Epub ahead of print]

Hereditary ataxias are a heterogeneous group of neurological diseases characterized by progressive cerebellar syndrome and numerous other features, which result in great diversity of ataxia subtypes. Despite the characterization of a number of both autosomal dominant and autosomal recessive ataxias, it is thought that a large group of these conditions remains to be identified. In this study, we report the characterization of five patients (three Mexicans and two Italians) who exhibit a peculiar form of recessive ataxia associated with coughing. The main clinical and neurophysiological features of these patients include cerebellar ataxia, paroxysmal cough, restless legs syndrome (RLS), choreic movements, atrophy of distal muscles, and oculomotor disorders. Brain magnetic resonance imaging (MRI) revealed cerebellar atrophy, while video polysomnography (VPSG) studies showed a severe pattern of breathing-related sleep disorder, including sleep apnea, snoring, and significant oxygen saturation in the absence of risk factors. All patients share clinical features in the peripheral nervous system, including reduction of amplitude and prolonged latency of sensory potentials in median and sural nerves. Altogether, clinical criteria as well as molecular genetic testing that was negative for different autosomal dominant and autosomal recessive ataxias suggest the presence of a new form of recessive ataxia. This ataxia, in which cerebellar signs are preceded by paroxysmal cough, affects not only the cerebellum and its fiber connections, but also the sensory peripheral nervous system and extracerebellar central pathways.

Reliability and validity of a Spanish version of the Impact of Pediatric Epilepsy Scale in a Cuban population.

Garóffalo N, Fernández O, Gómez AM. Epilepsy Behav. 2013 Nov;29(2):357-60.

The Impact of Pediatric Epilepsy Scale (IPES) is a brief, accurate, and acceptable measurement scale of the impact of pediatric epilepsy on the health-related quality of life (HRQOL) of both the child and the child's family as perceived by the child's parent(s). The aim of this study was to validate a Spanish language version of the IPES in Cuban children with epilepsy. The IPES was translated and adapted to Cuban culture and administered to 76 parents of children with epilepsy. The principal component analysis indicated that two factors accounted for 72% of the variance of the IPES (family relationships and health and social well-being). The IPES was also able to detect differences in HRQOL between subjects according to epilepsy severity. The internal consistency coefficient was 0.962, and the test-retest reliability was 0.979. The Cuban version of IPES can be used to measure a child's epilepsy-specific HRQOL in Cuba.

Role of CC chemokine receptor 1 and two of its ligands in human dengue infection. Three approaches under the Cuban situation.

Sierra B, Pérez AB, García G, Aguirre E, Alvarez M, González D, et al. Microbes Infect. 2013 Oct 22. pii: S1286-4579(13)00213-X. doi: 10.1016/j.micinf.2013.10.011. [Epub ahead of print]

Any of the four dengue serotypes can cause a severe disease, partly due to systemic inflammation orchestrated by mediators like cytokines and chemokines. We addressed the role of CCR1 and its ligands CCL3/MIP-1 α and CCL5/RANTES in dengue infection using three different approaches: an ex vivo model exploring memory immune response in subjects with a well characterized dengue immune background, an in vivo study in patients with primary or secondary dengue infection, and an approach in fatal dengue. CCR1 and CCL3/MIP-1 α gene expression showed differences after homotypic and heterotypic challenge according to dengue immune background of subjects, in correspondence with previous observations in Cuban dengue outbreaks. CCL5/RANTES gene expression was higher after homotypic challenge. CCR1 and CCL3/MIP-1 α gene expression was higher in patients with secondary infection during critical days of the dengue disease, while the increase in RANTES expression started earlier than the observed for CCR1 and CCL3/MIP-1 α . CCR1 and CCL3/MIP-1 α gene expression was as high in brain as in spleen tissue from necropsy. Our results confirm the strong influence of previous immunity in subsequent dengue infections, and confer a possible pathogenic role to CCR1 and CCL3/MIP-1 α in dengue disease and a possible protective role for CCL5/RANTES, probably through CCR5 interaction.

The relationship between economic status, knowledge of dengue, risk perceptions and practices.

Castro M, Sánchez L, Pérez D, Sebrango C, Shkedy Z, Van der Stuyft. PLoS One. 2013 Dec 12;8(12):e81875. doi: 10.1371/journal.pone.0081875.

