

# The 2<sup>nd</sup> International **Neurotrauma** Congress

## The 4<sup>th</sup> International **Roads Safety** Congress



The Supplement of the Neuroscience Journal of Shefaye Khatam, 2015  
Volume 2, No. 4, Suppl. 3



## Abstract Book of the 2<sup>nd</sup> International Neurotrauma Congress & the 4<sup>th</sup> International Roads Safety Congress

18-20 February, 2015, Tehran, Iran.

Published: 18 February, 2015

These abstracts are available online at [http://www.shefayeKhatam.ir/index.php?slc\\_lang=en&sid=1](http://www.shefayeKhatam.ir/index.php?slc_lang=en&sid=1)

### Oral Presentations

#### O1

##### Roads Safety and Neurotrauma

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O1

Road traffic accidents account for approximately 3000 deaths on a daily basis, and 50 million injuries and 1.2 million deaths each year. In low-income and middle income countries, road traffic accidents account for 85% of deaths and 90% of annual disability. Casualties of this magnitude are a serious problem throughout the world and create a significant impact on society. In addition, neurological disorders due to traffic accidents are a major problem for the health system. Prevention of road accidents saves life and reduces the morbidity and the rate of neurological disorders. Iran and other Middle Eastern countries have one of the highest incidences of fatality rates due to road traffic crashes in the world. To develop effective road safety programs in the region, establish and maintain regional road safety partnerships, and attract funds and resources, a close cooperation among the countries in this region is essential.

#### O2

##### The 4<sup>th</sup> Road Safety and the 2<sup>nd</sup> Neurotrauma Congresses in Khatam Alanbia Hospital

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O2

Every 6 seconds someone is killed or seriously injured on the world's roads. With 1.3 million road deaths each year this is a global epidemic comparable to malaria or Tuberculosis. Nine in ten road deaths and injuries are

in developing countries. By comparison to other global killers, road injury is neglected. Road crashes are the leading global cause of death for young people under 25 years, and by 2015 are predicted to be the leading cause of premature death and disability for children in developing countries aged five and above. Already, according to UNICEF and the WHO, 260,000 children die and another 10 million are injured in road crashes every year. The international community has failed to respond to this epidemic. Road safety needs more attention from all governments in the World. This neglect means that developing countries are not received the financial support and technical advice they need to improve road safety. While road deaths in the industrial countries are falling, fatalities in the developing world are rising sharply. Improved road design and a focus on pedestrian safety, safer vehicles, motorcycle helmets, seat belts, driver training and licensing, and tackling speed is how road deaths can be decreased. Immediate actions are necessary to prevent these casualties.

#### O3

##### Roads Safety in Developing Countries

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O3

The investigation showed that the increasing number of deaths and fatalities resulting from driving accidents is mostly related to developing countries especially with intermediate and low social classes which it is resulting from industrialization of the mentioned societies without considering necessary infra structures such as health, safety and environment (HSE). Increasing number of cars, users' different traffic behaviors, inappropriate and insufficient infrastructures especially in the field of ITS, inappropriate driving skills are the main causes of high accidents and fatalities number. Based on the conducted studies, accidents and fatalities expenditures allocated 6 percent of national treasures of Islamic Republic of Iran.

According to these expenditures, the main aim of traffic police which is extracted from the Quran signs (which are mentioned above) and also from Iran supreme leader statements who said that “the authorities should attempt to decrease the accidents and fatalities to minimum level” so that the strategies for decreasing accidents and its fatalities have been determined which include: 1. The especial attention to development of standardization and strengthening of road infrastructures safety, car, public transportation of loads and passengers. 2. Daily analyzing of road accidents by the help of traffic experts society based on the different indexes such as accidents causes, safety indexes by the type of traffic users and so on. 3. Attempting to make integrate management and assistance of different organization for strengthening of traffic health. 4. Revising traffic laws and regulations in the Islamic parliament of Iran after 40 years. 5. Suggesting development of programs devoted to accidents and fatalities reductions in the realm of (HSE) and rescue and emergency after post-crash. 6. Especial attention to training of different age, sex, social and risky traffic users such as motorcycle riders and pedestrians with the help of different organizations such as media, higher education, education organization, road and rail transportation organization and so on. 7. Establishing of training course for traffic police professionalism with the help of specializing traffic sciences and courses and standardization of their behaviors in social transactions. The sum of these efforts in addition to triple number of vehicles, distance covered in urban and rural roads and those who have taken driving certificate in 2006, caused that we have experienced 18000 reductions of fatalities and accidents that are equals to 10000 deaths during past 8 years in 2014. This rate of deaths and fatalities is improper for such a country as Iran and we should try to decrease it to the probable minimum level.

## O4

### Status of Road Safety and Injury Burden: Europe

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O4

Road traffic injuries are an ongoing global health burden and cause more than 1.2 million deaths per year. In Europe, the annual socioeconomic impact accounts for €130 billion. In 2011, the United Nations set a

special focus on road safety and injury prevention by the proclamation of the “Decade of Action for Road Safety.” This initiative focuses mainly on developing countries. In Germany, many measures have been undertaken to improve the mortality rates associated with traffic injuries. Among these are countrywide mandatory helmet laws for motorcyclists, speed limits on the Autobahn, speed limit reinforcements associated with fines in and outside the cities, and a network of overlapping rescue helicopter coverage throughout the country. Despite a general decrease in mortality, the European Commission in 2001 set a new law to reduce the number of road traffic fatalities by another 50%. Until 2009, a reduction of more than one third (38%) was achieved. The improvements observed seem to be a result of improvements in education, engineering, and technical improvements in active and passive car safety. These have had effects for cyclists and pedestrians, as well. In addition, a 1% reduction of distance traveled by motorized vehicles has occurred, which may have contributed to a decreased incidence of accidents (1.8%). Based on these prerequisites, this article provides an overview on the current situation in Europe and focuses on 2 questions: 1. How can the improvements in road traffic-associated fatalities in Europe be explained? 2. Is there a special patient group that should be aimed at in the future? The observed decline of fatalities over the last decades can be explained by different factors. The highest number of fatalities was observed in the age group between 15 and 29 years. Furthermore, most pronounced decrease in fatalities was found for children younger than 14 years of age (55%). The age group between 15 and 24 years demonstrated a decrease of 40%. In elderly persons, the reduction was only 9%. This may be explained by the fact that more elderly people continue to drive. Moreover, if involved in a car accident, their chances of death are higher than in all other age groups.

## O5

### Technical Accident Reconstruction-What Can be Learned to Improve Medical Treatment in Trauma patients.

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O5

Annually, more than 1 million people were killed in road traffic accidents worldwide every year and an uncounted number were severely injured. In 2012 fatal injuries caused by road traffic accidents are under the top ten lists of causes of death in the world. It's expected

that in the near future road traffic accidents become one of the main causes of death in the world. Most of these fatal injuries in road traffic accidents are avoidable and prevention is needed. To prevent severe traffic accidents a multidisciplinary approach is needed. The Ministry of transportation, road planners, police services, school teachers, employees of driving schools, rescue organizations and medical experts has to work together to find solutions to decrease the numbers of accidents. To identify the most effective solutions to reduce fatal accidents in every single country good statistics, proper demographic data and traffic accident research is needed to understand the specific circumstances in each region of the world. Technical reconstruction of severe accidents can help to understand the cause of accidents but it's a cost-intensive and time-consuming method to get information road traffic accidents. For technical reconstruction of road traffic accidents specific trained and equipped teams are essential and in general the number of investigated cases are limited. In recent decades these well documented data of traffic accident researcher teams in the UK, Germany etc. could help to improve road safety and to develop prevention strategies to decrease the number of fatal injuries in the world. Technical reconstruction of road traffic accidents is a very effective way to prevent fatal injuries.

## O6

### **Road Traffic Accidents Lead to Different Patterns of Injuries Depending on Impact, Age and Premedical Condition-Specific Attention Must be Provided by Multi-Disciplinary Trauma-Teams**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O6

The approximate number of road traffic accidents that occur in Germany every year is 4.8 million. In 15-25% of these accidents patients die on scene, while about 35,000 severely injured patients are admitted to the resuscitation units of trauma centers in Germany, out of which about 10% do not survive. To continuously observe and improve their treatment and management, polytraumatized patients are documented in the trauma registry of the German Society for Trauma Surgery. A retrospective study of patients differing as to impact, age and premedical condition shows that special attention is needed depending on their actual pattern of injuries. While elderly trauma patients are regularly exposed to neurotrauma increased by their level of activity in an aging society, trauma in children usually involves passive participants with little chance of escape. Both

need to be treated in specialized trauma centers. While healthcare professionals are working hard to control the quality of trauma management and communication, a multi-disciplinary approach to specific programs in accident prevention needs to include all professionals dealing with road safety and education. Programs on accident prevention such as Preventing Alcohol Related Trauma in Youth (P.A.R.T.Y.) are just as important as certified trauma courses. A recent study on an evaluation of the P.A.R.T.Y.-program supports its importance and efficiency in changing behavior of young drivers.

## O7

### **Orthopedic Trauma Surgery in Germany-Influence on a Better Road Safety**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O7

Each year over 50 million humans are injured worldwide in traffic accidents (WHO). 1,200,000 fatalities are registered at the same time. Everybody agrees, that we must fight against. Beside law enforcement, education, car technology and road construction a well organized rescue chain is mandatory, chain links are: Emergency call center (Europe TEL. 112), SAR system, Treatment in a competent hospital, Early rehabilitation. In Germany the trauma surgeon is the "Team Leader" Emergency medical doctors (trauma surgeon, anesthesiologist ...) are treating the polytrauma patient at the scene. By helicopter or ambulance the patient is transported to a trauma center with the necessary specialists (neurosurgeon, visceral surgeon, orthopedic trauma surgeon). The knowledge of all trauma centers is collected in a register and shared with the government (laws), car manufacturers (safer cars) and all interested institutions. It is evidence based that due to this organisation the number of fatalities and heavy injuries are diminished from year to year, not only in Germany but in all European countries as well.

## O8

### **A Report Base on the Observation Regarding to Percentage of Death in Road Accident**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O8

Based on the release statistic in Iran, there are three major causes of death which included; heart attacks, death due to road accident and cancer. Prevention from

heart attacks needs one or two decade and changing in life styles, eating diet and etc. About the cancer regarding to previous finding and progresses in medicine, we are still far from finding the cause of death, and we could not suggest a preventive method and treatment. Death through trauma after road accident has been suggested as the second cause of death in Iran. Traumas due to accident with motorcycle are the most common cause of trauma. However, in trauma of accident with car or motorcycle death prevention is possible and providing a useful treatment for injured people could cause significant differences. Statistic in our country showed that every 20 or 25 minute one person is dead as result of road accidents. Furthermore, based on the provided statistic from world health organization in 2012, Iran always was in the list of countries which have the highest number of death due to road accident, although the number is about decreasing but still is so high. The percentage of death from accident in Iran are 2 times and the number of injured from road crash are 5.1 time more than global standards. Even the number of death because of road accidents was more than the number of dead from eight year war with Iraq. Deaths mostly happen among the ages 20 to 40 cause 4 million years lost in Iran each year. The cost of this accident in Iran is about 4 milliard dollar per year. In this study, 51.7 % of injured people were with motorcycle, 5.6% was with bicycle, 17.5% was pedestrians, 17.9% was in bus and 11.3% was in lorry. In about 40 up to 60 percent of all accident a motorcycle driver had the major role in accident. In about 58.2 percent of death, head trauma was the cause of death. Regarding to the Size of country, transportation of injured always could not be done by ambulance, which is a critical problem. At the end in order to reduce damages and provide better treatment we suggested some points: using seat belt for all passengers, using helmet for motorcycle drivers, using airbag for auto, providing sufficient role by police and applying it around the country, improve controlling and enhance fine, change road structure and correct dangerous areas, enhance the number of ambulances, using of telemedicine in ambulance, having expert in ambulance, transportation of injured to medical center by helicopter when there is long distance from the accident site to hospital, provide education from elementary school, using mass media special radio and television, improving some roles for pedestrian and using of aforementioned points will reduce the number of death and prevent road accident which destroy both society and families and abolish the young nation of country.

## O9

### Role of Neuroimaging in Head Trauma

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O9

Cranio-cerebral injuries are a common cause of hospital admission following trauma, and long- term morbidity and mortality. Neuroimaging plays an essential role in brain injuries. In the X ray field however simple skull X ray is useful but there is shift toward recognition of intracranial pathology by CT scanning. CT is the most appropriate initial study for acute evaluation of the head-injured patient who may harbor lesion(s) that require immediate neurosurgical intervention. Early and sometimes repeat CT scanning may be required. Cerebral angiography has a role in demonstrating and managing traumatic vascular injuries such as pseudo aneurysm, dissection, fistulae, or diagnosis and neurointerventional treatment of uncontrolled hemorrhage. Dynamic spiral CT angiography (CTA) and magnetic resonance angiography (MRA) have a role as less invasive screening tools for detecting traumatic intracranial, skull base, and/or neck vascular lesions. Intracranial and neck MRA with fat- suppressed T1-weighted neck MR are helpful for screening vascular lesions such as thromboses, pseudo aneurysms, fistulae, or dissection. CTA of the aortic arch and neck vasculature may reveal carotid or vertebral dissection, although angiography remains the gold standard for depicting dissection. MRI in imaging of head trauma is limited while CT is sensitive for detecting injuries requiring a change in treatment, MRI is also used for acute head-injured patients with nonsurgical, medically stable pathology. Hemosidrin-sensitive T2-weighted gradient echo and susceptibility-weighted sequences are helpful for imaging small or subacute or chronic hemorrhages. Diffusion-weighted sequences improve detection of acute infarction associated with head injury. Although management of surgical injuries is not likely to be altered by the substitution of MRI for CT, superior depiction of nonsurgical lesions with MRI may affect medical management and predict the degree of neurologic recovery. Diffusion-weighted MRI and apparent diffusion coefficient (ADC) mapping depict cytotoxic injury almost immediately. In acute brain trauma, focal contusion and DAI may show restricted diffusion and evolve over time to atrophy or encephalomalacia. Perfusion imaging with CT or MRI may prove helpful as a marker for disorders of vascular autoregulation or ischemia. Diffusion tensor imaging and MR spectroscopy (MRS) are ancillary tools that may offer additional insight into the biochemical and structural patterns of injury following head trauma, as well as prognosis.

## O10

### The Changing Landscape of TBI Research

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O10

Traumatic brain injury (TBI) is a major cause of death and disability, leading to great personal suffering to victim and relatives, as well as huge direct and indirect costs to society. Strong ethical, medical, social and health economic reasons therefore exist for improving treatment. A clear, concise definition of Traumatic Brain Injury is fundamental for reporting, comparison and interpretation of studies on TBI. Researchers and clinicians have welcomed a change in nomenclature from “head injury” to the more precise “traumatic brain injury”. However, this change has not directly alleviated a sometimes Babylonian confusion as to what should really be considered under the umbrella of TBI. New insights and the development of new biomarkers and imaging tools have led to the understanding that milder insults and less typical presentations now fit under this umbrella. The diagnostic confound by non-TBI pathologies has increased confounding precise epidemiologic description, clinical management and rational research strategy development. Shifts of research are currently occurring in two directions: first, towards personalized treatment which would require better characterization of the disease TBI in individual patients, and secondly, towards broader approaches with greater generalizability. Improved characterization will aid Precision Medicine, a concept recently advocated by the US National Academy of Science, facilitating targeted management for individual patients. Improvement is much needed as treatment approaches differ widely, and evidence underpinning treatment choices low. Since the first publication of the guidelines on management of severe TBI in 1996 strong evidence in support of treatment recommendations has not been forthcoming. Specific challenges in TBI research relate to the heterogeneity of the disease and the lack of early mechanistic endpoints which can serve as intermediate outcome markers. Conventional approaches to clinical TBI research have been reductionistic, attempting to isolate out one single factor which is treated and by attempting to limit heterogeneity by the use of strict enrolment criteria. These approaches do not reflect the clinical reality of TBI heterogeneity and substantially limit generalizability of results. Modern computational techniques facilitate more holistic approaches allowing us to broaden the scope of current reductionistic thinking. A comparative effectiveness research (CER) framework offers opportunities for addressing both directions. High quality contemporaneous data, on which to base such research, are however lacking. International collaborations are being developed offering vats opportunities both in terms of concentration of knowledge and in terms of increased numbers; recently, InTBIR, the International Initiative for Traumatic

Brain Injury Research, was formed as a collaboration of funding agencies (European Commission, NIH and CIHR) to stimulate and support these initiatives.

## O11

### Iatrogenic Nerve Injuries

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O11

Nerve injuries are called “iatrogenic” if they have happened during a medical procedure. They are a relevant problem. We report our personal experience with 340 such patients operated from 1990 to 2012. Among the potential causes surgical procedures and among these orthopedic and traumatological interventions are the most frequent ones. They are followed by lymph node resection in the lateral triangle at the neck and by carpal tunnel release. If a patient has been neurologically normal before surgery but after surgery suffers from a functional deficit attributable to a peripheral nerve, common sense should come to the conclusion that something must have happened to the nerve during this procedure. However, in reality, if at all, this conclusion is often taken rather late. Only 35% of such patients arrived at our department within an interval of 6 months after injury. Although it is well known that the results of nerve repair are best when it is done as early as possible. Among 148 patients examined at least 3 months after our surgery, 26% had significantly improved. Another 45% were better than before surgery, 26% had remained unchanged so far and 3% were worse. We like to emphasize the importance of an early diagnosis and treatment of these iatrogenic nerve injuries.

## O12

### Direct and Indirect Insults of Traumatic Brain Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O12

In Traumatic Brain Injury (TBI) primary injuries result immediately from the initial trauma. This injury occurs at the moment of trauma and includes contusion, damage to blood vessels, and axonal shearing. The blood brain barrier and meninges may be damaged in the primary injury, and neurons may die. In treatment terms, this type of injury is exclusively sensitive to preventive but not therapeutic measures. The secondary insult (delayed non-mechanical damage) represents consecutive pathological processes initiated at the moment of injury

with delayed clinical presentation. After TBI, CBF autoregulation (i.e. cerebrovascular constriction or dilation in response to increases or decreases in CPP) is impaired or abolished in most patients. It is important to note that diagnosing hypoperfusion or hyperperfusion is only valid after assessing measurements of CBF in relation to those of cerebral oxygen consumption. Both cerebral ischaemia and hyperaemia refer to a mismatch between CBF and cerebral metabolism. For example, low flow with normal or high metabolic rate represents an ischaemic situation whereas high CBF with normal or reduced metabolic rate represents cerebral hyperaemia. This 'ischaemia-like' pattern leads to accumulation of lactic acid due to anaerobic glycolysis, increased membrane permeability, and consecutive oedema formation. Since the anaerobic metabolism is inadequate to maintain cellular energy states, the ATP-stores deplete and failure of energy-dependent membrane ion pumps occurs. The second stage of the pathophysiological cascade is characterized by terminal membrane depolarization along with excessive release of excitatory neurotransmitters. This event leads to increase the intracellular concentration of free fatty acids and free radicals, DNA fragmentation and inhibition of DNA repair. These events lead to membrane degradation of vascular and cellular structures and ultimately necrotic or programmed cell death (apoptosis).

