

Leading article

DEAR READERS!

We present to you the special issue of the Slovenian Medical Journal, devoted to Neuroscience, which has been compiled and edited by members of the Slovene Neuroscience Association: Mara Bresjanac, Maja Trošt and Grega Repovš.

Neuroscience has made a remarkable progress in the last few decades. Despite the age long human curiosity and interest in the nervous system, many key questions remain unanswered. When the journal Science was celebrating its 125th anniversary it published the top 125 unanswered questions still challenging scientists. The following two neuroscience-related questions found their way into the top 25: *What is the neurobiological basis of consciousness?* and *How are memories stored and subsequently retrieved?* Many more neuroscience-related questions were among the other 100 on the list including mechanisms of prion disease, addiction, Alzheimer disease, schizophrenia, autism, explaining the need to sleep, to dream ...

Slovenian neuroscientists work in different environments from the Universities, hospitals to research institutes, where we employ different methods to study the nervous system from the molecular to the systems level, and from isolated neural cells in vitro, experimental animals to human subjects. However, not many organized forms of collaboration between different institutions and individual neuroscientists exist, which undoubtedly contributes to suboptimal exploitation of the available research resources.

In the past five years, SiNAPSA, Slovenian Neuroscience Association, has made systematic efforts to improve communication between Slovenian neuroscientists. Two international neuroscientific conferences and a few symposia have been organized under the auspices of SiNAPSA. These events have always been accompanied by activities aimed at improved communication between scientists across disciplinary and geographical borders. SiNAPSA conferences are strings of independent thematic symposia, organized by their proponents with financial and organizational help from SiNAPSA. With the intent to diversify program and facilitate international collaboration, every symposium has at least one presenter who comes from a country other than Slovenia.

The second SiNAPSA Neuroscience Conference took place at the Medical Faculty of the University of Ljubljana between October 5 and 7, 2007. It had 5 symposia: cognitive neuroscience, neurobiology of Alzheimer disease and other conformational disorders of the brain, pediatric neurology, neurodegenerative disorders and cerebro-vascular disorders. Selected presenters were invited to submit their manuscripts for the special issue of the Slovenian Medical Journal. In order to reach the widest readership we opted to publish the selected papers in English. Final selection

and preparation of manuscripts was done by the guest-editors and a number of Slovenian and foreign invited reviewers, whom we wish to express our gratitude.

Allow us to invite you to reading the issue by presenting a short overview of its contents: the introductory paper by David Vodusek and coworkers follows the example of the European Brain Council, which recently published its analysis revealing a huge burden on the European economies, including Slovenia, posed by neurological and psychiatric disorders. This leads to increased requirements of the modern societies for advances in neuroscientific research and their efficacious and timely transfer into clinical practice.

The paper by Currais and coworkers addresses an interesting topic of cell cycle reactivation in neurons – otherwise highly differentiated, non-dividing cells. It points to the role this reactivation plays in the pathogenesis of Alzheimer disease. The review paper by Eva Žerovnik describes some characteristics of amyloidogenic proteins, based on the in vitro studies of human Stefin B. The use of this model protein allows insight into amyloid fibril formation, a central process in the deposition of pathological proteins in the brains of neurodegenerative disorders' patients.

Long-term effectiveness of L-DOPA treatment in Parkinson disease patients is hampered by dyskinesias. The research contribution by Gordana Glavan and Marko Živin employs experimental animals to test the hypothesis that dyskinesias are related with dopaminergic hypersensitivity of the striatal neurons denervated through initial dopaminergic injury.

A review paper by Nina Mohorko and Mara Bresjanac describes a new classification of neurodegenerative disorders with pathological protein tau deposition in the brain, and discusses possible new diagnostic methods based on detection and recognition of different forms of tau deposits. Neuroimaging methods which can reveal structural and functional changes in living brains of patients with dementia are gaining in importance as diagnostic aids. Lojze M. Šmid and Mara Bresjanac offer a review of the main neuroimaging methods and their key findings in neurodegenerative dementias.

In a review article by Metka Derganc and Damjan Osredkar about hypoxic-ischemic brain injury in the neonatal period different cellular mechanisms responsible for the neuronal death are described and new treatment approaches are listed. Mental retardation in early childhood is often caused by infantile spasms, which have a negative influence on cortical development in the critical period of early brain development. As shown in the review by Zvonka Rener Primec, early treatment may have a favorable prognosis on cognitive and behavior impairments.