The reemergence of dengue as an important public health problem reflects the difficulties in sustaining vertically organized, effective, control programs and the need for community-based strategies for *Aedes aegypti* control that result in behavioral change. We aimed to disentangle the relationships between underlying determinants of dengue related practices. We conducted a cross-sectional study in 780 households in La Lisa, Havana, Cuba. A questionnaire and an observation guide were administrated to collect information on variables related to economic status, knowledge on dengue, risk perception and practices associated with *Aedes aegypti* breeding sites. To test a conceptual model that hypothesized direct relationships among all these constructs, we first used Exploratory Factor Analysis with Principal Component Analysis to establish the relationship between observed variables and the underlying latent variables. Subsequently, we tested whether the observed data supported the conceptual model through Confirmatory Factor Analysis. Exploratory Factor Analysis indicated that the items measured could be reduced into five factors with an eigenvalue >1.0: Knowledge on dengue, Intradomiciliar risk practices, Peridomiciliar risk practices, Risk perception and Economic status. The proportion of the total variance in the data explained by these five factors was 74.3%. The Confirmatory Factor Analysis model differed from our hypothesized conceptual model. Only Knowledge on dengue had a significant, direct, positive, effect on Practices. There was also a direct association of Economic status with Knowledge on dengue, but not with Risk perception and Practices. Clarifying the relationship between direct and indirect determinants of dengue related practices contributes to a better understanding of the potential effect of Information Education and Communication on practices and on the reduction of *Aedes aegypti* breeding sites and provides inputs for designing a community based strategy for dengue control.

Timing and tuning for familiarity of cortical responses to faces.

Bobes MA, Lage Castellanos A, Quiñones I, García L, Valdes-Sosa M. PLoS One. 2013 Oct 9;8(10):e76100.

Different kinds of known faces activate brain areas to dissimilar degrees. However, the tuning to type of knowledge, and the temporal course of activation, of each area have not been well characterized. Here we measured, with functional magnetic resonance imaging, brain activity elicited by unfamiliar, visually familiar, and personally-familiar faces. We assessed response amplitude and duration using flexible hemodynamic response functions, as well as the tuning to face type, of regions within the face processing system. Core face processing areas (occipital and fusiform face areas) responded to all types of faces with only small differences in amplitude and duration. In contrast, most areas of the extended face processing system (medial orbito-frontal, anterior and posterior cingulate) had weak responses to unfamiliar and visually-familiar faces, but were highly tuned and exhibited prolonged responses to personally-familiar faces. This indicates that the neural processing of different types of familiar faces not only differs in degree, but is probably mediated by qualitatively distinct mechanisms.

Study of airborne fungus spores by viable and non-viable methods in Havana.

Almaguer M, Aira MJ, Rodríguez FJ, Rojas TI. Grana. 2013 Sep 20;52(4):289–98.

The Havana aeromycobiota diversity was studied from November 2010 to October 2011 using two complementary volumetric methods. A total of 35 fungal genera were characterised, 26 of them were recognised only by non-viable methods, six with viable methodology and the other three with both sampling methods. Furthermore, 47 species were identified by cultivation and the spores collected with the non-viable methodology. These could not be included in a specific genus, and thus, were categorised into five fungal

types. In general, the main, spread worldwide, mitosporic fungi also predominated the Havana atmosphere. The predominant species were *Cladosporium cladosporioides*, *Aspergillus flavus* and *Penicillium citrinum*. Moreover, several Zygomycetes (*Syncephalastrum racemosum*, *Rhizopus stolonifer* and *Rhizopus oryzae*), Ascomycetes (*Chaetomium globosum*) and Basidiomycetes such as *Coprinus* or *Ganoderma* were isolated. In the present paper, the review of the airborne fungi conducted in previous studies in Cuba was completed by the detection of two new genera and the first isolation of ten new records in the Cuban atmosphere. Most of the fungi detected showed a diurnal pattern with high spore peak at 11.00–12.00.

Zolpidem Arousing Effect In Persistent Vegetative State Patients: Autonomic, Eeg And Behavioral Assessment.

Machado C, Estevez M, Rodríguez R, Pérez J, Chinchilla M, Defina P, et al. Curr Pharm Des. 2013 Sep 10. [Epub ahead of print]

Objective To study the Zolpidem arousing effect in persistent vegetative state (PVS) patients combining clinical evaluation, autonomic assessment by heart rate variability (HRV), and EEG records. **Methods** We studied a group of 8 PVS patients and other 8 healthy control subjects, matched by age and gender. The patients and controls received drug or placebo in two experimental sessions, separated by 10-14 days. The first 30 minutes of the session were considered the basal record, and then Zolpidem was administered. All participants were evaluated clinically, by EEG, and by HRV during the basal record, and for 90 minutes after drug intake. **Results** We found in all patients, time-related arousing signs after Zolpidem intake: behavioral (yawns and hiccups), activation of EEG cortical activity, and a vagolytic chronotropic effect without a significant increment of the vasomotor sympathetic tone. **Conclusions** We demonstrated time-related arousing signs after Zolpidem intake. We discussed possible mechanisms to explain these patho-physiological findings regarding EEG cortical activation and an autonomic vagolytic drug effect. As this autonomic imbalance might induce cardio-circulatory complications, which we didn't find in any of our patients, we suggest developing future trials under control of physiological indices by bedside monitoring. However, considering that this arousing Zolpidem effect might be certainly related to brain function improvement, it should be particularly considered for the development of new neuro-rehabilitation programs in PVS cases. According to the literature review, we claim that this is the first report about the vagolitic effect of Zolpidem in PVS cases.