## O13

### Posttraumatic Epilepsy-Epidemiology, Pathophysiology and Principles of Treatment

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O13

Traumatic head injury is the underlying cause of approximately 5% of all persons with epilepsy and is the major cause of epilepsies starting in young adulthood. Penetrating head injury, particularly among soldiers, carries a risk of almost 50% of developing posttraumatic epilepsy (PTE), mostly within 6 months to two years after the trauma. Early seizures (within one week of the trauma) are dependent on the severity of the trauma and do not independently contribute to the risk of developing PTE. The pathophysiology of development of chronic seizures is not fully understood. The process of epileptogenesis and postinjury recovery share some characteristics such as neurogenesis and axonal sprouting. Unspecific hippocampal damage as well as hemosiderin remnants from bleedings may play a role. There is no evidence supporting routine use of antiepileptic drugs beyond the first week after trauma for seizure prophylaxis. Treatment after the first seizure beyond 1-2 weeks after the trauma is indicated because the risk of seizure recurrence within 2 years is almost 90%. As of yet, no anticonvulsant has been singled out

as being particularly effective in PTE. Seizure remission with medical treatment can be expected in 25%- 40% of the patients. Epilepsy surgery may be an option, but seems to be less effective when compared with other etiologies such as hippocampal sclerosis or benign tumors.

## O14

### Cellular and Molecular Mechanisms of Spinal Cord Trauma

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O14

The prevalence of spinal cord injury (SCI) is about 2.5 million in the worldwide and more than 130,000 new injuries reported each year. Regeneration in the CNS versus the PNS is very different from the other tissues and many factors can prevent regeneration in PNS and specially CNS. Previous researches demonstrated that regeneration of CNS can inhibit by inhibitory molecules and glial scar. Therefore, creating new approaches to CNS injury treatment is a hot topic in this field. Providing a permissive growth environment by transplanting neural cells and stem cells with using tissue engineering and nanofiber scaffolds, promote the survival and growth of damaged axons. In addition, using neurotrophins like stromal-derived factor-1 and granulocyte colony-stimulating factor, neutralizing inhibitory molecules improve the regeneration condition. Functional electrical stimulation such as standing and walking after spinal cord injury, combination treatment with different methods versus mono-therapy, and gene therapy are some of new approaches in this field. Our presentation will comprehensively summarize basic aspects of cellular and molecular mechanism of spinal cord injury, critically evaluate current experimental models that are used in basic research, and provide an overview on established and emerging neuroprotective, neurorestoration and gene therapies.

## O15

### Update on Guidelines for the Treatment of Penetrating Brain Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O15

Conceptually traumatic brain injury (TBI) can be classified from a mechanistic perspective as: 1) closed, 2) penetrating, 3) blast, and 4) crush injuries. Thus, TBI is a heterogeneous disease and each type of brain injury has different characteristic features often necessitating different approaches to management. The first edition of the guidelines for management and prognosis of penetrating brain injury was published in 2001. An update on these guidelines is currently in preparation and is coordinated by Dr. James Ecklund and Dr. Beverly Walters in the US. Substantial advances have been made in diagnostic imaging for TBI, also for penetrating brain injury (PBI). A specific feature relevant to PBI is a traumatic intracranial aneurysm (TICA) which is reported in variable but sometimes high frequencies. Any patient with an intracerebral hematoma or a missile tract crossing one of the major arteries should be considered at increased risk for a TICA and appropriate imaging should be implemented. The risk of intracranial infection and of seizures following PBI is sufficiently high to warrant prophylactic medication. In the absence of a mass lesion, surgical therapy may be limited to more superficial debridement and wound closure. Prognostic analysis is less well developed compared to the field of closed TBI. Nevertheless, CT features represent one of the main and most objective predictors following PBI. Prognostic CT features are different in PBI compared to closed TBI. This presentation will present an overview of the current evidence for imaging, management and prognosis of Penetrating Brain Injury.

## O16

### **Evaluation of the Immediate and Early Role of Decompressive Craniectomy in the Treatment of Refractory Intracranial Hypertension in Cases of Severe Traumatic Brain Injury**

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*The Neuroscience Journal of Shefaye Khatam*, 2015; 2(S3): O16

When intracranial pressure (ICP) was uncontrollable among patients with severe traumatic brain injuries (STBI) and especially if it raises above 40 mmHg 100% mortality was reported. Eighty four percent of head injured patients would die if their initial ICP is greater than 25 mm Hg. Decreasing ICP through decompressive craniectomy (DC) theoretically may revert increased ICP to normal and decrease mortality. However some data indicated increased morbidity and mortality related to DC. The ability of early DC to decrease ICP in traumatic brain injury patients is still under evaluation. This is a prospective randomized study on 80 consecutive patients who sustained severe traumatic brain injury and increased ICP above 20 mm H<sub>2</sub>O who failed to respond to conservative medial measures to lower ICP. Forty-

three patients under went outright DC, while thirty-seven patients were in the conservative medical arm. Wide DC was performed and early results within one week are compared for responsiveness and complications. Most patients have a low admission Glasgow coma score (GCS). Thirty seven percent of patients scored less than 5 on GCS at the time of inclusion in the study. Associated extra-cranial injuries were commonly encountered and resulted in hypoxic episodes in 63% of patients and in hypotensive episodes in 53% of victims during the first 24 hours post injury. After decompressive craniectomy ICP dropped from a mean of 34 cm H<sub>2</sub>O to 19.2 cm H<sub>2</sub>O. Higher mortality was significantly associated with: 1. Hypotension ( $P=0.001$ ), 2. Extra-cranial injuries ( $P=0.019$ ); and 3. High preoperative ICP ( $P=0.002$ ). Fifty four percent of patients have died. There was a significant correlation between ICP and outcome ( $P=0.002$ ). Complications were frequent. In all patients DC succeeded to decrease ICP below 20 cm H<sub>2</sub>O in the immediate P.O. period. This was maintained below 20 cm H<sub>2</sub>O in those who improved. An increase of ICP to above 20 cm H<sub>2</sub>O after 1 week was noted in those who died or became vegetative. Decompressive craniectomy decreased high ICP in patients with STBI. High M&M was encountered. Only patients who maintained a lowered ICP below 20 mm H<sub>2</sub>O showed clinically significant recovery. Patients who showed a later secondary increased ICP either died or became vegetative. Those who failed to maintain a lowered ICP after one week are candidates for further studies & treatment alternatives.

## O17

### **Cerebroprotection in Severe Brain Injury**

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*The Neuroscience Journal of Shefaye Khatam*, 2015; 2(S3): O17

Formula one legend Michael Schumacher hit his head severely while skiing on December 29, 2013. He was operated on for brain decompression and left in a coma fighting for life. In such severe brain injury with cerebral contusion and hemorrhage following head trauma, refractory to medical therapy and with increasing cerebral oedema and intracranial pressure, critically low cerebral perfusion can cause anaerobic cerebral metabolism with secondary severe brain lesions and even death. The prevention of primary brain lesions is only possible by accident prevention measures. Prevention of secondary lesions is a medical challenge. Many medications with suspected cerebroprotective properties show an effect in animal experimental studies but not in human studies. Up

to now, the only promising methods in severe cerebral energy crises seem to be hypothermia and/or barbiturate administration. Additionally, clinical and experimental studies showed a close relation between the amount of hypoxic intervals and secondary injury of neural tissue (1), where the application of hyperbaric oxygen (HBO) is the only way to improve oxygen supply to the tissues with higher amounts of oxygen freely dissolved in the plasma. So we examined these methods in experimental studies and clinical application. In experimental studies we used a hypoxic standardized model of brain slices to examine the effect of hypothermia. In clinical cases with critical perfusion pressure below 50 mmHg and severe brain oedema we performed active body cooling with lowering body temperature from 38.2 °C to 35 °C. In 60 patients with reduced cerebral perfusion we administered the barbiturate methohexital and measured lactate concentrations in the blood taken from the appropriate internal jugular vein. EEG analysis was used to reveal electrical brain activity and burst suppression pattern while administrating barbiturates. Ninety-nine patients with midbrain syndrome after severe head injury were randomized. All patients received comparable monitoring and intensive care, while every second patient was additionally subjected to a series of HBO treatment. Neurological follow-up and EEG during and after HBO were registered. Our experimental studies confirmed the cerebroprotective effect of hypothermia in vitro and in vivo in cerebral energy crises, but in contrast a lack of protective effect once hypoxia had occurred under normothermic conditions. In patients with critically low cerebral perfusion, hypothermia is able to improve the clinical outcome. The administration of barbiturates in patients with reduced cerebral perfusion showed a normalization of increased cerebrovenous lactate concentrations with correlation to burst suppression time. The survival time of brain injured patients under HBO was distinctively longer and the survival rate significantly higher (group B patients). At the end of the study, 74% of the patients in group A. Were dead or apallic as compared to 53% in group B. Complete recovery occurred in only 6% in group A and 33% in group B. In the situation of cerebral energy crises it is a challenge to avoid secondary ischemic brain lesions. Our investigations showed that administration of hypothermia and barbiturates reduces cerebral metabolism and glycolysis with an improved outcome in humans. However, this treatment needs to be administered as soon as possible after reduced cerebral perfusion occurs. As another or additional treatment HBO may be discussed to improve oxygenation of ischemic hypoxic brain tissue in reduced cerebral perfusion. Further investigations and randomized studies should be performed to discuss the best treatment options for patients with a cerebral energy crisis following severe head injury.

## O18

### Iranian Quality Registry of Spinal Cord Injury, Key Considerations for Implementation

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O18

Prevalence of spinal cord injury (SCI) in Iran is considerable and developing a national registry is substantial. Registry can be a foundation of efforts for patient care improvement, clinical research facilitation, preventative strategy formulation and policymaking for better support of patients. With respect to long-term and multiple consequents of the lesions that will have a negative impact on patient quality of life, implementation of quality registry would be more appropriate. There are some considerations for this due to the special nature of medical condition, which is SCI, and development objectives. In this paper will be discussed on the key considerations. The study has been performed by discussion groups and brainstorming sessions as well as literature review on international experiences about develop and implement spinal cord registry. Key considerations for implementing the quality registry of SCI are related to defining detailed objectives, inclusion criteria for both traumatic and non-traumatic, methods for case finding according to distribution and movement of individuals across the country, identifying data sources, data registration and clinical assessments standards, processes, controls and auditing, confidentiality and administrative and technical infrastructures. Given the complexities that are available in the nature of injury, care and follow up processes and budget limitations, successful implementation depends on the appropriateness of the defined administrative structure, processes and quality control and registry auditing instructions with regard to key considerations that implied. In addition, the spirit of cooperation related originations and authorities, commitment to the principles of the program, comply with the ethical framework such as confidentiality and using the loop of feedback in the development process of registry are critical success factors for implement it.

## O19

### **Being a Neighbor to Syria: A Retrospective Analysis of Patients Brought to Our Clinic for Cranial Gunshot Wounds in the Syrian Civil War**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O19.

Our experience as a result of this war shows that early intubation, aggressive resuscitation and GCS score are important factors for survival. The time of arrival has great importance on mortality. Despite the diversity of views in the literature, patients with GCS of 4 and above should be operated if surgical pathologies exist, and decompressive craniectomy must be made wide. If duraplasty is necessary, fascia lata could be preferred considering the possibility that the galea may be contaminated. In craniocerebral firearm injuries in war, there are several factors affecting mortality. For that reason, we suggest that it may be appropriate to consider GCS as the basic criteria in assessments. The evaluation was carried out on 241 patients who were injured in the Syrian War and brought to, followed up and treated in the Neurosurgery Clinic of Mustafa Kemal University, Faculty of Medicine in Hatay, a Turkish city on the Syrian border, between April 2011 and October 2014. The physiopathology of the injuries, clinical findings, injury patterns (penetrating, perforating, tangential and superficial) and injury types (blunt trauma, bullet injury, shell fragment injury, mine injury, bomb, missile and blast) were investigated. For all patients, age, gender, Glasgow coma score (GCS), time to arrival at the hospital, Glasgow outcome score (GOS), CT images, cranial pathologies, postoperative complications, mortality and morbidity rates and surgical methods were evaluated. A total of 241 patients were evaluated in a period of more than 3 years. Of these, 87% were adults. The age of victims ranged from 2 months to 67 years with an average of 31 years. In terms of injury types, 148 patients (61.4%) had shell fragment injuries and 93 patients (38.6%) had suffered from bullet injuries. In terms of injury patterns, 91 patients (37.7%) showed penetrating injuries, 51 patients (21.1%) had injuries crossing both hemispheres at any plain, 39 patients (16.1%) had tangential injuries, 26 (10.7%) had perforating injuries, 6 (2.4%) patients had injuries from ricocheting bullets, and 28 (11%) had superficial injuries. According to admission GCS of the patients, GCS was 3 in 42 patients (17.4%), between 4 and 7 in 93 patients (38.5%), and between 8 and 15 in 106 patients (44%). 80 of the 241 patients (33.19%) died. In regard to distribution of the patients who died, in the surgical treatment group, all the 6 patients who had a GCS of 3

(100%), and 13 of the 72 patients who had a GCS score of 4-7 (18%) died. 2 of the 35 patients who had a GCS of 8-15 died (5.7%). In the conservative treatment group, all the 36 patients who had a GCS of 3 (100%), 14 of the 21 patients who had a GCS of 4-7 (66.6%), and 9 of the 71 patients who had a GCS score of 8-15 (12.6%) died. As it is seen, there is obviously difference between the mortality rate in the surgical treatment group and the mortality rate of the conservative treatment group, given the rates of surgical and conservative patients who had a GCS of 4-7. Our experience as a result of this war shows that early intubation, aggressive resuscitation and GCS score are important factors for survival. The time of arrival has great importance on mortality. Despite the diversity of views in the literature, patients with GCS of 4 and above should be operated, and decompressive craniectomy must be wide. If duraplasty is necessary, fascia lata could be preferred considering the possibility that the galea may be contaminated. In craniocerebral firearm injuries in war, there are several factors affecting mortality. For that reason, we suggest that it may be appropriate to consider GCS as the basic criteria in assessments.

## O20

### **Severe Traumatic Brain Injury Following Motor Vehicle Accidents: Pathogenesis, Pathophysiology and Prognosis.**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O20

Over half of all reported traumatic brain injuries are the result of a motor vehicle accident. Other than the direct head impact itself, the sheer forces of the accident can cause the brain also to collide against the internal bone of the skull. In fact, when a moving head comes to a quick stop, the brain continues in its movement, striking the interior of the skull. This can cause bruising of the brain and/or bleeding from vessels tearing. The consequences are immediate, with a scarcely predictable spectrum of lesions: from simple scalp lacerations (SLs), up to the most severe types of diffuse axonal injury (DAI). SLs can bleed profusely, causing dangerous acute hypotension and may act as a conduit for infection when associated with depressed skull fractures (SFs). SFs generally correlate with severity of injury, and patients with a SFs have a much higher likelihood of having an intracranial hematoma, such as extradural hematomas. Contusions are found to have a characteristic distribution, with the frontal poles, orbital gyri, the cortex above and below the Sylvian fissure, the temporal poles, and the lateral and inferior aspects of the temporal lobes. Lacerations of the frontal and

temporal lobes are frequently associated with acute subdural bleeding and/or intraparenchymal hemorrhage. DAI causes by itself 35% of all deaths after head injury, and may or may not be accompanied by intracranial mass lesion. Approximately half of severe cases of DAI exhibit focal lesions of the corpus callosum, the rostral brainstem, and microscopic evidence of widespread damage of the white matter. Urgent surgical candidates are those patients in whom a mass lesion is causing a significant mass effect. Radiographically, lesions are considerable when they are more than 25 cc of volume, and/or cause effacement of the basal cisterns or midline shift >5mm. More important, clinically significant lesions are those causing progressive neurologic symptoms. The decision to operate is based on a combination of the history of the trauma, significance of the patient's neurologic deficits, and the significance of findings on cerebral imaging. Prognosis for victims of severe brain injury has improved in the past two decades, with a decreasing mortality. Still, however, one out of two will face permanent neurological deficits. Undoubtedly, after the urgent surgical treatment that represents the crucial action to stop the "run against the clock", a better understanding of the pathophysiology and the development of new pharmacological strategies is mandatory. Continual improvements in the training of pre-hospital medical personnel, rapid transport of head injury victims to definitive care, and the increase of the Trauma Centers and Neuroscience Intensive Care Units will play a role in the next future.

## O21

### **Decompressive Craniotomy and Reconstruction with Cranioplasty: Perspective Study in 96 Patients**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O21

Autologous bone is considered the first choice as material of cranioplasty because of its biological and anatomical features. However in some situations such as skull fractures or tumors the bone flap is not available or it must be replaced with a heterologous cranioplasty because of the development of surgical complications. Authors of this study aimed to identify which are the best materials for cranioplasty and

which are the factors involved in the development of complications. Patients over 14 years of age and of both sexes that underwent the positioning of autologous and heterologous cranioplasty (Polyetheretherketone, Polymethylmetachrilate, Hydroxyapatite) between January 2008 and December 2013 have been collected after the analysis of neurosurgical registries of four different Neurosurgery Units of four Hospitals in Italy. For all these patients data about complications were prospectively collected. 96 patients met the study criteria. 7 patients (7.29%) developed complications which required re-operation. Complications included infection (4 cases), bone resorption (2 cases) and fracture of the cranioplasty (1 case). Statistical analysis of the factors revealed a relevance in the use of autologous bone compared to heterologous materials in the development of complications ( $P=0.3710$ ). No statistical significance has been revealed from the comparison of primary and secondary cranioplasties with heterologous materials. In order to predict which material is better to use for a cranioplasty, our experience suggests that cranioplasties with heterologous materials are burdened by a lower rate of complications compared to the autologous bone flap.