Neuronal activity is tightly coupled with regional cerebral blood flow. This functional link is called neurovascular coupling. The paper by Marjan Zaletel explains how the neurovascular coupling can be measured by visually evoked cerebral blood flow velocity responses (VEFR) and visual evoked potentials (VEP). Neurovascular coupling could be altered in older subjects and in migraineurs. Elderly often suffer from dementia. The most common dementias are neurodegenerative; Alzheimer and frontotemporal dementia. A clinical differentiation between them is often difficult but important. Clinical fea-

res and recent developments in genetics and neuropathology are presented in a review article about the differentiation between the two dementias by Rajka Liščić.

Alcohol dependence leaves numerous neuropsychological deficits even weeks after abstinence. Results of the neurocognitive study done by Lilijana Šprah and Tatjana Novak on abstinent alcoholics showed their specific neuropsychological profile and presented neurocognitive assessment that proved a useful approach for evaluation of alcohol abstinence functioning.

Mara Bresjanac, Maja Trošt and Grega Repovš
Guest-editors of the special issue of the Slovenian Medical Journal

Uvodnik

SPOŠTOVANE BRALKE IN BRALCI!

Pred vami je posebna številka Zdravniškega vestnika, posvečena nevroznanosti, ki so jo pripravili in uredili člani SiNAPSE, slovenskega društva za nevroznanost: Mara Bresjanac, Maja Trošt in Grega Repovš.

Nevroznanost se v zadnjih desetletjih razvija z izjemno hitrostjo. Zanimanje za vprašanja povezana z živčevjem so že dolgo v žarišču človeške radovednosti in številna med temi vprašanji kljub metodološkemu napredku zadnjih desetletij ostajajo neodgovorjena. Po zanimivem prispevku revije Science iz leta 2005, ko je revija praznovala 125. obletnico izhajanja, sta že med prvimi petindvajsetimi dve nevroznanstveni vprašanji: *Kakšna je (neuro)biološka podlaga zavesti?* in *Kako se spomini shranjujejo in ponovno priključijo?* Med nadaljnimi stotimi vprašanji je nevroznanstvenih še več in vključujejo mehanizem nastanka prirobnih bolezni, odvisnosti, Alzheimerjeve bolezni, shizofrenije, avtizma, razlago potrebe po spanju, po sanjanju ...

V Sloveniji smo nevroznanstveniki posejani na Univerzah, v kliničnem medicinskem okolju in na raziskovalnih Inštitutih, kjer z različnimi metodološkimi pristopi raziskujemo živčevje na vseh ravneh od molekularne do sistemske in od izoliranih celic prek živali do človeka. Med posameznimi inštitucijami in raziskovalci v našem okolju ni veliko organiziranih oblik sodelovanja in obstoječih raziskovalnih potencialov tudi zato verjetno ne izrabljamo najbolje.

V zadnjih petih letih slovenske nevroznanstvenike iz različnih okolij v skupnih akcijah sistematično povezuje SiNAPSA, slovensko društvo za nevroznanost. Pod okriljem SiNAPSE smo izpeljali dve večji mednarodni nevroznanstveni konferenci in nekaj simpozijev, ki jih vedno spremlja tudi program (npr. okrogle mize in panelne razprave) namenjen izboljšanju komunikacije med raziskovalci iz različnih okolij in znanstvenih panog na osrednje teme nevroznanosti. SiNAPSINE konference so zastavljene kot zaporedje neodvisnih tematskih simpozijev, ki jih organizirajo njihovi predlagatelji in jim SiNAPSA pri tem pomaga po finančni in organizacijski plati. Vsak simpozij ima za popestritev programa in za spodbujanje mednarodnega sodelovanja tudi vsaj enega tujega vabljenega predstavljalca.

Druga SiNAPSINA nevroznanstvena konferenca je potekala na Medicinski fakulteti Univerze v Ljubljani med 5. in 7. oktobrom 2007. Sestavljali so jo naslednji simpoziji: kognitivna nevroznanost, nevrobiologija Alzheimerjeve bolezni in drugih bolezni z odlaganjem amiloida v možganih, otroška nevrologija, nevrodegenerativne bolezni ter cerebrovaskularne bolezni. Avtorji vabljenih predavanj na konferenci so imeli možnost oddaje preglednih ali raziskovalnih prispevkov za posebno številko Zdravniškega vestnika. V želji, da osrednje strokovno glasilo slovenskih zdravni-

kov doseže najširši krog bralcev, smo se gostujoči uredniki odločili za izbor prispevkov v angleškem jeziku. Pri izboru in dokončni podobi člankov so sodelovali številni domači in tuji recenzenti, ki se jim za delo najlepše zahvaljujemo.