## O22

### **Report of the Milan Consensus Conference About Clinical Applications of Intracranial Pressure Monitoring in Traumatic Brain Injury**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O22

In recent years, the usefulness of intracranial pressure (ICP) monitoring has been questioned in several reports for traumatic brain injury (TBI) management. Therefore the needs of multidisciplinary groups of discussion of neurosurgeons and neurointensivists to update practical applications of ICP in severe adult TBI has been advocated in many parts of the world. A consensus conference was held in Milan on October 5, 2013, putting together neurosurgeons and intensivists with recognized expertise in treatment of TBI. Four topics have been selected and addressed in pro-con presentations: 1) ICP indications in diffuse brain injury, 2) cerebral contusions, 3) secondary decompressive craniectomy (DC), and 4) after evacuation of intracranial traumatic hematomas. The participants after elaborating the existing published evidence (without a systematic review) and their personal clinical experience provided some drafts. After

remarks and further contributions were collected, a final document was approved by the participants. The group made the following recommendations: 1) in comatose TBI patients, in case of normal computed tomography (CT) scan, there is no indication for ICP monitoring; 2) ICP monitoring is indicated in comatose TBI patients with cerebral contusions in whom the interruption of sedation to check neurological status is dangerous and when the clinical examination is not completely reliable. The probe should be positioned on the side of the larger contusion; 3) ICP monitoring is generally recommended following a secondary DC in order to assess the effectiveness of DC in terms of ICP control and guide further therapy; 4) ICP monitoring after evacuation of an acute supratentorial intracranial hematoma should be considered for salvageable patients at increased risk of intracranial hypertension with particular perioperative features.

## O23

### **Polytrauma with and without Neurotrauma: Experimental Animal Studies with Clinical, Immunological and Histopathological Features**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O23

Although the majority of the patients with traumatic brain injury presents with injuries involving the extremities, there was a clear paucity of adequate experimental polytrauma models. To close this gap, we conducted several studies to establish two different polytrauma mice models including both closed and open traumatic brain injury. Male C57BL mice with a mean weight of 23g were anesthetized with ketamine and xylazine. The anaesthetized animals were subjected to a controlled cortical impact (CCI)-(n=20) over the left parietotemporal cortex using rounded-tip impounder for application of a standardized brain injury. Following fracture of the right femur using a guillotine, a hemorrhagic shock was induced via blood aspiration. The control groups included animals with isolated CCI (n=20) and animals with fracture of femur plus hemorrhagic shock (n=20). The second model included weight-drop injury with femure fracture and hemorrhagic shock (n=20), isolated weight-drop (n=20), femure fracture and hemorrhagic shock (n=20). All subjects were sacrificed 96 hours following trauma. Intracardial blood samples were taken before. Brain, kidney, liver, lung and spleen were taken for histopathological examination. The inflammatory response measured by Il-6, TNFa, CD4+ and CD+8 cells was stronger in the polytrauma group, in comparison with the control groups. Within the histopathological investigations,

polytraumatized animals differ from those with a single trauma (traumatic brain injury or femur fracture with hemorrhagic shock) with various severity. The findings of the studies show that such polytrauma models can be standardized resulting in a reproducible damage. These models fulfill the requirements of a standardized animal model. It allows adequate analogies and inferences to the clinical situation of polytrauma in humans. It opens promising capabilities for more evaluation of possible posttraumatic drug therapy, heterotopic ossification and also studies with knock-out mice.

## O24

### **Management of Road Trauma Sufferers in Iran Accidents' Casualties**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O24

Iran is one of the countries with a high rate of accident casualties in highways and cities. We are amongst the pioneers in accident related deaths and casualties in the world. In just 2014, road and highway casualties and fatalities were 315,719 and 17,994 respectively. Motorcycles passengers and pedestrians are the main victims of these casualties. Definitely, by appropriate measures, the suffering of many of these trauma victims could be diminished. In our country, many facilities and instruments for this purpose are available, but are not used to their full potential which leads to higher traffic casualty and losses. Unfortunately, it takes between twenty minutes to five hours to transfer the accident victims to hospitals and consequently, many of them lose their life during this process. Many approaches could be used to overcome these problems such as improving highway and road qualities, educating the public regarding correct driving habits and better rescue team training. Fortunately, advanced trauma life support (ATLS) training classes are offered in Iran. By further expansion of these courses in different parts of the country, more victims of accident related traumas could be saved.

## O25

### **Orthopedic Trauma Surgery and Polytrauma Treatment in Germany and IRAN**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O25

Management of traumatized patients after road accidents is in many countries still a serious challenge. Apart from

technical problems in management of car accidents, the recovery and rescue of the patients and their transport to hospital need exact planning and efficient strategy. Present lecture compares the trauma management in an industrial country like Germany with this in Iran. Present work analyses the key points and step by step in management of trauma patients after road accidents in both countries. The medical aspects (emergency medicine) stands here in the centre of our focus. We hope, the present lecture helps us to better understand and optimize the management of injured traffic participants.

## O26

### **SOS System, National Initiation to Improve Emergency Services: Problem Solving in Iran**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O26

Dealing with life-threatening situations requires the quickest, most effective response. Each time the emergency phone number 115 is dialed, EMS is ready to act and dispatch the rescue services needed. Whether it is a fire, road accident, crime or medical crisis, the caller in distress should receive support from emergency services and lives should be saved. To be able to meet the required response times and to handle every complex situation, related studies showed that there are a lot of problems in emergency services in Iran such as: the lack of planning, Inadequate organizational management of resources, Insufficient coordination in the provision of health services in emergency and disaster, duplication efforts, wasting resources, wasting time: response time, organizational conflict, and most important different Emergency numbers with different dispatch system. This study has been done to develop integrated dispatch system between EMS, Fire brigade, Red Crescendo, Traffic Police and Road maintenance organization. This study has been done using multi method approach including, individual interview, FGD, Expert panel and reviewing international experiences. Study showed that developing PSAP: Public Service Answering Point (SOS) with integrated dispatch system can solve a lot of coordination and cooperation problem and improve the quality of care for people who needs life saving emergency services. The concept of providing emergency care for the seriously ill is one of the measures of a civilised society. Throughout the world, the emergency medical systems have been focused on the delivery of care to life-threatening emergencies. The provision of organised prioritisation and dispatching systems is the first step in the delivery of emergency medical support in the prehospital setting. Emergency medical dispatching

(EMD) with a single common number can play crucial role in saving life and improving quality of care in life treating situation.

## O27

### **Prevention of Road Crashes in Iran**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O27

Without any doubt, road safety (RS) needs a precise planning in road accident prevention. RS effects on different fields of the life. Therefore, response to this need in order to promote the RS as well as to save more lives is the most asset in each country. In the recent years, statistics have been shown that the numbers of mortalities due to road crashes decreased. This shows the true motion to improve the roads facilities and safety. It can be useful in all sectors and area in road engineering and cultural and social fields. In this regard, some points need more attention in RS such as to recognize the black spots, to arrange the police forces in appropriate situations, to interact with relevant organizations, to prepare the traffic signs.

## O28

### **The Study of Mortality Due to Car Accidents in Ten Years in Iran from the Point of View of Forensic Medicine**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O28

Accidents in the world today are a social problem. Disability and property damage accidents caused much appreciated. Anticipated traffic deaths in 2020 and placed third. This study is a cross sectional study from 2002 to 2011. All the victims were examined following the accident sent to the Forensic Medicine the questionnaire has been used in order to collect all data. After completion, the SPSS software has been used for analyzing data and the K&T has been used for assumptions test. Form the total number of 241236, 80.4% male and 19.6% female, One third of the victims were aged 18 to 29 years. During 2007 to 2011 the rate of 50.7% on the scene, 38.9% in hospital and 8.9% died during transport to hospital. Most died in the hospital is Tehran of Province (48%) and most died in transit is to Province of Kurdistan and the highest died at the scene is Ilam of Province (64.2%). The most common cause of death was trauma to head (55.2) and multiple fractures were to 33.7% and bleeding with 6.4 percent. In this study 24.2% of pedestrian and Tehran Province's highest

numbers, male 72.9% and. The average age of 50 and 44.9% was illiterate. 25.7% of vehicle used motorcycles. According to the research Authorities should plan to reduce the mortality of pedestrians and motorcyclists, and investigate the cause of death of the victims in transit and to hospital. Is it considered medical malpractice or lack of equipment or specialized personnel?

## O29

### **The Study of Negative Effects of Air Pollution on Serotonin Receptors (5HTR2a and 5HTR3a) and Mono Amino Oxidase A Gene Expression Alterations in Exposed Individuals and its Association with Urban Traffic Accident**

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*The Neuroscience Journal of Shefaye Khatam*, 2015; 2(S3): O29

In recent years, with the rapid development of science, especially Neurogenetics, we could find different genes, especially genes that influence our behavior and cause behavioral changes. Culture is one of the important factors in urban traffic and correct way of driving But this is only effective when the biological conditions are healthy and with appropriate interaction of an endogenous gene and an appropriate biological and psychological balance in person. Serotonin and receptor genes and enzymes that control this neurotransmitter are one of the major factors controlling the behavior, thus were selected as target genes in this study. In this study, according to the municipal air quality control center most polluted parts of the city in 2012 were revealed. Blood samples were collected from Individuals who are deployed for 6 months from September to March in the contaminated areas. The PBMCs were extracted and RNA isolated and through reverse reaction cDNA synthesis was performed. Then, using the specific primer pairs, 5H2Ra, 5H3Ra, MAO and B-Actin genes were measured and amplified By the Real- Time PCR. For statistical analysis REST software was used ,then by comparing the gene expression levels in healthy individuals and individuals located in contaminated area in Tehran The results confirmed statistically significant changes in the genes serotonin receptors 5H2Ra, 5H3Ra that regulate mood and behavior. But there was no significant change of mono amino oxidase enzymes which control serotonin. Due to significant changes in the genes that are responsible for controlling our behavior, there was a stress-strain behavior in people who have a track daily traffic jams, and pollution area compared with individuals outside the city. This behavior leads to restlessness, impatience, and non-compliance with laws and regulations. Thus, it leads to conflict with

each other or officers of the law and will create a high risk of accidents. In respect with this study, Further studies are necessary to prevent human injury .It is also recommended that the traffic police forces also used as rotation in the affected areas to be less susceptible to the damage caused by air pollution.

## O30

### **Sleep Disorders and Traffic Accidents**

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*The Neuroscience Journal of Shefaye Khatam*, 2015; 2(S3): O30

One of the leading causes of death and disability in the Middle East is road traffic accidents. There are multiple factors that cause these traffic accidents, and the most important of which is fatigue, drowsiness and lack of concentration. The risk of road traffic accidents due to sleepiness, which were reported by police, increased by more than sevenfold in low alertness hours during circadian rhythm (0-6 A.M.) compared to other times during the day. The risk of road traffic accidents due to fatigue and sleepiness decreased in hours with maximum of alertness (6-10 P.M.) of circadian rhythm compared to other times during the day. Public health officials, road traffic designers and the police should co-operate in an interdisciplinary method to implement the proven effective measures to lower this increasingly heavy social and economic burden. Sleep and fatigue-related vehicle accidents are not only more common than is generally realized, but are more likely to result in death and serious injury owing to the relatively high speed of the vehicles on impact. To examine and address this public health issue, a screening program for drowsiness in commercial drivers is under development. Driver's sleepiness due to sleep disorders are an important preventable cause of morbidity and mortality. Screening of commercial drivers is a topic of growing interest in occupational sleep medicine.

## O31

### **Head Injury in Road Traffic Crashes in Iran: a Cross Sectional Study**

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*The Neuroscience Journal of Shefaye Khatam*, 2015; 2(S3): O31

Road traffic injuries (RTIs) are a leading cause of death and disability worldwide. Head injury is one of the most important causes of death in various types of road users particularly among motorcycle and bicycle riders. Epidemiological pattern of head injury among victims

of road traffic injury can improve road safety measures and it is an implication for any intervention. The current study was designed to map epidemiology of head injury as a result of road traffic injury in Iran. A cross-sectional study was designed among fatal road traffic injury those registered in a national database called Forensic Medicine System. Data collection was between 23 March 2011 till 23 March 2014. There were 20069 fatal road traffic injuries in the study period. Finding of study indicated that 88% of fatal RTIs were men and more than 87% of fatal road traffic injury had head injury. Close to 25% of head injured were illiterate and around 44% were at primary and secondary school. Only 10% had higher education. The most important cause of death was head injury (60%) following by multiple-trauma (28%) and internal bleeding (12%). Among them, 58% of death occurred at crash scene and 45% at pre-hospital and hospital phase. Moreover, 76% of fatal road traffic injuries were car riders and 23% of them were pedestrian. Close to 80% of victims were transported by ambulance system. There is various measures for head injury prevention in Iran that are included speed management, wearing helmet and seat belts as well as crashworthiness and improving visibility in all car riders particularly for pedestrian. Severity of injury is one important cause of death. However, regarding post crash care it is also an implication for preventable death study in Iran.

## O32

### **Crash Analysis: Powerfull Tool to Assess Vehicle Safety**

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Motor vehicle crashes are among the leading causes of traumatic injuries and mortalities in Iran. Understanding the injury process is the first step to predict and later on preventing the injuries. Among the main factors that are defined as the cause of a motor vehicle crash (human, road, and vehicle), the vehicle performance is one the most important factor that contributes to the injury since traumatic injury is defined as a process rather an event. Crash investigation and evaluation of the vehicle performance are the basic elements that define the injury causation scenario. The process of crash investigation combines the collected data from the crash scene with professional multidisciplinary analysis of medical and engineering evidence to determine the injury causation in every case. This process aims to improve the prevention of motor vehicle crash injuries to reduce deaths, disabilities, and human and economic costs.

## O33

### **The “Hub & Spoke” System: a Model of Integrated Neurosurgical Trauma Care System**

### **in the Geographical Area of Western Emilia Romagna, Italy**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O33

Guidelines for the management of severe traumatic brain injury (TBI) have been published both in the USA and Europe. Unfortunately, none of these guidelines contain clear statements about which patients should be admitted to a neurosurgical centre. Neurosurgical care is limited in many parts of the world to one or two Hospitals serving a large geographical area. Therefore still under debating is about the best TBI management between the centralization of all patients in one neurosurgical hospital (NSH) or the selection of the patients in a previous general hospital (GH) rough telecounselling after trauma. The quality of the imaging, the feasibility of the sharing-pictures softwares play an important role on the efficacy of TR. The technological knowledge should be rapidly upgraded in the cultural background within healthcare organizations. The referral protocol of the patients is another important aspect of TR, but the developing of guidelines is depending from the different scenarios where the TR could be applied, even in rural areas and in metropolitan healthcare system. The combination of teleradiology and guidelines for head injury management could allow in so different areas a better selection for patients’ referral to Neurosurgery. The “Hub & Spoke” system provides one high specialized trauma center (Hub) and several peripheral hospitals (Spokes) all connected with telemedicine systems and equipped with shared protocols for the management of the patients. The authors report the territorial organization of TBI management in an area of 1.200.000 people, in the western part of Emilia Romagna region, Italy. The Hub is a II level trauma center, with high expertise for any traumatic complexity, with neurosurgeon on duty 24h. The Spokes are dislocated in nine general hospitals with a lower helath care level in the treatment of trauma patients, with emergency facilities and CT scan 24h. Moreover, as specific feature of this regional rauma system, one Spoke is a trauma center of I level with neurosurgeon on duty from 8 a.m. to 8 p.m. and on-call during the night. The Hub and the Spokes are connected with differents telemedicine systems, through a radiology information system (RIS)/picture archiving and communication system (PACS) off site workstation and server connection. Patients with severe TBI or with complex polytrauma need management in the Hub. Patients with mild TBI can be managed in hub and in

Spokes with similar results if specific area protocols are applied. The patients with spine trauma can be managed in the Spoke with neurosurgical facilities as in the Hub, if prompt treatment is required. Otherwise the treatment is planned according to area protocols.

### O34

#### Adaptation of Traumatic Brain Injury Clinical Guideline in Iran

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O34

Traumatic brain injury guidelines of two well-known sources were selected for adaptation in Iran. In this brief report, we aimed to highlight our modifications according to domestic situation of a developing country. The guidelines were selected using the AGREE (Appraisal of Guidelines for Research & Evaluation) instrument. Fourteen Iranian expert neurosurgeons reviewed all key recommendations, related levels of evidence were evaluated and possible revisions were considered. Following items were the most challenging which were modified according to domestic situation: Age as a risk factor for referral or computed tomography scan, medical comorbidities and pregnancy, consultation and referral to a neurosurgical unit, teleconsulting and observation before discharge. Modifications in these topics were done based on experts views and very limited and controversial evidences. This report underlines the

importance of further studies in Iran to fill the current knowledge gap.

### O35

#### Psychological Evaluation of Traffic: Computer-Based Assessment of Fitness to Drive Safety and Mobility in Road Traffic

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O35

Considering the large number of car accidents happening in Iran raises concern about the causes of them. Three categories of environment, vehicle and human errors are the main reasons lead to car accident. Human errors by playing the main role, cause 60 percent of car accident directly and contribute in 85 percent of cases. Human error is the result of many different issues in related to personality, human thought, attitude, behavior, and cognitive, sensory and motor abilities which together effect drivers' performances. Evaluation of these aspects by either paper based or subjective tools is inaccurate, time consuming and very difficult. There are some software packages which are helpful for evaluating these parameters such as Vienna that is being used by more than 2400 traffic centers. These packages assess attention, cognitive ability, reaction and visual performance, sensory- motor factors, and personality characteristics related to driving. All of these packages are based on local culture and regulations. Necessity of redesigning and localizing these kinds of packages, in order to be used in Iran and control the car accident reasons, is an undeniable fact.

### O36

#### Three-Dimensional Transplantation of Adult Neural Stem Cells in an Acute Brain Injury Model

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O36

Brain injury is the leading cause of death and disability in the most active population. There is no definite clinical treatment for repair of damaged brain tissue. Application of nanoscaffolds supporting stem cells can be helpful. The present study examined the effects of autologous adult neural stem/progenitor cells (NS/PCs) seeded in PuraMatrix in acute brain injury. The right brain subventricular zone of adult wistar rats was stereotactically harvested. Then, NS/PCs were cultured using neurosphere assay. At day 45, brain injury was performed in left side of brain and PBS, PuraMatrix, NS/PCs or PuraMatrix+NS/PCs was injected into the created cavity. The neurological status was evaluated for 4 weeks. Then, morphological and immunohistochemical studies were done. The neurologic status improved after treatment of brain injury with PuraMatrix, NS/PCs or PuraMatrix+NS/PCs. The lesion volume was decreased in PuraMatrix+NS/PCs. By 3D transplantation of NS/PCs, not only the rate of inflammation was reduced but also the survival rate in the site of injury was increased. In addition, the transplanted cells expressed the differentiation markers after 4 weeks. Transplantation of adult NS/PCs in PuraMatrix may be a feasible method for reduction of tissue damage following brain injury.

## O37

### Justice in the Health of the City

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O37

Justice gap have been suggested as one of the most important effort in matter of improving urban health. Among some major documents significant relation between the living conditions and health level is found. There is long time that World health organization has identified the importance of equity. Based on information of this organization in 1999, equity in all nations is the most critical point to reach justice. Equity in health can be described as the having same chances of all people to have the highest and best health status. This requires an action to reduce justice gap in health status among the citizen of a city or a country. In 21 century reduction of these gaps to reach equality in health service require Intensive Corporation. In this regards, some action have been done by Tehran Town

hall to reduce justice gap and improve health status. The most important one include performing justice intervention in Tehran different towns. In order to do this at the first step an instruction should be set up and send to various sites of city to be used. Moreover, in different stages of action required qualification should be done. Regarding to town hall policy to enhance active social cooperation for reaching the best health condition, a program for improving health system and reducing social and justice gap between different regional and local group in 20 states have been started.

## O38

### Citizens Participation and Empowerment in Solving the Urban Problems

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O38

Empowerment of citizens defined as providing chances and experience which allowed active involvements of participation in decisions making and programing. However, lacking an accepted program which could involve active collaboration of all citizens is feeling. Wide definition from the citizens' cooperation is the most critical problem. Collaboration of citizen without knowledge and experience is impossible. The second major discussion of programmers and specialist in decision making in order to involve citizen association is the concern which they have about future exception of citizen involving in other matters and problems. It seems that citizen cooperation could provide programs stability and expand social justice in city local and could empower citizens, however previous information about such cooperation is rare. The third and the most important discussion are finding a way which through designer and programmer could be able to use the capacity of citizens. Put this together, without association of citizen of local in different cities, a complete and powerful controlling of city and providing a useful program is not possible. Still, most of researchers are doubtful about aforementioned cooperation's consequences and believe that this may be dangerous as the specialists are not sure weather in long term such cooperation could help. Experts are worry that if the situation change or mistakes happen this could cause problem for citizen who is involved. Base on previous experiences, attitude, belief and ordinary behavior among the expert, they believe in level of power as their right and maybe they are not willing to share their power with citizen. Therefore, continuing such cooperation and using from its numerous advantages will be impossible.

## O39

### Improvement of Public Awareness and

## Reduction of Traffic Accidents

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O39

Nowadays, there are an increasing number of people who lived in city, which made more usage of vehicle. However, these may have a lot of advantage but there should be a culture promotion in order to reduce road and traffic accident. Road crash have significant impact on society, culture, and economy of a nation. One of the major problems in this regards is the lack of knowledge about the importance of this matter. Road crash damage up to 6-8% of gross domestic product of a country and could destroy economy. However, based on resistive economy policy, enhancements of safety culture among nation and society could have significant correlation with sustainable development and improvement of life levels in society. Based on our studies which were done we found that road accidents are the ninth cause of human death around the world, however in the Iran it is the second cause of human death. Average ages of Victims are almost between 15 to 44 years old. Furthermore, 79 % of deaths are men. The crash of two car with each other include 48% of death and 30% of this accident mostly are due to fatigue of drivers. Human mistake which lead to road accident and crash are including: Widespread disease and effects of drug usage and addictive drugs are the most important one for diabetes, high blood pressure, somniferous drugs and etc. Psychology problems and mental disorders are the other one such as stress, aggressive driving, anger and others. Special situation of driving including driving at night or in the winter and etc and also lack of knowledge of people. Road accidents are one of the major causes of death in Iran and the important point in this regards is to establish some policy which could be as Precautionary policy. In this regard, using effective potential of our society such as social workers can make a significant difference. This will change anti-social attitude of some people who think that why I should obey all of the traffic roles. This people are thinking that I should change the social as well as traffic role and adopt them to their own Idea. Therefore, there should be some permanent education for different ages from children up to elder consist of various themes such as Safety, first aid, psychology accident in order to enhance social culture. Moreover, test of safety, precaution of accident and analyze of psychological state of drivers before giving them driver license should be done. We should also name a day of year as a national day of reduction in road accident and crash to absorb the attention of different social group to produce new idea about road safety.

## O40

### The Role of Citizens in Reduction of Traffic Accidents

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O40

Association of citizenry is known as a major factor in order to reach developmental goal, especially urban development. As much as higher cooperation of people in their own urban developmental could be absorb, there will be higher percentage of success. Now day cooperation of people in their own urban development is a critical factor, critical to make a persistent urban development. When the people association is considered weak point and positive point, chances and threats are more necessary to be evaluated. In modern city management and in the world, which are consistently move toward urbanization, citizenry association are so important. Aim of the present study was prevention of road accident and crash through emphasizing on the active role of citizen cooperation. For this purpose, number of 30 adult citizen of a region in Pasdaran town as a voluntary group, who had taken a part in an organized program were selected and various class set for them. At the end of the programs with respect to the survey which have been done. We concluded that citizen have an active role in management of their own areas and were satisfy from the administrative process. This clearly represented that such association by enhancements of two side responsibility feeling could have significant impact and could lead to positive outcome. Finally, partnership and involvements of citizen in the process of programing could guaranty successfulness of city management.

## O41

### The Role of Public Intervention in the Prevention of Traffic Accidents in Zibadasht Area, Tehran, Iran

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O41

Priorities which have been selected were in order to run the analyzing program of health house of Zibadasht about the factor of road safety. This study was based on couple Matrix among priority of selected studies. Results are from personal and group interview with fire

officials, traffic police and crisis Management Staff of 22 districts about the causes of traffic accident and a field visit from various highways and autobahns which were placed in Zibadasht were another factor of choosing this methods. With respect to this point that the significant number of accident and crashes was due to such a high ways in this region. Reduction in the number of traffic accident require consideration and policy which limit insecurity, which in association with education and cultural programs provide high expectation regarding to significant reduction in number of traffic accident. However, it should be mention that after personal and group interview with locals and identification of problems and discussion with police station and fire station elimination of traffic problems was suggested as the second solution. Therefore, we decided to make some pedestrian bridge at some critical sites, set up some traffic sign, some mirror to enhance drivers vision in entrance of underpass and cutting some tree, which reduced drivers vision in site of turn. Moreover, some class in Mosque, university was hold to enhance information of locals about traffic safety and about 70% of local was attended in these programs. These programs have made significant impact on locals' information. Important and positive point of choosing this priority included: 1. Involvement of people in finding a solutions, 2. Reinforcement of group collaborations, 3. Enhancement of safety and security and 4. notification of citizen about traffic accident. However, negative point included: 1. Difficulty in absorbance of organizations association, 2. weakness of school collaboration and 3. absence of goof facility. Intensive monitoring on traffic rules performance, modification of infrastructure, survey from local about running of construction project, making some safe place for local to pass the highways, good emergency services, set up some traffics signs, paying more attention before construction of highway.

## O42

### **The Role of Public Intervention in the Prevention of Traffic Accidents in Sazman-e Barnameh Area, Tehran, Iran**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O42

Every day thousands of people are losing their life or injured during road crashes. Therefore, it has high priority to set a strategy in order to reduce the number of death and injured people of road accident. Four important factors in road safety including: 1. Safety belief, 2. respecting of roles, 3. Access to safety requirements and 4. Knowledge

of the correct use of safety devices. After analyzing and considering the result of our result in the north program in the Aban of 2013 in cooperation with development committee and a discussion and study on final factor of the program and regarding to this point that the rate of traffic accident in the north program was 4.8 % and the average in Tehran was 8.7% and in the fifth region was 7% higher, This factor with acceptance of Board of Trustees and member of developmental committee by using of couple matrix were selected as a priority of intervention. In addition, absence of zebra crossing line and lack of safety requirements was selected as another important factor. Total aim of choosing road accident was prevention of traffic accident which included: 1. Reduction in the number of traffic accidents, 2. Decrease in the number of traffic accidents death, 3. Decline in the number of traffic accidents injuries and disabilities and 4. reduction of financial burdens of road accidents. The methods of gathering information included personal and group review and also brainstorming method in order to identification of causes and offering of solutions was done. Then, intervention team in order to collect the idea, have suggested these programs for intervention. 1. Organizing different period of classes for road accident from the psychological point of view, 2. Holding some classes for traffic accident form the point of road, driving, vehicles and distribution of some Leaflet, 3: The attendance of children in Traffic Park (As a learning program) and 4. Organizing different period of classes in cooperation with bus drivers and 5. Organization of some meeting to set up some Signs and warning signs. In this program 40 number of citizen of town were participated, which have average of 35 years old. Included: 10 people with master degree, 7 with advanced Diploma, and 23 diplomas. From the number of 40 person who have taken part in this program. The number of 23 had a continuous attendance. The children of 18 attendances have taken part in traffic park have satisfaction.

## O43

### **Reduction of Road Crashes in Public Transportation**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): O43

The project is defined in order to reduce accidents caused by drivers of public vehicles. In the first phase, we will hold the educational workshops with drivers of public vehicles. The teachers of these workshops are the best professors in the field of road safety. The main topics of the program are non-standard roads and drowsiness, nutrition and drowsiness, sign and symptoms in sleep medicine, prevention of drowsiness, and conditions of inside the car.

## Workshop Presentations

### W1

#### Animal Models of Traumatic Brain Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): W1

Traumatic brain injury (TBI) leads to tissue damage by primary and secondary mechanisms. Several factors such as location, nature and severity of the primary injury, age, health, sex, medication, alcohol and drug use, and genetics influence the pathophysiology of TBI in clinic, so TBI is a heterogeneous event and consequently, TBI modeling faces some difficulties. In the fluid percussion injury model, a fluid pressure pulse is generated to the intact dura through a craniotomy and produces a combination of focal and diffuse neuronal injury. The controlled cortical impact injury model uses a pneumatic or electromagnetic impact device to drive a rigid impactor onto the intact dura and creates tissue loss, haematoma, axonal injury and concussion. In the penetrating ballistic-like brain injury, projectiles are transmitted with high energy to produce a cavity in a defined area of the brain. In the weight-drop model, a weight falls from specified height. In the blast brain injury model, trauma can be caused by the primary injury related to the blast. By choosing a proper animal model, we can address the biomechanical aspects of brain injury and assess the potential treatments.

### W2

#### An Animal Model of Brain Injury for Evaluation of Tissue Engineering Treatment Strategies

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): W2

Brain injury is a complex event leading to tissue damage and functional deficits by primary and secondary mechanisms. Since the application of tissue engineering

approaches is a new topic in the treatment of brain injury, producing a proper experimental model to evaluate the effects of tissue engineering products on damaged brain tissue is required. In the present study, a simple and reproducible model of brain injury was introduced. Adult Wistar rats were anesthetized by ketamine and xylazine and their heads were fixed in stereotaxic device. Then, after prep and drape, a midline incision was made in the skull skin by surgical knife. Using a dental drill, a rectangle window was made in the left side of the skull bone. After removing the dura mater by a micro scissors, a defined cavity was created in the cortex of the left hemisphere by slowly inserting a rotary biopsy punch with 2 mm diameter into the cortex. Following performing treatments (neural stem cells + a hydrogel scaffold), to repair of the dura and consequently prevent leakage of materials, we used a piece of the loose connective tissue located between skull bone and skin as well as a piece of dural path. Finally, the skin was closed by 2-0 surgical suture. Neurological evaluations were performed using modified neurological severity score for 28 days. Histological analysis was done after one month. This method produced a mild brain injury model and created a defined cavity in the brain cortex. The cells transplanted in the cavity survived after 28 days. We introduced an applied animal model of brain injury for evaluation of tissue engineering treatment strategies.

### W3

#### A Controllable Brain Injury Model with a Defined Size for Evaluation of Tissue Engineered Products

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): W3

Brain injury has a multiple pathophysiology for which there is no definite treatment. In this regard, tissue engineering is one of the probable strategies for repair of damaged tissue. But creating a proper model for testing the engineered products faced some difficulties, specially, when we want to evaluate the effects of a product on the volume of injury. The current brain injury methods couldn't provide defined brain tissue damage. We propose a new method to solve the problem. Previously, we introduced a new method for harvesting subventricular tissue from adult rat brain using a modified semi-automatic biopsy needle. We showed that

a defined volume of tissue harvested from a specific area of brain without any adverse effect on other regions. We suggest using this biopsy procedure for creating a brain injury model with a defined size. Using this controllable biopsy method, we can test engineered products in a rat model of brain injury and assessed the volume of cavity after performing treatments in different groups.

#### W4

### A New Animal Model of Traumatic Brain Injury in Rat

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): W4

This study was designed to develop a modified TBI weight drop model for induction of focal mild cerebral injury. A stereotaxic coupled weight drop device was designed. Principle arm of device carries up to 500g weights which their force was conveyed to animal skull through a thin nail like metal tip. To determine the optimal configuration of the device to induce mild TBI, six different trials were designed. The optimal configuration of the instrument was used for evaluation of behavioral, histopathological and molecular changes of mild TBI. Histological studies revealed a remarkable increase in the number of dark neurons in trauma site. TBI increased the expression of apoptotic proteins, Bax, Bcl2 and cleaved caspase-3 in the hippocampus. Our designed TBI device is capable to produce variable severity of TBI from mild to severe. The main advantage of the new TBI model is induction of mild local unilateral brain injury instead of traumatization of the whole brain. This model does not require craniotomy for induction of brain injury. This novel animal TBI model mimics human mild focal brain injury. This model is suitable for evaluation of pathophysiology as well as screening of new therapies for mild TBI. Details of this study were published (Ghadiri, et al. 2014).

#### W5

### Animal Models of Spinal Cord Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): W5

Spinal cord injury (SCI) leads to a significant health problem associated with a broad range of secondary complications and disabilities. In this regard, animal models can help us to understand the pathobiology of SCI and evaluate the effects of potential treatments for SCI. In contusion models of SCI, different devices including surgical spring-loaded clips, balloons, forceps, weights and the computer-controlled reproducible impact contusion devices were used to create a defined lesion in the spinal cord. To evaluate treatments that target axon regeneration or in case of implantations, transection models may be utilized in which an incision is created into spinal cord. The transection may be complete or incomplete. The unilateral hemisection injury can be a good alternative to complete transection in which structural integrity, function of one side of the spinal cord and bladder and bowel function were preserved. By choosing an appropriate SCI method, we can test numerous possibilities for novel therapeutic strategies before clinical investigations.

#### W6

### Self-Assembling Peptide Nanofiber Containing Biologic Motif Induces Neural Differentiation, Tubulin Polymerization and Neurogenesis; In-Vitro, Ex-Vivo and In-Vivo Studies

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): W6

Spinal cord injury (SCI) in humans remains a

devastating and incurable disorder. A very important obstacle in axonal regeneration after spinal cord injury is astroglial scarring. The use of self-assembling peptide nanofiber, a hydrogel mimicking extracellular matrix, has been suggested as a scaffold for spinal cord regeneration and inhibition of astrogliosis. However, neurogenesis potential of laminin has been proved. The purpose of this study was to investigate the role of self-assembling peptide nanofiber containing long motif of laminin (SAPN-LL) in neural differentiation of human endometrial-derived stem cells (hEnSCs) in-vitro, in polymerization of tubulin isolated from sheep brain ex-vivo and assess the supportive effects of this hydrogel in an animal model of SCI. Results showed that although nanofibers strongly differentiated hEnSC towards neuron and there were not significant differences between their neural differentiations but motor recovery results demonstrated that concentration of laminin influences motor recovery and tubulin polymerization. However, both of in-vitro and in-vivo results showed that SAPN-LL inhibited astrogenesis. Based on our results it might be concluded that, SAPN containing long motif of laminin holds great promise for spinal cord injury.

## W7

### In Vitro Traumatic Brain Injury Models

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): W7

Traumatic brain injury (TBI) is caused by rapid deformation of the brain, resulting in a cascade of pathological events and ultimately neurodegeneration. In vitro models of TBI can help us to describe the pathobiological mechanisms. In vitro models of brain injury support a platform for performing repeatable, well-controlled, environmentally isolated experiments. Other advantages of in vitro models of injury are monitoring in real time and evaluation of specific region. Acute preparations, organotypic cultures, dissociated primary cultures, and immortalized cell line have been used to study neural injury in vitro. Several in vitro models of TBI have been designed, they include the following: Transection: in vitro transection models leading to axotomy. Compression: this model of TBI can be induced primary and secondary injury by the impactor. Hydrostatic pressure: using transient or static

pressure, deformation is induced. Fluid shear stress: culture cells have been deformed using a fluid shear forces. Shear strain: in vitro shear strain model has been simulated for closed-head TBI. Stretch injury models: in vitro models of Stretch injury have been developed to reproduce the mechanics which occur during in vivo TBI. Using appropriate in vitro models, we can understand mechanisms of injury in details and evaluate the effects of potential treatments.

P1

**Comparing Emotion Regulation Difficulties in Mild Traumatic Brain Injury Patients and Normal People**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P1

Emotion regulation difficulties are from the factors that caused the incidents and automobile accidents and work related. This study aimed to comparing emotion regulation difficulties in mild traumatic brain injury (TBI) patients and normal people in Kashan. The study was performed on 30 TBI patients referred to Shahid Beheshti Hospital in Kashan city and 30 normal people in Kashan. TBI patients and normal people were selected by convenience sampling. Two groups filled out the demographic sheet, the difficulties in emotion regulation scale (DERS). The data was analyzed by SPSS-19 software with multivariate analysis of variance. The results of this study showed there were significant differences between TBI and control groups in total scores and subscales of DERS ( $F=58.80$ ,  $P=0.00$ ). Based on the survey results there is significant difference between the mild TBI and control groups in emotion regulation.

P2

**Correlation between Working Memory and Mental Disorder in Traumatic Brain Injury Patients**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P2

Working memory impairment is one of the most important cognitive deficits in patients with mild traumatic brain injury that affect mental health status even in the early stages of the disease. The purpose of this study was to evaluate the correlation between the working memory and mental health status in traumatic brain injury (TBI) patients. This cohort study was performed on 50 TBI patients and 50 healthy (control) participants. Working memory and mental health status were assessed using Wechsler adult intelligence scale and the brief symptom inventory (BSI), respectively. Results showed a significant difference between the two groups in the means of working memory in both auditory ( $P<0.001$ ) and visual span ( $P<0.0001$ ) as well as mental disorder ( $P<0.04$ ). Moreover, logistic regression analysis showed that TBI disease had an impact on components of mental (OR= 0.929 and CI= 0.857-0.998). Findings of the study indicate that cognition is an effective factor to engage in activities of daily living. Moreover, the relation between the working memory impairment and mental disorder in TBI patients highlights the importance of the early recognition of cognitive deficit.