Dovolite, da vas k branju posebne številke povabimo s kratkim preletom vsebine:

Uvodni pregledni prispevek Davida Voduška s sodelavci se zgleduje po analizi Evropskega sveta za možgane, ki opozarja na izjemno velikost bremena nevroloških in psihiatričnih bolezni za proračune evropskih držav, vključno s Slovenijo. Zato se povečujejo tudi potrebe sodobne družbe po napredku v nevroznanosti in učinkovitem ter pravočasnem prenosu novih raziskovalnih spoznanj v klinično medicino.

Antonio Currais s sodelavci v svojem preglednem prispevku odpira zanimivo temo reaktivacije celičnega ciklusa v nevronih, ki so sicer visoko diferencirane, nedeleče se celice, in o vlogi te reaktivacije v patologiji Alzheimerjeve bolezni. Pregledni prispevek Eve Žerovnik prikazuje nekatere značilnosti amiloidogenih beljakovin na temelju *in vitro* študij človeškega stefina B. Uporaba te modelne beljakovine omogoča podroben vpogled v nastajanje amiloidnih fibril, pomembnega procesa v odlaganju patoloških beljakovin v možganih pri nevrodegenerativnih boleznih.

Učinkovitost kroničnega zdravljenja Parkinsonove bolezni z L-DOPA krnijo zapleti v obliki motenj gibanja (diskinezij). Raziskovalni prispevek Gordane Glavan in Marka Živina na poskusnih živalih preverja domnevo, da so tovrstni zapleti povezani z dopaminergično preobčutljivostjo striatalnih nevronov, ki je posledica dopaminergične denervacije.

Pregledni prispevek Nine Mohorko in Mare Bresjanac podaja opis in sodobno razvrstitev bolezni, pri katerih se v možganih odlaga patološko spremenjena beljakovina tau ter možnosti za razvoj novih diagnostičnih pristopov, temelječih na prepoznavi posameznih tipov odlag tau. V diagnostiki demenc igrajo danes vse pomembnejšo vlogo sodobne slikovne metode, ki lahko prikažejo strukturne in funkcijske spremembe v možganih bolnikov. Pregled teh metod in njihovih izsledkov pri nevrodegenerativnih demencah podaja prispevek Lojzeta Šmida in Mare Bresjanac.

V preglednem članku Metke Derganc in Damjana Osredkarja o hipoksično-ishemični okvari možganov v neonatalnem obdobju so opisani celični mehanizmi okvare nevronov in predstavljena novejša priporočila glede zdravljenja. Umsko manjrazvitost zgodnje otroške dobe pogosto povzročajo infantilni spazmi, saj negativno vplivajo na razvoj možganske skorje v kritičnem časovnem obdobju zgodnje razvojne faze možganov. Kot kaže prispevek avtorice Zvonke Re-

ner Primec, so kognitivni in vedenjski primanjkljaji blažji ob hitrejšem začetku zdravljenja.

Aktivnost možganskih nevronov je tesno povezana s področnim možganskim krvnim pretokom. Tej funkcijski povezanosti pravimo živčnožilna sklopitev. V svojem prispevku Marjan Zaletel predstavi, da živčnožilno sklopitev lahko ocenjujemo z merjenjem evociranih možganskih odgovorov krvnega pretoka (VEOP) in vidnih evociranih potencialov (VEP). Motnje živčnožilne sklopitve so v tem prispevku opisane pri starostnikih in bolnikih z migreno. Vedno pogostejša spremljevalka starostnikov je tudi demenca. Najpogostejše demence so nevrodegenerativne demen-

ce; npr. Alzheimerjeva in frontotemporalna. Klinično razlikovanje je pogosto težko a pomembno. V preglednem članku Rajke Liščić o razlikovanju med omenjenima demencama so poleg kliničnih značilnosti obeh predstavljena tudi najnovejša odkritja molekularne genetike in nevropatologije.

Odvisnost od alkohola pušča številne nevropsihološke primanjkljaje tudi po večtedenski abstinenci. Rezultati študije nevrokognitivne ocene abstinentov, ki je predstavljena v prispevku Lilijane Šprah in Tanje Novak, so prikazali nevropsihološki profil abstinentov in predstavili nevropsihološki instrumentarij za klinično oceno njihovega funkcioniranja.

Mara Bresjanac, Maja Trošt in Grega Repovš

Gostujoči uredniki posebne številke Zdravniškega vestnika