P3

**Isolation of Neurosphere-Like Bodies from Adult Human Amygdala**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P3

In the last century, neural stem cells are used in a lot of studies for basic and therapeutic investigations. Several sources are identified for neural stem cells including embryonic, fetal and adult stem cells. Although most of studies have focused in embryonic as well as fetal cells due to their capacity to generate progenies, these cells have some problems such as immunological, availability and ethical concerns. Among adult sources for neural stem cells, two areas in adult mammalian brain including the subventricular zone of lateral wall of lateral ventricle and the subgranular zone of hippocampus are identified as niches with neural stem/progenitor cells (NS/PCs). According to previous studies, other adult mammalian brain regions may have the quiescent cells which generate stem-like cells in vitro. To date, a few researches have addressed the isolation of NS/PCs from adult human amygdala. The aim of the present study was to evaluate the ability of human amygdala tissue to generate neurospheres. The amygdala specimens were obtained from five patients suffering from refractory temporal lobe epilepsy and subjected to amigdalotomy. After removing the pia mater and

associated blood vessels, the tissue was dissociated enzymatically. Then, the single cells were cultured in neurosphere medium containing 20 ng/ml Fibroblast growth factor, 20 ng/ml epidermal growth factor, B27 supplement and N2 supplement in non-coated flasks. Growth factors were added twice a week. Additional neurosphere medium was administered once every week. The efficacy and number of spheres and cells were evaluated. Four days after primary culture of amygdala tissue, small free floating spheres were appeared. The proliferation of the cells slowly continued to day 15 at which passage was done and neurospheres dissociate into single cells. The number of spheres and cells increased after each passage. Here, we showed for the first time in Iran the possibility of isolating proliferating neurospheres from patients with refractory epilepsy during interventional surgery.

#### P4

### Evaluation of Urinary Interleukin-8 Levels in Patients with Spinal Cord Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P4

Interleukin-8 (IL8) is the protein released by different cells. Increased of IL8 indicated the infection in any part of body so increased of IL8 in urine is indicated the urinary tract infection. Patients with spinal cord injuries have to use catheter for long time and or for all of life, and they are high risk to recurrent urinary tract infections and other infections. To determine of increasing urinary IL8 in patients with spinal cord injuries the present study is the survey of this. Clean catch midstream urine samples were collected from spinal cord injury patients who admitted to "Brain and Spinal Injury Repair Research Centre" in Imam Hospital in duration almost one year. Urine samples were collected from 97 spinal cord injury patients included 85 male and 12 female and then were analyzed by biochemical and microscopically surveys and then, IL8 were measured in samples by ELISA method. In total 97 patients, 87 patients were IL8 positive ( $>10$  pg/ml) and in 87 positive samples, 59 patients had bacteriuria and 54 patients had pyuria. Statistical analysis showed that the significant relationship between bacteriuria and pyuria with urinary IL8 positive patients ( $P<0.05$ ). The patients with spinal cord injury need to monitor for urinary tract infection although without any symptoms of infections and sometimes. The measurement of IL8 is a fast and easy method for monitoring of urinary tract infection in these patients.

#### P5

### Evaluating the Toxicity of L-Glutamic Acid on Brain via Histological and Locomotion Measures in Mice

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P5

Following severe head injury, there is elevated extracellular glutamate in brain. "About 30% of severely head injured patients develop cerebral ischemia". Increased levels of glutamate (glutamate toxicity) have been considered as an important factor in post-traumatic outcomes. Some articles have reported the effectiveness of antagonists of glutamate for treating head injury. In this study we tried to evaluate the toxicity of glutamate on brain via histological and locomotion measures in mice, to see to what extent glutamate can induce histological and locomotion impairment. In this study, 96 mice were studied which divided into three groups in terms of age: infant, immature and mature. Then in each age group, mice were divided into four groups which three of them received 0.5, 1 or 2 mg/kg of L-glutamic acid and the control group received distilled water. 30 minutes after the injection, the motor activity impairments were evaluated with the classical EAE scoring scale. Then, mice were tested by a grid walk test, and a narrow beam test, to assess specific aspects of locomotion impairments. For histological effect of glutamate on brain, histological slides were prepared from different parts. L-glutamic acid in three doses 0.5, 1 and 2 mg/kg and three age groups increased the mean of scores in classical EAE scoring scale and the mean of footfall errors in grid walk test, significantly ( $P<0.001$ ), and decreased the mean of scores in narrow beam test, significantly ( $P<0.001$ ) compared to the control group. Histological showed significant necrosis in the cortex, hippocampus, olfactory bulb, and in lesser extent in the striatum. Glutamate can cause locomotor and histological impairments, so using antagonists of glutamate may be able to be as a one of treatments in head injury in future.

#### P6

### Neuroprotective Effect of Estrogen against Brain Edema and Blood Brain Barrier Disruption: Roles of Estrogen Receptors $\alpha$ and $\beta$

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P6

Estrogen (E2) has neuroprotective effects on blood-brain-barrier (BBB) after traumatic brain injury (TBI). In order to investigate the roles of estrogen receptors (ERs) in these kind of effects, ER- $\alpha$  antagonist (MPP) and, ER- $\beta$  antagonist (PHTPP), or non-selective estrogen receptors antagonist (ICI 182780) were administered as regulators of CNS cytokines levels and neuroinflammation after TBI. MPP (150  $\mu$ g/Kg), PHTPP (150  $\mu$ g/Kg) or ICI182780 (4 mg/kg) was injected daily 48hr before TBI, then E2 (33.3  $\mu$ g/Kg) or oil were administered 30min after TBI. BBB disruption (Evans blue content) and brain edema (brain water content) were evaluated 5hr and 24hr after the TBI, respectively. Brain levels of anti-inflammatory (IL-10 and IL-1ra) and proinflammatory (IL-1 $\beta$ , IL-6, and TNF- $\alpha$ ) cytokines were quantified 24hr after TBI induced by Marmarou's method. Results revealed that, in the presence of each selective estrogen receptor antagonist there was a significant increase of IL-10 and significant decrease of IL-1 $\beta$ , IL-6, and TNF- $\alpha$  24hr after TBI but there is no significant differences between the results of combined use of selective receptor antagonists and the non-selective one. Taken together, these studies identified a dramatic cytokine-mediated neuroinflammatory response that is regulated through both ER- $\alpha$  and ER- $\beta$  receptors. This may suggest a therapeutic potential in the brain trauma for ER-specific agonists.

## P7

### Salutary Effects of Progesterone for Traumatic Brain Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P7

The sex hormone progesterone has been shown to improve outcomes in animal models and two early-phase trials involving patients with traumatic brain injury (TBI). The aim of this clinical study was to

assess the effect of progesterone on the improvement of neurologic outcome in patients with diffuse and acute TBI. A prospective, randomized, double-blind trial of progesterone was conducted in our teaching hospital. A total of 50 patients with diffuse acute TBI who arrived within 4 hours of injury with a Glasgow coma score  $\leq 12$  were enrolled in the study. In a randomized style, 25 received progesterone (1 mg/kg per 12h for 5 days) and 25 did not. The primary efficacy endpoint was the Glasgow outcome scale score 3 months after brain injury. Secondary efficacy endpoint included the mortality. The demographic characteristics and the mechanism of injury were similar for the two groups. After 3 months of treatment, the Glasgow outcome scale score analysis exhibited more favorable outcome among the patients who were given progesterone compared with the control individuals ( $P=0.05$ ). The mortality rate of the control group was 20.8%, whereas any of patients in progesterone group did not die. Instances of complications and adverse events associated with the administration of progesterone were not found in any of patients. Our data suggest that the administration of progesterone for diffuse and acute TBI patients improved neurologic outcomes and reduced mortality. These results indicate that progesterone can be considered as a promising neuroprotective drug.

## P8

### Efficacy of Life Review Therapy with Emphasis on Islamic Ontology on Decreasing PTSD Symptoms

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P8

Life review therapy has been used for reducing post-traumatic stress disorder (PTSD) symptoms in older ages. Using life review therapy with elements of religious ontology, this study introduces an intervention for decreasing PTSD symptoms in younger adults. The study population included clients referred to the two counseling centers in Tehran during 2008 and 2009. The sample consisted of 18 clients who referred for treatment with PTSD diagnosis by their psychiatrist and were willing to participate in the study. After completion of diagnosis process and a pre-test, clients were randomly assigned to two groups of intervention and control. PTSD symptoms were assessed by PTSD questionnaire before and after the intervention. The intervention group received ten sessions of life review therapy and the control group was invited to attend treatment sessions after the study and the post-test. None of the members of the two groups took any medication during the study period and they were followed up three months later to check the persistence of the effects. Analysis of data by t-test showed a significant decrease in PTSD symptoms

in the experimental group. Findings showed that life review therapy with emphasis on islamic ontology was effective in reducing PTSD symptoms. Using elements of religious ontology for those who believe with a process of life review therapy can be effective in reducing PTSD symptoms.

## P9

### Incidence of Spinal Cord Injury Caused by Road Traffic Crash in Tehran

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P9

Spinal cord injury (SCI) is a devastating condition with enormous personal and social costs. To develop preventive strategies, the determination of epidemiological features and causes is required. Due to Iran's high incidence of road traffic crash (RTC) injuries, epidemiologic data concerning specific causes of SCI may assist in reducing this national health dilemma. In a retrospective study in Tehran hospitals, the records of traumatic SCI patients, admitted between March 2010 and July 2011 were surveyed. A total of 138 traumatic SCI patients were admitted, of which 56 (40.6%) were due to RTC that the majority of them were male (78.6%) and the mean age was  $32 \pm 15$  years. The most common spinal fractures/dislocations due to RTC among SCI patients were related to the thoracolumbar region. However, RTC was the most frequent cause of tetraplegia (cervical SCI)-(56%) and also hospital death ( $OR=3.2$ ,  $CI=0.9-11.5$ ). Each SCI-RTC patient paid averagely  $79,000,000 \pm 56,000,000$  Iranian Rials. Whereas the cervical SCI is the most frequently hospitalized SCI in the developed countries, here, most of cervical SCI patients are passed away in the scene of accident due to inadequate emergency medical services. On the other hand, based on an approved national policy, all medical services are free-of-charge for RTC victims. But the payment of above mentioned huge sums by patients could be related to law breaking in hospitals or weak law enforcement. More studies are suggested to evaluate the incidence of severe RTC injuries which lead to pre-hospital deaths were not considered in our study.

## P10

### Effects of Female Gonadal Hormones on Neuromedin S and its Receptor Following Experimental Traumatic Brain Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P10

Brain edema plays an important role in secondary tissue damage following traumatic brain injury (TBI) but the underlying mechanisms are not entirely elucidated. The G protein coupled receptor FM-4 and its ligands, neuromedin S (NMS) and neuromedin U (NMU), are expressed in diverse brain areas, and have a variety of roles in nociception, inflammation, and stress but their probable changes after brain trauma has not yet been investigated. In the current study, we investigated the effect of low and high physiological levels of progesterone (P4) and  $17\beta$ -estradiol (E2) replacements on brain NMS and NMU and expression of FM-4 as well as cerebral edema following TBI. Female Albino N-Mari rats were given female sex steroid hormones by capsule implantation for one week before brain injury or were not given hormone replacement therapy. The animal groups were included: Ovariectomized (OVX)+low estradiol (LE), OVX+high estradiol (HE), OVX+low progesterone (LP), OVX+high progesterone (HP), OVX+TBI, blank, vehicle (Veh). At 24 hrs after trauma, brain edema was estimated by measuring the brain water content. expression of prepro-NMS and FM-4, and the NMU protein content were evaluated. The results demonstrated that following TBI, the cerebral water content in (OVX+HP) and (OVX+HE) groups was less than in TBI untreated groups ( $P<0.01$ ). Quantitative real time PCR indicated the higher expression of FM-4 gene and western blot analyses revealed an increase in prepro-NMS protein expression in progesterone-replaced rats compared to the both traumatic-unreplaced and estradiol-replaced groups. Our findings suggest that progesterone-replacement attenuates brain edema and induces an enhance in prepro-NMS and FM-4 mRNA expression which may mediate the anti-edematous effects of this hormone following TBI.

## P11

### Evening Primrose Oil Improves Nerve Functions Following Crush Injury of Sciatic Nerve in Rats

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P11

Repairing the damaged nerves caused by physical injury

(trauma), is one of the major challenges facing modern medical sciences. Evening primrose oil (EPO) extraction of *oenothera biennis* seed that enriches with omega-6,  $\gamma$ -linoleic acid and linoleic acid that they have essential role in myelination and neural membrane structure. The aim of this study was to evaluate the functional recovery of sciatic nerve after EPO administration in crushed sciatic nerves. Eighteen male Wistar rats with 180-200g weight were divided in to 3 groups: sham, saline, and EPO. In 12 anesthetized rats in saline, EPO groups, the right sciatic nerve was crushed using a small hemostatic forceps. EPO, 450 mg/kg/day, was orally administrated for 28 days. Gastrocnemius muscle atrophy was investigated using light microscopy. Functional recovery of the nerves was assessed using sciatic functional index SFI one day before injury and 7, 14, 21 and 28 days after injury. The result of this study showed that in EPO group, functional recovery of sciatic nerve significantly accelerated compared with group 2 that received saline. In addition the muscular atrophy improvement was greater in EPO group compared with saline group. The present study showed that EPO induced improving effect on motor function and muscular atrophy caused by nerve crush injury.

## P12

### Cultivation of Neural Stem-Like Cells from Adult Human Amygdala

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P12

Several sources were introduced for cell therapy after neurotrauma. There are some evidences that quiescent stem cells are located in the various regions of the adult mammalian brain including cortex, hippocampus, amygdala and striatum. But more study is needed to identify the characteristics of these cells. In the present study we investigated the possibility of isolating neural stem cells from adult human amygdala. The amygdala specimens were obtained from five patients suffering from refractory temporal lobe epilepsy and subjected to amygdalo-hippocampectomy. After removing the pia mater and associated blood vessels, the tissue was dissociated enzymatically. Then, the single cells were cultured in neurosphere medium containing 20 ng/ml Fibroblast growth factor, 20 ng/ml epidermal growth factor, B27 supplement and N2 supplement in non-coated flasks. Growth factors were added twice a week. Additional neurosphere medium was administered once every week. To characterize the isolated cells, immunocytochemistry was done against nestin, Sox2, Oct4, GFAP and MAP2. The isolated cells highly expressed neural stem cell markers nestin, Sox2 and

Oct4. But there was a few cells expressed mature neuron marker MAP2 and astrocyte marker GFAP. Here, we showed for the first time in Iran the possibility of isolating neural stem-like cells from patients with refractory epilepsy during interventional surgery.

## P13

### Cognitive Failures in Mild Traumatic Brain Injury Patients Compared to Normal People in Kashan

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P13

Head trauma associated with multiple destructive cognitive symptoms. Cognitive destruction leads to impairment in cognitive tasks and cognitive failure. Cognitive failures include problems with memory, attention, and operation. This study aimed to comparing cognitive failures in mild traumatic brain injury (TBI) patients and normal people in Kashan. The study was performed on 40 TBI patients referred to Shahid Beheshti Hospital in Kashan city and 40 normal people in Kashan. TBI patients and normal people were selected by convenience sampling. Two groups filled out the demographic sheet and cognitive failures questionnaire (CFQ). The data was analyzed by multivariate analysis of variance and multiple regressions analysis. The results of this study showed no significant difference between the TBI and control groups in cognitive failures. But the study indicated cognitive failures increase with increasing age and cognitive failures have a negative correlation with education. Among the demographic variables, education is the best predictor of cognitive failures. Based on the survey results there is no significant difference between the TBI and control groups in cognitive failures. Cognitive failures are inversely related to education and directly correlated to age. Also education is the best predictor of cognitive failures.

## P14

### The Impact of Psychological Problems Caused by the Trauma of War on Mental Quality of Life in Veterans Wives

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P14

Iran-Iraq war during the 1980–1988 has left many consequences on veterans and their families that persist long after the war ended. In this research we evaluated the

relationship between psychological problems caused by the trauma of war in veterans with mental quality of life in their wives 24 years after the war ended. The sample was all children of veterans in Isfahan city that registered by Veterans and Martyrs Affair Foundation (VMAF). 226 veterans were selected by systematic randomized sampling and the symptom checklist 90-revised (SCL-90-R) were administered for them. Their wives fill out the short form health survey (SF-36). The data from 226 couples was analyzed by multiple regressions analysis. From Global severity index (GSI) and 9 subscale scores of veterans in SCL-90-R, depression and obsession scores were inversely correlated with scores of wives' mental quality of life. Veteran's depression is the best predictor of the mental quality of life in their wives. The obsessive thoughts and behaviors of Veterans is the second predictor of mental quality of life spouses.

## P15

### Analysis of Receptor's Distribution in Entorhinal Cortex after Induction of Spreading Depression in Juvenile Rats

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P15

Spreading depression (SD), discovered by Leao in 1944, is a pathophysiological wave which propagates slowly in the brain (3 mm/min) and cause dramatic ionic and hemodynamic changes. SD appears to act through several mechanisms and receptors which have not completely understood. Here, we studied the effect of inhibitory system in animal model of SD using immunohistochemistry technique. After implanting recording electrodes and cannula over the brain, repetitive SD was induced by KCl injection (2 M) in juvenile rats for four consecutive weeks. Then all rats were decapitated and the brains removed. Mean number of dark neurons in entorhinal cortex were determined using Toluidine blue staining. To identify the prevalence and distribution of  $\gamma$ -aminobutyric acid A (GABA-A) subunit receptors and glutamic acid decarboxylase (GAD), immunohistochemistry technique was performed. The mean number of SD induced by KCl injection was statistically increased during four weeks of experiments ( $P=0.036$ ). The mean number of dark neurons in entorhinal cortex was significantly increased in SD group compared to sham rats ( $P\leq 0.001$ ). Also, expression of GAD 65 receptor in the entorhinal cortex significantly increased in SD group compared to control group ( $P<0.05$ ). GABA-A $\alpha$  and GABA-A $\beta$  receptors didn't show significant change in that region. These data suggest that SD is able to damage

neural cells and also it could lead to enhancement of GAD, the enzyme which is responsible for synthesizing an important inhibitory neurotransmitter, GABA receptor, in the central nervous system.

## P16

### Iranian Quality Registry of Spinal Cord Injury, Key Considerations for Implementation

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P16

Prevalence of spinal cord injury (SCI) in Iran is considerable and developing a national registry is substantial. Registry can be a foundation of efforts for patient care improvement, clinical research facilitation, preventative strategy formulation and policymaking for better support of patients. With respect to long-term and multiple consequences of the lesions that will have a negative impact on patient quality of life, implementation of quality registry would be more appropriate. There are some considerations for this due to the special nature of medical condition, which is SCI, and development objectives. This paper will be discussed on the key considerations. The study has been performed by discussion groups and brainstorming sessions as well as literature review on international experiences about develop and implement spinal cord registry. Key considerations for implementing the quality registry of SCI are related to defining detailed objectives, inclusion criteria for both traumatic and non-traumatic, methods for case finding according to distribution and movement of individuals across the country, identifying data sources, data registration and clinical assessments standards, processes, controls and auditing, confidentiality and administrative and technical infrastructures. Given the complexities that are available in the nature of injury, care and follow up processes and budget limitations, successful implementation depends on the appropriateness of the defined administrative structure, processes and quality control and registry auditing instructions with regard to key considerations that implied. In addition, the spirit of cooperation related originations and authorities, commitment to the principles of the program, comply with the ethical framework such as confidentiality and using the loop

of feedback in the development process of registry are critical success factors for implement it.

## P17

### **HCG and Trolox Reduced the Apoptotic Hippocampus Neuronal Cells in Ischemia-Reperfusion Mice Model**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P17

Ischemia has an important role in spread of pathologic injuries in the neuropathies. It is widely accepted that most damages such as reperfusion injuries, are related to the activity of free radicals. Apoptotic signaling was exacerbated by free radicals. The aim of this study was to evaluate the neuroprotective effect of human chorionic gonadotropin (HCG) and vitamin E (trolox) in the hippocampus. In this study we used 40 male mice. Then, animals randomly divided into 5 groups: ischemia, HCG, trolox, HCG+trolox, and control. We cut off 2 sides of carotid vein about 15 minutes to induce ischemia. Then through reperfusion, Trolox was injected in inner Peritoneum and after 48hrs HCG was injected in muscle for 5 days. We extract protein from the brain tissue for western blotting test and the brains were fixed for nissl staining. Western blotting test shows significant increase of NF-KB (anti apoptotic protein) expression and decrease ratio of Bax/Bcl2 (the apoptotic proteins) expression in the treatment groups. Injection of HCG+Trolox after ischemia-reperfusion increased density of normal cells and significantly enhances the number of CA1 pyramidal neuronal cells. Our findings indicated that the application of Trolox and HCG in the same time after ischemia-reperfusion had neuroprotective effect and improved the neuronal cell survival.

## P18

### **The Biomarkers of Cardiovascular Responses among Thirty-Four Male War Veterans with Post-Traumatic Stress Disorder**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P18

Perhaps, due to the impact of post-traumatic stress disorder (PTSD) on biological markers of cardiovascular such as systolic and diastolic blood pressure, heart rate,

body temperature, physiological response to reminders of trauma has become an essential part and hallmark of the diagnostic and statistical manual of mental disorders (Fifth edition-DSM-5, American Psychiatric Association, 2013). Therefore, this study aimed to investigate the biomarkers of cardiovascular responses among thirty-four male war veterans with PTSD. In this cross sectional study, Participants were selected from Iraq imposed war against Iran in the province of Kermanshah in 2014. They were approved by medical committee as patients who suffer from PTSD and chosen by available sampling. The data were collected by the post-traumatic stress disorder Checklist-Military version (PCL- M) and digital Barometer and Thermometer. In additional, with 0.95 confidence level and IBM SPSS22 software was used for data process. Result showed that the mean of age, percentage of injury and the years each individual spent in the front, for all participations was 53.73, 45.72 and 4.07. Mean scores of systolic blood pressure; diastolic blood pressure, heart rate and body temperature were respectively 123.72, 82.94, 89 and 36.51. With regard to the results of this study can be stated that biological markers of cardiovascular as a risk factor for heart attacks in the war veterans is at a high level. The heart attacks caused by increased blood pressure can lead to PTSD in survivors.

## P19

### **Investigate the Effect of Family Meetings Are Conducted on the Level of Consciousness of Patients in ICU**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P19

The purpose of this study was to determine the effect of a guided family visiting, as an auditory and tactile stimulation, on the consciousness level of comatose head injury patients. A randomized controlled trial design was used. Sixty-four comatose head injury patients were randomly allocated into a control group or an intervention group. Patients in the intervention group were received auditory and tactile stimulations for 45-60 minutes by a family member for 14 days. In control group, in routine way, meetings with the family will be every other day for 30 minutes. Consciousness level was measured half hour before and after each meeting (twice daily) with Glasgow coma scale score and 4 score. The independent t-test results demonstrated that the means of the consciousness level at the first day before intervention had no significant difference in both groups. The repeated measured ANOVA results demonstrated

that the consciousness level alterations were significant between the two groups over the 14 days of intervention. The results of the present study provided evidence to support that a guided family visiting could induce the stimulation of comatose patients. Therefore, it can be considered as a potential nursing intervention.

## P20

### Computational Model for the Effects of Phenobarbital and the NKCC1 Inhibitor Bumetanide in the Pilocarpine Model of Temporal Lobe Epilepsy

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P20

In this research, we have computationally investigated a mechanism for antiepileptic drugs (AED) and proposed bumetanide as a possible temporal lobe epilepsy (TLE) treatment. Experimentally it is difficult and devastating to determine the ionic mechanisms of depolarizing currents. It is obvious that chlorine and potassium transients are challenging to isolate pharmacologically and much  $\gamma$ -aminobutyric acid (GABA) signaling occurs in small, difficult to measure, dendritic compartments. So many computational studies have been done to confirm the mechanisms of TLE. Despite widespread acceptance of GABA as the transmitter of inhibition in the central nervous system, in one of the most frequent reported TLE data, GABA plays role of excitatory neurotransmitter. In this computational study we have modeled three hippocampal neurons. We have modeled healthy, patient and bumetanide treated neuron and the compared the firing rate of these three neurons. The computationally based model neuron was morphologically reconstructed from hippocampal pyramidal neuron n123 taken from the published Duke Southhampton neuronal morphology: from the published Duke Southhampton neuronal morphology: [http://www.compneuro.org/CDROM/nmorph/index/n123\\_t.html](http://www.compneuro.org/CDROM/nmorph/index/n123_t.html). The model was modified to include an axon, as described in Poirazi and et al. The neuron contains 183 compartments. Voltage gated ionic currents were modeled as in Poirazi and et al modified by Naomi Lewin et al. The extracellular space was modeled as a cylindrical shell surrounding each compartment with a volume 15% of the intracellular compartment. The initial intracellular concentrations of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ ,  $\text{Ca}^{2+}$  and  $\text{HCO}_3^-$  were based on the intracellular and extracellular concentrations described in Smirnov et al. The concentrations of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$  and  $\text{Ca}^{2+}$  were allowed to fluctuate in both the intracellular and extracellular compartments, except where specified. The results showed that blocking the  $\text{Cl}^-$  importer Na-

K-Cl cotransporter 1 (NKCC1) is significantly reducing firing rate so NKCC1 blockers such as bumethanide are potential anti-epileptic drugs. Due to these computations, we are experimentally testing bumetanide's effect on animal subjects. In conclusion combined treatment with bumetanide and phenobarbital after status epilepticus (SE), increase inhibition and maximize the anticonvulsant power of the GABA system and might be useful in the treatment of epilepsy patient.

## P21

### Comparing Hostility and Sleep Disorders among Nursing Students of Islamic Azad University, Toyserkan Branch with and without PTSD

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P21

Both at 11<sup>th</sup> edition of the international classification of diseases (ICD-11) and in Fifth edition of the diagnostic and statistical manual of mental disorders (Fifth edition-DSM-5), have pointed out that attitudes and quality of sleep can be seriously impaired by post-traumatic stress disorder (PTSD). The present study was conducted to compare hostility and sleep disorders among nursing students of Islamic Azad University, Toyserkan branch with and without PTSD. This descriptive-comparative causal study was performed on 190 (140 girls & 50 boys) nursing students. Participants were chosen by available sampling. They completed three scales: the post traumatic stress disorder checklist-military version (PCL- M); hostility subscale from Buss & Perry aggression questionnaire and sleep disorder subscale from Mississippi scale for combat-related post-traumatic stress disorder. Data were analyzed and processed using descriptive statistics and T test, by SPSS18. Result revealed that overall, 56 out of the 190 students identified with PTSD and they obtained significantly higher scores on hostility and sleep disorders ( $P<0.05$ ). Due to considerable prevalence and impact of post-traumatic stress disorder on sleep quality and hostility patients who suffer from this disorder, it is essential that substantial interventions to diagnose and treatment of patients to be performed.

## P22

### The Role of Religious Coping in Predicting Post-Traumatic Growth in Patients with Breast Cancer

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P22

Breast cancer is the most common cancer among women that creates stress in physical, mental and spiritual aspects of patients' lives. Adjustment consequences for these patients may lead to post-traumatic growth including positive changes following the traumatic experience and/or return to the higher psychological level from what there was before that traumatic event. Given the impacts of spirituality on post-traumatic growth, the present study aimed to examine the role of religious coping in predicting post-traumatic growth in patients with breast cancer. This is a descriptive-correlational study. The study population included all patients with breast cancer referred to health centers in Kerman in 2014. The sample consisted of 121 patients whom were selected through applying convenience sampling method. Variables were evaluated using religious coping style (Iranian Religious Coping, 2011) and the post-traumatic growth inventory (PTGI, 1996). To analyze the obtained data, the Pearson correlation and stepwise regression analysis were applied. Findings indicated that dimensions of active religious activities ( $r=0.42$ ), benevolent evaluation ( $r=0.63$ ) and religious activities (dimensions of religious coping) ( $r=0.43$ ) were positively correlated with post-traumatic growth and these relationships were significant at the 0.99 confidence level. The results of regression analysis, conducted to predict post-traumatic growth, demonstrated that in the first step, benevolent evaluation (0.39) predicted the post-traumatic growth. Therefore, benevolent evaluation can predict post-traumatic growth (Beta= 0.63,  $P<0.001$ ). With regard to these results, it can be deduced that religious coping can predict post-traumatic growth in patients with cancer. Hence, religious coping can be regarded as a strategy to achieve post-traumatic growth in patients with cancer.

## P23

### The Emergency Care in Spinal Cord Injuries

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P23

A high number of people in the world suffered from spinal cord injury (SCI). Spinal cord injuries are happen due to falls from height, accidents, climbing, sports and etc. Emergency care according to the standards not performed immediately after SCI. A significant enhancement in the number of mortality and complications was observed every year. The aim of this study is to prevent the mortality, neural injuries, hypoperfusion, ischemia, biochemical, and inflammatory changes. The first act in acute spinal cord trauma is to establish a secure airway with the fixing of the spine. Keeping the airway clear,

oxygen supply, adequate ventilation, and maintain sufficient perfusion of the spinal cord must be noticed. Neurological damages may be occurred without proper fixation of the SCI. All victims of spinal cord trauma must be immobilized immediately and correctly (collar and splint and etc.). After stabilization of the airway and hemodynamic of the patient neurological status must be evaluated. Neurological injury can be distinguished from hemorrhagic shock by controlling pulse, temperature, urine output. Maintain blood pressure above 90 mmHg is necessary to prevent secondary ischemic injury. Stabilization of blood pressure is very important because low blood pressure hampers the development of microcirculation the spinal cord. While high blood pressure causes bleeding and edema (Arterial blood pressure should be 80-100 mmHg). Methylprednisolone protocol must be done after the evaluation and diagnosis of spinal cord injury. Fans rush in surgery believed that systemic effects of SCI decrease in the first 24 hours, but fans delay in surgery prefer to stable situation of neurological surgery. The results of this research revealed that promptly evaluation and management of SCI can considerably decrease the complications and mortality. Therefore, we can put treatment protocols of these patients in the emergency department and training nurses and physicians in this field.

## P24

### Minimally Conscious State Improvements with Thalamic Ventralis Intermedius Nucleus Stimulation after Severe Traumatic Brain Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P24

Methods of modulating brain neural plasticity, improving memory and learning, improving recovery from traumatic brain injury, preventing epilepsy, treating memory disorders, and treating persistent impairment of consciousness in humans and animals by nerve stimulation are provided. Widespread loss of cerebral connectivity is assumed to underlie the failure of brain mechanisms that support communication and goal-directed behavior following severe traumatic brain injury. This study was tried to clarify with the effect of deep brain stimulation in patients who had severe traumatic brain injury. Recent studies have shown unexpected preservation of large-scale cerebral networks in patients in the minimally conscious state (MCS), a condition that is characterized by intermittent evidence of awareness of self or the environment. These findings indicate that there might be residual functional capacity in some patients that could be supported by therapeutic interventions. This study was followed after

6-month indicated that bilateral deep brain electrical stimulation (DBS) of the ventralis intermedius thalamus modulates behavioral responsiveness in a patient who remained in MSC for 6 years following traumatic brain injury before the intervention. Primary outcome measures was mediated by the frequency of specific cognitively behaviors and functional limb control and oral feeding (secondary outcome measures) increased during periods in which DBS was on as compared with periods in which it was off. Our studies demonstrated early DBS treatment discontinuation for patients with only inconsistent interactive behaviors and motivate further research to develop therapeutic interventions.

## P25

### **Driver Cognitive Fatigue Detection Based on Changes in EEG Frequency Bands in Non-Professional Drivers During a Simulated Driving Task**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P25.

Driver fatigue may impose the risk of crashes and is a leading cause of death in transportation industry. This study aimed to detect driver cognitive fatigue based on changes in EEG frequency bands in non-professional drivers during a simulated driving task. In a descriptive-analytical study, 12 healthy male car drivers took part in a two hour driving session on a simulated monotonous road, while EEG signals were recorded. The four EEG frequency bands, including delta, theta, alpha and beta were extracted and calculated using Fast Fourier Transform technique. The findings suggest significant differences in delta, theta, alpha and beta activities at the prefrontal, parietal sites, and also in the average activity during the driving sections. There were significant differences at the central site for delta, theta and alpha activities. At the temporal site, significant differences were found for delta and beta activities. No significant differences were observed for the four frequency bands at the occipital site. To prevent the risk of cognitive fatigue in transportation industry, it is necessary to estimate the changes in EEG activities during driving. The findings proposed the drop in beta activity as a potential fatigue indicator, but for developing a fatigue

countermeasure device, some implications still exist that need further investigation.

## P26

### **Determination the Effectiveness of Cognitive-Behavioral Therapy in Reducing Symptoms of Post-Traumatic Stress Disorder in Victims of Road Accidents**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P26

Post-traumatic stress disorder (PTSD) is the one of the main disorders arising from disastrous experiences. Road accidents are common reasons for mental disorders which are associated with trauma. With regard to the prevalence and effects of PTSD, treatment of these disorders is very important. The aim of the present study is to determine the efficacy of cognitive-behavioral therapy in reducing symptoms of PTSD in road accidents victims. Population of this study consists of 50 subjects of road accident victims hospitalized in different wards of 3 hospitals in Esfahan city. Thirty nine subjects have earned maximum score of the PCL questionnaire and 30 subjects were randomly selected and divided into two groups as the experimental group and control group. The experimental group received eight ninety-minute sessions of cognitive-behavioral therapy and the control group did not receive any therapy program. After the end of therapy sessions, the two groups were tested and the results compared with the primary scores. Data were analyzed using spss16 software. Results showed that there are significant differences between the control and experimental groups in terms of PTSD mean ( $P < 0.05$ ). Based on these findings, we conclude that cognitive behavioral therapy dramatically, leads to reduce symptoms of PTSD in road accidents.

## P27

### **The Relationship between Risky Driving Behavior with Extroversion and Consciousness and Affect**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P27

The purpose of follow study concerned review of relation between extraversion, consciousness, negative and positive affect risky driving behavior. The population of this study is involved whole men driver in Tehran and divided in two groups including: 202 men with risky driving behavior and 192 men without risky

driving behavior. They are selected by random sampling method. Gordon five factor questionnaire is applied for measuring of consciousness, extraversion. Also it is applied the scale of positive and negative experience for measuring of the negative and positive affect. The data were analyzed using SPSS21 software and Pearson's correlation coefficient. Regression analysis was used to interpretation the data. The results of this research showed that high-risk driving behavior does not have significant relation with consciousness. How researches that done about five factor show that however similar elements in several culture are general but major difference are characterized in their importance. Based on this research, it have been resulted that consciousness variable have many importance for participants and their in answer to questions that measure this variable show more defiance toward other variables. Extraversion and positive affect up to 14% and negative affect and extraversion up to 11% of high-risk driving behavior can predict. Positive and negative affect could not reduce the relation between extraversion and risky driving behavior or reduced to zero. Also, they are as moderator variables on the relation between extroversion and risky driving behavior, in order to reverse the effects of direct and darned. So that extraversion driver have positive affect risky driving behavior increase and extraversion driver have negative affect risky driving behavior decrease.

## P28

### Estimating Bus Driver Fatigue through Performance Measures in a Virtual Driving Environment

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P28

Driver fatigue is one of the main causes of road accidents. This study aimed to estimate bus driver fatigue through performance measures in a virtual driving environment. The study was conducted on thirty professional male bus drivers participated in a two-hour drive session. The driver subjective fatigue was assessed by fatigue visual analogue scale (F-VAS) on 10 min intervals. At the same time, the performance measures of lane drifting as mean and standard deviation of bus lateral position (SDLP) were calculated during the simulated driving task. The findings presented a rising trend in subjective fatigue level with increasing the time-on-task of driving. Time-on-task of driving was the most effective

factor on fatigue self-evaluation. The drivers showed a significant correlation between F-VAS score and SDLP. The findings revealed a strong correspondence between SDLP and driver subjective fatigue based on group mean data, but individual differences may affect the driving performance which should not be ignored in future investigation.

## P29

### A Survey on the Cognition of the Car Drivers about the Traffic Signs: A Case Study in Yazd, Iran

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P29

Today, the number of drivers and traffic users is increasing. So, it is necessary to know that the human factor has the most important factor in the traffic. Thus, any behavior change or fault that arises from human factor (for example drivers) can have inappropriate impacts on the traffic. So, it is important that traffic users be trained about the effectiveness and attention to the traffic signs is the one of the legal and major instances of the good driving, and the risk free driving. It has been reported that in the most traffic accidents there were some warnings and informative signs that drivers did not care. This study conduct a field study on the cognition rate of the drivers about the traffic signs, among the statistical population of Yazd city's drivers. The results indicate that there are significant differences between driver's demographic properties, and cognition rate about the traffic signs. In conclusion, by using the obtained results, it is possible to increase the acknowledgement rates and attention rates of the drivers about the training system changes, and about continuous training and informing, after receiving the certificate.

## P30

### Investigation of Sustainability in Road Transportation: A Case Study in Isfahan, Iran

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P30

Sustainable road transportation requires integration with economic, social and environmental aspects of

transportation. It depends on term and condition of each society. In the recent decades, transportation is growing fast in Iran and Isfahan follows this scenario. The aim of this study is to study the traffic, parking road properties of Isfahan Metropolitan Area who are actively implementing TDM Plans. Isfahan is the third city in Iranian population and one of Iran metropolis Isfahan contains different types of transportation including airport, metro, intercity public transportation and railroad transport. In the case of transportation in Isfahan is currently under heavy expansion which began during the last decade. Its lengthy construction is due to concerns of possible destruction of valuable historical buildings. Outside the city, Isfahan is connected by modern highways to Tehran. The highways also service satellite cities surrounding the metropolitan area. In this paper firstly try to analyze the definition of road transportation and relationship with transportation demand management TDM. Secondly discuss briefly theory of SWOT analysis for assessment of strengths, weaknesses, opportunities and threats of road transportation

### P31

#### Cross-Cultural Comparison of Iran-Georgia Major Driving Behavior Problems

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P31

Ninety percent of road traffic deaths occur in low- and middle-income countries, which claim less than half the world's registered vehicle fleet. Iran and Georgia have a strategic position in the region and as a bridge connect Europe to Asia. Almost all over the world countries are planning and implementing solutions to stop tsunami of road accidents. In this paper the main challenges of road safety in both countries have been discussed and then using a road safety survey among Iranian-Georgian experts, main findings and priorities have been identified and compared. Comparison of surveys showed that we have lots of similar problems in both countries that mainly come from cultural unsafe habits and also level of perceived risk by road users. Since both countries have close cultures are categorized as middle income countries it could be predicted that successful efforts in one country could be possibly effective in another one. At the end an example of root cause analysis for aggressive driving problem is provided to clarify the possible solutions for future teamwork. Necessarily same solutions do not lead to successful achievements. Cultural norms, educational and enforcement methods vary from one country to another and to stop wasting the time it is better to start regional road safety cooperation for sharing the experiences and benefit each other.

### P32

#### Road Traffic Injuries in Aq-Qala City, Golestan Province, Iran, 2007-2012

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P32

Road traffic injuries are the leading cause of death and disability in the world. So, the aim of current study was investigated the epidemiologic survey of road traffic injuries in patients admitted in Al-Jalil hospital in Aq-Qala. This study was conducted on 5774 patients during 2007-2012, to evaluate the profile of 2784 injury patients due to road traffic accidents, admitted in Al- Jalil hospital in Aq-Qala. Data were collected from their personal forms and were analyzed using SPSS18 software. Among 5774 injuries, accident with 2784 cases (48.2%) was the most injury, of the people who have had accident, 81.9% (2280) were male and 18.1% (504) were female. Average age was  $25.2 \pm 13.3$  years. 20-29 years old group and 10-19 years old group have the most accident with 36.4% and 30.1% respectively. The findings from this study showed that accidents involve motorcycle accident 55.7% (1552), car accident 25.4% (708) and 18.8% (524) for pedestrians. Also, most accidents have been occurred in urban areas (57.3%), in rural areas (34.3%) and out of town and village (8.4%). The majority of accidents have been occurred in the spring and summer. Incidence of accident in hospitalization during the years of 2007 to 2012 was calculated 327.1, 492.6, 352, 270.7, 407.5 and 488.6 in 100000 person. 1.8 % of accidents (50) cause death. This study showed that the majority of accidents were occurred for men. Also, motorcycle accidents involve more than half of the accidents. So, this current paper suggests that applying the safe community-based interventions for high- risk groups can be useful.

### P33

#### The Study of the Mistakes and Errors Made by Distracted and Undistracted Drivers in Road Safety of Users

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P33

Road users such as drivers, motorists, motorcycle riders, bike riders and pedestrians play an important role in traffic safety. Most accidents can be prevented by accurate and regulated driving based on the traffic laws and regulation. In fact by recognizing the errors made by violated drivers we are able to find the appropriate lawful solution for them and to avoid repeating violations

made by drivers in the near future and saving the life of road users such as pedestrians and drivers. This study aims to examine the kind and nature of mistakes made by drivers when distracted and not distracted. In fact this study examined what kinds of errors made in two situations and to compare them. In this study was asked from the participants drove an equipped vehicle around an urban test route both while distracted and while not distracted. Two in-vehicle observers recorded the driving errors and mistakes made, and a range of other data such as driver verbal protocols, video and the data of vehicle (speed, brake, steering wheel angle and so on). Categorization of the errors and mistakes showed that distracted drivers (drivers being distracted by playing mp3 player, talking to mobile phone and talking to occupant seating in the car) significantly make errors although undistracted driver's errors were prevalent. However the natures of errors made by both drivers were not significant. This study showed that in addition to making different types of errors, distracted drivers simply make a great number of the same errors type they make when not distracted. Understanding of the relationship between distraction and driving errors and mistakes are discussed along with the advantages of using a multi-framework for studying driver's behavior. Distracted drivers made 268 mistakes and errors while undistracted made 180 errors. The general estimation equations (GEE) showed that distracted drivers had 48 percent errors more than undistracted drivers. The result also showed the common mistakes of both drivers such as turning left or right fast; hit the brake inappropriately and so on.

### P34

#### Identifying and Reducing Occupational Road Safety Risks

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P34

Occupational road traffic crashes account for a large portion of killed and seriously injured road traffic victims. Several organizations have introduced driver-training programs in order to determine a safety culture and improve the safety of employees and society, as well as to comply with insurance company requests to reduce risks. The aim of these programs is to identify and promote desirable traits and remove attitudes and behaviors that are associated with higher crash

involvement. The factors, which predict involvement in road traffic collisions, were driver personality; behavior; attitude and personal exposure are important determinants. It does show that driver attitudes and behaviors are a predictor of crash involvement, although their impact seems lower than exposure variables such as mileage, hours driven and having an aggressive personality. Where this is impossible or unpractical, efforts to assess attitudes and behaviors associated with poor driving and to improve these through training and other interventions do appear to be validated as worthwhile. It is useful for greater effort to be taken by organizations to promote a safety culture and make use of education programs to improve driver related attitudes and behavior. Hazard perception and knowledge of the rules do not appear to be strong predictors of accident involvement, but they are important in underpinning attitude, behavior, personality and exposure. Absolutely, where practical, the attention of safety programs should be directed to those with aggressive, impulsive and impatient personalities. The findings support that drivers with these personality types have greater involvement in road traffic collisions.

### P35

#### Neuroprotective Effect of Noscapine on Cerebral Oxygen-Glucose Deprivation Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P35

The present study aims to investigate the effect of noscapine (0.5-2.5  $\mu$ M), an alkaloid from the opium poppy, on primary murine fetal cortical neurons exposed to oxygen-glucose deprivation (OGD), an in vitro model of ischemia. Cells were transferred to glucose-free DMEM (Dulbecco's Modified Eagle Medium) and were exposed to hypoxia in a small anaerobic chamber. Cell viability and nitric oxide production were evaluated by MTT assay and the Griess method, respectively. 0.5  $\mu$ M noscapine were significantly inhibited the neurotoxicities produced by 30 min OGD. The neurotoxicity decreased by noscapine treatment in the concentration-dependent manner. Pretreatment of cells with MK-801 (10  $\mu$ M), a non-competitive NMDA (N-Methyl-D-aspartate) antagonist, and nimodipine (10 nM), a L-type  $Ca^{2+}$  channel blockers, increased cell viability after 30 min OGD, while the application of NBQX (30  $\mu$ M), a selective AMPA ( $-\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid)-kainate receptor antagonist partially attenuated cell injury. Noscapine attenuated nitric oxide (NO) production in

cortical neurons after 30 min OGD. We concluded that noscipine had a neuroprotective effect, which could be due to its interference with multiple targets in the excitotoxicity process. These effects could be mediated partially by a decrease in NO production.

### P36

#### Effectiveness of Safety Seats on Reduction of Head Injuries and Fatalities of Children in Accidents

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P36

Children under 5 years old are the most vulnerable age group in car accidents. Researchers showed that application and correct use of child safety seats can reduce the risk of fatal injury by 71 percent for infants and 54 percent for toddlers. The purpose of this review is to identify factors and procedures that declare the correct use of child car seats which prevent children head injuries that are close to fatal ending. The information presented in this paper describes the importance of safety seats, the correct use of them referring to data which are collected in USA, Shanghai and Sweden. Children under 5 years old are potential victims of car accidents, mostly because of head crashes. Car safety seats can definitely prevent injuries and fatalities. Safety seats are designed upon age groups and the correct use of them is so important to prevent head injury and fatality.

### P37

#### Relationships between Memory Dysfunction and Driving Ability in Alzheimer's Disease

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P37

Alzheimer's disease (AD), a common and debilitating neurodegenerative disorder, affect more than 65 million individuals throughout the world. This disability plays a crucial role in daily activities such as driving. Several studies have investigated the relationship between cognitive functions and driving safety. The current study

revises the literature on the relation between road safety and AD. Results from a recent study showed that a person with moderate to severe dementia is certainly no longer fit to drive, whereas driving ability may be maintained in mild dementia for some time. So, impaired driving performance in elder compared to younger is the main reason for their driving cessation. It is suggested that driving competence must be addressed because many older adults with dementia continue to drive.

### P38

#### Spinal Cord Injury and Body Mass Index

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P38

Obesity is one of the most prevalent diet-related problems and increases the risk for diabetes mellitus, hypertension, atherosclerosis and dyslipidemia. Cardio vascular disease is a major cause of morbidity and mortality in spinal cord injury (SCI) patients. Increased fat mass has also been identified as an important risk factor in chronic SCI and weight management is recommended as a key cardio vascular disease prevention strategy. The aim of this study is to determine the prevalence of overweight and obesity in persons with spinal cord injury. An observational analytic cross sectional study on 850 files of SCI patients registered in the current database in Khatam Alanbia Hospital from 2008 to 2013 was undertaken. Data collected for each patient included age, sex, height, weight, duration of spinal cord injury and the level of spinal cord injury. The body mass index (BMI) was subsequently calculated for each patient and the prevalence of overweight and obesity were determined. 833 patients were male and 17 were female. In all, 50.2% of patients had a normal BMI and 7.6% of patients were undernourished. The prevalence of overweight and obesity were 32.1 % and 10 % of patients, respectively. Prevalence of overweight and obesity are high in persons with spinal cord injury and there is a significant positive correlation between BMI and age.

### P39

#### Effect of Injured Brain Extract on Proliferation of Neural Stem/Progenitor Cells Cultured in a 3-Dimensional Scaffold

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P39

Neuroinflammation occurring after traumatic brain injury (TBI) is a complex phenomenon comprising distinct cellular and molecular events involving the injured cerebral tissue. Mechanical injury to adult rat brain elucidated the accumulation in the affected area of trophic activity. In the tissue adjacent to the injury, trophic titers began to rise after the lesion. This study aimed to determine the effect of injured brain extract on proliferation of neonatal rat neural stem/progenitor cells (NS/PCs). NS/PCs were isolated from olfactory bulb of neonatal rat then cultured as neurospheres. After second passage, cells were seeded in PuraMatrix scaffold by injection method and incubated with intact or injured brain extracts. The proliferation assay was carried out by MTS assay 10 days later. For preparation of the injured brain extract, we used a rat brain injury model and collected the extract 48 hrs after injury. The experimental results showed that NS/PCs derived olfactory bulb have a good potential to proliferate. MTS assay demonstrated that NP/SCs proliferation rate was increased in injured brain extract. Injured brain extract could be benefit for NP/SCs proliferation.

#### P40

### The Effect of Post-Surgery Social Isolation on the Traumatic Brain Injury in Rat

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P40

Traumatic brain injury (TBI) is one the most common cause of disability between young adults. These people have been socially isolated during post-surgery traumatic brain injury. In this study we investigated the effect of social isolation on the structural deficits after TBI in the young rats. Young rats were divided into control group with social interaction, sham group with social isolation and TBI group with social interaction, and TBI with social isolation. During four weeks after brain injury in young rats, we evaluated structural changes by histological procedures in the hippocampal areas. Our findings showed an increase of the mean number of dark neurons, apoptotic cells, and caspase-3 positive cells in the hippocampal areas in TBI rats with and without social isolation compared to sham rats. Furthermore, social isolation significantly increased the number of dark cells, apoptotic neurons, and caspase-3 positive cells in the hippocampal CA3 region in rats with TBI. This study indicates social isolation exacerbates the pathological effects of TBI in the hippocampal tissue

in the young rats. Prevention of social isolation may improve the outcome of TBI.

#### P41

### Therapeutic Effect of Transplanting Neural Stem Cells Derived Bone Marrow Stromal Cells Using Bioactive Substance TNT, for Enhance Recovery from Spinal Cord Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P41

Bone marrow mesenchymal stem cells can differentiate into neurons and astrocytes after transplantation in the spinal cord injury of rats. Although bone marrow mesenchymal stem cells are known to protect against spinal cord injury through anti-apoptotic effects, but generation of neural stem cells with large number and safety protocols unclear. In the present study, described the differentiation of bone marrow stromal cells (BMSC) into a neural stem cell-like under the influence of a factor inducing non-toxic bioactive substance TNT. In the present study, bone marrow mesenchymal stem cells were cultured and proliferated, then induced with bioactive substance TNT. That these cells differentiate as a neurosphere-like structures and neural stem cells. These cells approved by immunocytochemistry and RT-PCR technique. These cells transplanted into rats with spinal cord injury. Immunohistochemistry and immunofluorescence with subsequent quantification revealed that the expression of the axonal regeneration marker and the neuronal marker, microtubule-associated protein 2, significantly increased in rats with bone marrow mesenchymal stem cell transplantation compared with those in rats with spinal cord injury. Our results suggest that bone marrow mesenchymal stem cell transplantation promotes neurite growth and regeneration and prevents autophagy. These responses may likely be mechanisms underlying the protective effect of bone marrow mesenchymal stem cells against spinal cord injury. Transplanting BMSCs can enhance the protein expression of neural growth factor in the rats which undergo injury to their spinal cord. It can be significantly improved the rehabilitation of the motor function. The improvement is associated with the transplantation of BMSCs which are beneficial for regeneration and repair of the rat's spinal cord injury.

#### P42

## Luteolin Counteracts ER Stress in PC12 Cells through Moderating ER Chaperones and Heat Shock Proteins

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P42

Luteolin, as a natural polyphenolic compound, has neuroprotective effect and exerts its function by attenuation of apoptosis and oxidative stress factors. Emerging evidences indicate that oxidative stress leads to neurodegeneration but is not the initial event and endoplasmic reticulum stress (ER) is often considered to be the stimulus event which is caused by accumulating of misfolded proteins. The activation of the unfolded protein response (UPR) outcrops as the one of early occurrence in brain injury when the agglomeration of mis- or unfolded proteins occur in the ER lumen. So, the present study try to define whether any neuroprotective effect is seen when Luteolin is administered in used H<sub>2</sub>O<sub>2</sub>-injured PC12 cells. PC12 cells were cultured and exposed to different concentrations of H<sub>2</sub>O<sub>2</sub> with different concentrations (10, 25, 50, 100 µM) of Luteolin for 2 hrs prior to our experiments, then the cells were exposed with H<sub>2</sub>O<sub>2</sub> (150 µM) for 24 hrs. Western blot analysis was performed in PC12 cells to evaluate the levels of Heat shock proteins (Hsp70 and Hsp90) and ER stress chaperon GRP78/BiP and CHOP. Cell viability was evaluated by the conventional MTT reduction assay. Pretreatment of PC12 cells with different concentration (10, 25, 50, 100 µM) of Luteolin followed by exposure to H<sub>2</sub>O<sub>2</sub> increased cell viability (about 46, 35, 78 and 80%, respectively) relative to the H<sub>2</sub>O<sub>2</sub>-treated cells. In the group that received (25 µM) concentration of Luteolin, ER stress chaperones such as GRP78/BiP and CHOP decreased compared to H<sub>2</sub>O<sub>2</sub> treated cells, while HSP70 increased in Luteolin treatment of 25 µM. The level of hsp90 decreased in Luteolin (25 µM) treatment. In conclusion, our data suggest that flavonoid has therapeutic potential following brain trauma.

### P43

## Secondary Demyelination in Spinal Cord Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P43

The pathology of spinal cord injury (SCI) comprises multiple processes characterized by extensive cell death and glial scar formation, which together limits axonal regeneration. In particular, variations in chronic demyelination of the lesion have been found to be largely independent of injury intensity, suggesting a secondary pathologic origin. This chronic demyelination results in progressive tissue degeneration and constitutes a significant component of the pathology in many cases of SCI. Widespread demyelination is resulted from oligodendrocyte apoptosis which has been seen after ischemic or traumatic injury to the central nervous system which also could be found within remote degenerating fiber tracts. Both secondary degeneration at the site of SCI and the chronic demyelination of tracts away from the injury appear to be due in part to apoptosis. Furthermore, secondary pathology is coincident with dense invasion of the lesion by macrophages and their phagocytosis of the membranous debris remaining from the initial hemorrhagic necrosis. Prolonged demyelination enhances axonal vulnerability to degeneration, and is thereby thought to contribute to the axonal degeneration that underlies the permanent functional losses associated with SCI. Recovery of conduction in demyelinated axons may permit recovery of function and can be mediated by several mechanisms including remyelination by oligodendrocytes and Schwann cells transplantation alone or in co-transplantation with other cellular types such as bone marrow mesenchymal cells or neural stem cells. In addition, combination cellular transplantation strategy with the complementary administration of neuro-protective agents/growth factors, improves the effect of cellular transplantation after SCI.

### P44

## Combination Therapies after Traumatic Brain Injury by Bumetanide and Dexamethasone Administration; a Hypothesis Study.

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P44

Traumatic brain injury (TBI) initiates a cascade of numerous pathophysiological events that evolve over time. Despite the complexity of TBI, research aimed at therapy development has almost exclusively focused on single therapies, all of which have failed in multicenter clinical trials. A variety of brain insults, including traumatic brain injury, encephalitis, stroke, and status epilepticus (SE), have the potential to induce the development of epilepsy, particularly temporal lobe epilepsy (TLE) in humans and rodent models of TLE. The

mechanisms underlying this process, which is termed epileptogenesis, are only incompletely understood, but include inflammation, neurodegeneration, blood–brain barrier disruption, alterations in expression and function of diverse receptors and ion channels, and development of hyperexcitability of neurons and neuronal circuits. The goal of the present study was to directly address this hypothesis by treating rats with the NKCC1 inhibitor bumetanide after a TBI. For the present experiments, Wistar rats, weighing 200–230 gr must be used. As previous studies on animal model of TBI treat by co-administration of dose dependent bumetanide and dexamethasone. Predict result: the result may show dexamethasone can inhibition second injury also combination of these two drugs may have reduction and inhibition of neural injury and inflammatory process. Co-administration of dose dependent bumetanide and Dexamethasone may have therapeutic role in traumatic brain injury.

## P45

### The Role of Blood-Brain Barrier Breakdown Following Traumatic Brain in Post-traumatic Epilepsy

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P45

Traumatic brain injury (TBI) refers to a brain injury caused by an external mechanical force such as an impact to the head, concussive forces, acceleration–deceleration forces, blast injury, and a projectile such as a bullet. Traumatic brain injury is recognized as a critical public health problem worldwide, TBI is accompanied with mortality and morbidity with an occurrence of approximately 200 cases per 100,000 people a year. It is also a known major risk factor for focal epilepsy. The incidence of post-traumatic epilepsy (PTE) ranges from 2–50% in different studies, accounting for approximately 20% of symptomatic epilepsies. Seizures may occur immediately following the trauma, though PTE usually develops several months and even years later. While immediate post-traumatic seizures may be successfully treated with antiepileptic drugs, the mechanisms underlying the development of PTE remain unknown with no means for preventing it. The central nervous system is protected by the function of the blood-brain barrier (BBB), which regulates the passage of blood constituents in and out of the brain extracellular space. It seems that an increase in BBB permeability may be associated with the pathogenesis of neurological disorders. However, only recent animal experiments directly showed that primary prolonged opening of the BBB leads to the development of delayed, long-lasting

epileptiform activity. Furthermore, it has been suggested that the most common serum protein, albumin may underlie astrocytic activation and dysfunction, further leading to neuronal hyper synchrony and accumulated neuronal loss. On the other hand previous clinical studies showed that altered permeability is observed in neurological patients.

## P46

### Therapeutic Potential of Neural Stem Cells for Spinal Cord Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P46

Spinal cord injury (SCI) is a destructive condition that the cord can't send signals below the level of the injury. Despite advances in the medical and surgical care of SCI patients, no effective treatment exists for the neurological deficits of SCI. Cell therapy is a new approach for SCI, and preclinical models demonstrate that cell transplantation can improve some secondary events through neuroprotection and also restore lost tissue through regeneration. Neural stem cells (NSCs) are multipotent cells committed to the neural lineage that can self-renew. NSCs are found in both fetal and adult central nervous system (CNS). NSCs locate within specific niches in the adult CNS, including the subventricular zone in the lateral ventricles of the forebrain, the dentate gyrus of the hippocampus, olfactory bulb and the region of the central canal of the spinal cord. Transplantation of NSCs into injured tissue, promoted functional recovery with neuroprotective and neuroregenerative effects. Most studies with transplanted NSCs have shown modest recovery of the injured spinal cord. Adult mouse brain–derived NSCs transplanted into the injured rat spinal cord with concomitant infusion of growth factors promoted oligodendrocyte differentiation of the grafted NSCs, remyelination, and improved locomotor function. NSCs derived from fetal rat spinal cord differentiated into neurons that integrated into the injured cord and improved recovery, and transplanted NSCs combined with valproic acid administration promoted neuronal differentiation, resulting in restoration of disrupted neuronal circuitry and enhanced recovery. NSCs have also demonstrated some immunomodulatory and pathotropic ability by

homing toward damaged tissue as well as secreting various neurotrophic factors and cytokines. Neural stem cells also express nerve growth factors that are essential to the healthy function of the CNS. These could protect the patient's own neurons from further degeneration due to injury. By solving some limitations in future, cell therapy can open a new window for treatment of SCI.

#### P47

### Application of Induced Pluripotent Stem Cells in Spinal Cord Injury Treatment

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P47

Stem cell therapy can be useful for spinal cord injury (SCI). Induced pluripotent stem cells (iPSCs) are generated by reprogramming mature, fully differentiated cells into a pluripotent state. The ability to generate pluripotent cells from adult somatic cells without the need for an embryo was a major development in stem cell biology. iPSCs were established from mouse fibroblasts and demonstrated therapeutic potential for treating SCI in animal models. It has been reported that the human iPSCs differentiated into neurons, astrocytes, and oligodendrocytes in the injured spinal cord and promoted motor functional recovery. It is hypothesized that the transplantation of human iPSCs could result in a wide range of positive effects, including angiogenesis, axonal regeneration, and local-circuitry reconstruction. Recent study has demonstrated that iPSCs cells possess properties of embryonic stem cells generated from Patients with amyotrophic lateral sclerosis can be differentiated into motor neurons. Our hypothesis suggests that human iPSCs represent a promising cell source for transplantation into the injured spinal cord.

#### P48

### Self-Assembling Peptide Nanostructures as a Good Scaffold for Treatment of Spinal Cord Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P48

To date, various approaches have been used in attempt to treat spinal cord injury (SCI) but there is no definite treatment for repair of the damaged tissue. It is well known that SCI results in a loss of neural tissues and formation of cystic cavities that inhibit regeneration of axons. Tissue engineering, in which cells, signals and scaffolds are combined, is one of the most promising areas of research due to its potential to regenerate damaged or lost tissues. Peptide nanostructures formed through molecular self-assembly are increasingly important for material science and regenerative medicine. Peptide self-assembly allows the design and fabrication of supramolecular architectures at nanoscale. Self-assembling peptides (SAPs) have been developed under physiological conditions that can form 3 dimension structures of nanofibers. SAPs are amenable to injection due to their water solubility and exhibit dramatic morphology changes immediately after injection due to the addition of salts from the cerebro- spinal fluid. SAPs can reduce the glial reaction and support the host cells to migrate and fill the cavity. In addition, SAPs provide a 3 dimensional environment for axonal elongation and angiogenesis. With application of the biocompatible, non-toxic and biodegradable SAPs in SCI, we can help the injured tissue to repair and reconstruct.

#### P49

### The Role of Extra Cellular Matrix in Brain Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P49

Traumatic brain injury (TBI) results from a sudden and external physical impact to the head, and often leads to motor and cognitive impairment. Using tissue engineering strategies, we aimed to review aspects of extra cellular matrix (ECM) based scaffold that could be delivered to the injured brain. The ECM is produced intracellularly and secreted to form a

dense network of proteins and glycans, occupying the parenchyma of virtually all cells. It is a source of diverse molecular signals that guide cellular growth, activity and survival. It is well known that changes to the ECM inhibit axonal regeneration; it is also becoming clear that such alterations, particularly chondroitin sulphate proteoglycans (CSPGs) accumulation, impair oligodendrocyte function and remyelination. In order to enhance therapeutic efficacy, many studies have reported benefits from remodeling the extracellular matrix to provide a suitable scaffold for regeneration of cells and axons. Therefore, due to the effects of various ECM components on signaling events, it is very difficult to design controlled experiments for ECM-based cell signaling. It is also difficult to gelatinize nano or picogram quantities of collagen or the other single ECM component alone. Meanwhile, our ability to maintain stable cell density throughout experiments is limited when using several cell lines that do not have consistent adherence to culture flasks. ECM can be focused in basic investigations for understanding its roles and making engineered scaffolds mimicking ECM to treat SCI.

## P50

### Post-Traumatic Stress Disorder after Motor Vehicle Accidents

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P50

Post-traumatic stress disorder (PTSD) is a chronic and progressive disorder that occurs after some traumas and accident. Injuries and harm to health caused by motor vehicle accidents (MVAs) have become an issue of global concern, as MVAs are expected to be the third largest contributor to the worldwide burden of disease by the year 2020. Chronic PTSD is a common consequence of MVA and that it may persist for years. Women have higher rates of PTSD than men after MVA. In the last years, many studies have evaluated the psychological consequences of MVAs. However, there are discrepancies in epidemiological studies. As an additional issue, other predictors of PTSD immediately after MVA have been established; Signs such as heart rate (HR) and respiratory rate (RR) immediately after injury predict subsequent PTSD remains controversial. Although many studies have shown an association between HR and PTSD, but recent study did not report an association between HR, RR, and PTSD. Elevated HR and RR might reflect initial fear conditioning and thus would be important factors in the mechanism of genesis of PTSD. It seems that, HR and RR they might

not be useful indicators of subsequent PTSD among accident survivors in clinical protocols, but any physical reactions like pounding heart might be an alternative to predict subsequent psychiatric morbidity.

## P51

### Thermogel Nanofiber Induces Human Endometrial-Derived Stromal Cells to Neural Differentiation and Improves Motor Dysfunction Following Spinal Cord Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P51

Although spinal cord injury (SCI) is one of the most common injuries after a road accident, there is no definite treatment for it. In this regard, nanotechnology has focused to retrieve damaged tissue function by designing of a biomaterial as a mimicking extracellular matrix to reduce inflammation, scar and lactate dehydrogenase, to fill the cyst and improve the graft integration, cell proliferation and differentiation in site of injury. In this study, the neuronal differentiation potential of thermogel nanofibrous Matrigel as a self-assembling nanofiber was investigated. Human endometrial-derived stromal stem cells (hEnSCs) were isolated and encapsulated into nanofiberoustermogel and cell viability and cell membrane damage were assessed. Encapsulated hEnSCs into Matrigel were treated with neural differentiation medium for 21 days, and then neural genes and protein markers were analyzed using real time-PCR and immunocytochemistry assays. In addition, Matrigel was implanted into an animal model of SCI and followed

up for 45 days using Basso-Beattie-Bresnahan (BBB) test. Our results showed higher cell viability and lower cell membrane damage in cells encapsulated into the nanofiber as compared to 2D cell culture. Also, it was seen neural differentiation in the level of genes and proteins and significant improvement in motor function of the injured animals. Matrigel with the ability of neural induction and motor function improvement could be as an applied scaffold in tissue engineering for SCI.

## P52

### In Vitro Investigation of Genes Which Derive BMSC-Derived Neurosphere Motility

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P52

It is estimated that annually 10 million people are affected by traumatic brain injury and it is one of the major causes of death and disability in accidents. Studies have shown the potential therapeutic value of neural stem cell therapies. Also, neural stem cell motility and migration to the site of injury has a great regeneration value of the damaged tissues. Extracellular and intracellular factors orchestrate this complicated process. In this work, we tried to elucidate the intracellular and indeed effectors of the cell motility and migration in neurosphere formations under in vitro conditions. After isolation and culture of bone marrow stromal cells (BMSCs) from rat; the cells were cultured in DMEM/F12 medium supplemented with 2% B27, 20 ng/ml basic fibroblast growth factor, 20 ng/ml epidermal growth factor, 100 U/ml penicillin, and 100 mg/ml streptomycin. After passing the incubation time; total RNA were extracted from the cells and cDNA synthesis were performed for different time i.e. at the times of 0, 1, 5 and 30 minutes as well as 1, 2, 4, 6, 12 and 24 hours. These cDNA were subjected to RT-PCR and real time RT-PCR reactions. At aforementioned different time courses; RT-PCR and real time RT-PCR results showed that there are substantial differences in the expression of the genes which regulate polymerization and depolymerization of intracellular actin protein and thus cell cytoskeleton dynamics including; Cdc42, Ctnn, Pak1, Rock1 genes. Actin protein dynamic causes cell membrane protrusions and filopodia formation and thus cell migration. Discovering of the underlined signaling mechanisms and pathways that guide the cell motility has a great importance, especially neurosphere cell motility in the field of CNS

regeneration medicine. In conclusion, our results show that Cdc42, Ctnn, Pak1, Rock1 are effector genes in the cell motility of neurosphere formations.

## P53

### The Use of Fluoro-Gold for Retrograde Tracing of Cell Injection after Spinal Cord Injury: Improves Axonal Growth after Transplantation of Cells

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P53

Traffic accident has increased in the last decade. One of the most important outcomes of accident is spinal cord injury (SCI). So, cell therapy is obtained a greater attention in most fields of medicine because of its potential for incurable diseases through replacing of dead cells. The current study aims to describe the important of locomotor functional and structural connection of the spinal cord pathway innervating the sciatic nerve after SCI following transplantation of GDNF-transfected adipose derived stem cells. The isolated adipose stromal cells were cultured and then mesenchymal stem cell markers were evaluated by RT-PCR and immunocytochemistry assays. Third passage cells were used for ex vivo gene delivery. ADSCs were transfect by vector pLVPT-GDNF-trTR-KRAB-2SM2. Then the transfected cell transplant to contusion model of rat SCI that administrate valproic acid in acute phase. Rats were divided into three groups: (1) laminectomy (without SCI) only; (2) laminectomy+SCI+VPA (300 g/kg and 12h post injury); (3) SCI+ADSCs-TR infused 7 days post injury+VPA(300 g/kg and 12h post injury). Contusion injury was performed with a New York University (NYU) weight-drop device. Locomotors function was assessed by the H-reflex and Basso-Beattie-Bresnahan (BBB) test for 12 weeks. The retrograde fluorogold tracing method used for fate of injected ADSCs-TR. Spinal cord was examined histologically, and assessed in order to position of cell replacement three month after surgery. BBB test scores of SCI rats treated with ADSCs-TR at 7 days+VPA (300 g/kg and 12h post injury) were significantly improved as compared to scores of rats similarly injured ( $P<0.05$ ). The H/M ratio decreased following the treated with ADSCs-TR ( $P<0.05$ ). Fluorogold tracing method revealed that transplanted ADSCs-TR showed positive labeling after sciatic nerve injection. Thus, our results demonstrate that genetic engineering of adipose MSC was effective in promoting axonal outgrowth but could also lead to enhanced recovery after injury.

## P54

### Anti-Apoptotic Effect of Neural Regeneration Peptides (NRP) 2945 on Pentylene-tetrazole-Induced Seizures in Rats

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P54

Delayed neuronal death after seizure attack may be mediated by the induction of apoptosis-pathway. Caspase-3, a mammalian cysteine protease, promotes apoptosis after some neurological disorders. Neuron regeneration peptides (NRPs) are small synthetic peptides that stimulate neural proliferation, migration, and differentiation with no apparent toxicity and high target specificity in CNS. In the current study, we try to investigate the effect of NRP 2945 on the apoptosis after seizure activity induced by pentylenetetrazole (PTZ) in rats. The effects of different concentrations of NRP 2945 (5 and 20 µg/kg) were tested on expression of caspase-3 protein in the temporal cortex and hippocampal area after seizure induction by immunohistochemistry. In addition, the number of terminal deoxynucleotidyl-transferase-mediated dUTP nick end-labelling-positive neurons in the hippocampus and temporal cortex was investigated by tunnel staining after NRP 2945 application in epileptic rats. Application of NRP 2945 at 5 and 20 µg/kg decreased the expression of caspase-3 protein in the CA1 and CA3 hippocampal areas and the temporal cortex. In addition, application of NRP 2945 at 5 and 20 µg/kg reduced the number of apoptotic neurons in the both temporal cortex and hippocampal area. This study indicates that NRP 2945 is able to prevent the neuronal apoptosis induced by PTZ by suppressing of caspase-3 protease. Further studies are needed to elucidate the potential role of NRP 2945 as an anti-apoptotic drug.

## P55

### Neuroprotective and Neurogenesis Effects of Curcumin in the Adult Rat Brain Following Transient Global Ischemia

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P55

Traumatic brain injury resulting road accidents create damage to the brain. The severe brain injury may cause extensive tissue loss of several parenchyma which results in cavities due to primary destruction and secondary injuries such as ischemia and inflammation. Recent findings suggest that neuronal precursors in the adult mammalian brain can be a therapeutic target in ischemic brain injuries. It has been reported that curcumin reduces oxidative stress and stimulates neurogenesis in the brain. The present study was undertaken to evaluate the neuroprotective and neurogenesis effects of curcumin in a rat model of transient global ischemia (TGI). Forty-eight adult male Wistar rats were randomly chosen as control, sham (animals only underwent TGI), treatment (animals were treated with 100 or 300 mg/kg curcumin following TGI) and vehicle groups. 5-bromo-2-deoxyuridine was injected intra peritoneally twice daily for three consecutive days. Then, animals were decapitated for 3 and 4 weeks after treatment. Neurogenesis, cell injury and apoptosis in the hippocampus, somatosensory neocortex, subventricular as well as subgranular zone and posterior periventricular region were assessed. We found that the number of dark neurons and apoptotic cells increased after TGI. Treatment with curcumin reduced the number of dark neurons and apoptotic cells in a dose-dependent manner. In addition, application of curcumin increased neurogenesis at low concentration in comparison to control and ischemia groups while higher concentration of curcumin reduced the neurogenesis. The present investigation provides evidences supporting the neuroprotective potential of curcumin in vivo and opens a new horizon for future experiments.

## P56

### Epidemiologic Data of Spinal Cord Injury Due to Auto Accident

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P56

Spinal cord injuries (SCI) are highly disabling and injuries. This study aims to describe the demographic and epidemiologic data on auto accident patients who were admitted at Khatam Alanbia hospital. The results obtained from 73 SCI patients treated on the SCI inpatient units of the Khatam Alanbia Hospital (from March 2009 to March 2013) were evaluated retrospectively. Then patient gender, age at time of injury and etiology of injury, neurologic level, and movement status were analyzed. The study sample was limited patients with a history of motor vehicle collisions. In total, 69 (94.52%) of the patients were male and 4 (5.48%) were female.

The mean age at time of injury was  $25.8 \pm 7.84$  years. In all, the level of injury of 13 (17.8%) of the patients were cervical, 44 (60.3%) thoracic, 12 (16.4%) lumbar and 4 (5.5%) thoracolumbar. 58 (79.5%) of patients were wheelchair bound, 4 (5.5%) moved by using cane and 11 (15.1) needed help to move. The findings showed SCI because of road traffic accident is more common in early age and majority of them became wheelchair bound. Thoracic level is the most injured level. Further research to establish the protective interventions is required.

## P57

### The Neuroprotective Effect of Periodic Fasting on the Brain Damages

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P57

Apoptosis plays an important role in many pathological processes of the central nervous system. The neuroprotective effect of periodic fasting (PF) in contrast to severe fasting or starvation has been suggested. However, these beneficial effects seem to depend on the type and duration of the used feeding protocol. This study was designed to evaluate the effects of different PF protocols on the apoptosis in the epileptic rats. Recurrent generalized seizures were caused by repetitive injection of Pentylene-tetrazole (PTZ) for a period of 4 weeks every other day. While control animals had free access to food and water, animals on a PF diet were on intermittent fasting for 24 hours every 48 hours for 4 weeks before (T1), after (T2), or both before and after (T3) the injection of PTZ. Histological investigations were performed after the experiments were completed. Dark neuron densities in hippocampal CA1 and CA3 areas were decreased in PF groups, but never in the temporal cortex. The PF-diet also decreased the number of terminal deoxynucleotidyl-transferase-mediated dUTP nick end-labelling-positive neurons in the hippocampus in both areas and all PF-diet protocols. These results support the idea that a PF-diet has neuroprotective effect on the epileptic rats but underlines different PF-diet protocols can have varying effects. The dark neurons number was decreased and apoptosis was prevented by all PF-diet protocols investigated in this work. Further evaluation of PF-diet protocols for possible clinical neuroprotective effect is suggested.

## P58

### Neurological Outcomes after Traumatic Brain Injury Affected by Concomitant Administration

### of Progesterone and Erythropoietin

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P58

Traumatic brain injury (TBI) is one of the most common neurological diseases with no definite treatment. Erythropoietin (Epo) and progesterone (Prog) have been shown to have neuroprotective effects in different types of experimental brain injury models. This study was designed to determine the effect of Epo, Prog and combination of Epo/Prog on neurological outcome after traumatic brain injury. Fifty-four male Wistar rats were divided into 5 groups including; intact (n=6), TBI (n=12), TBI + 16 mg/kg Prog (n=12), TBI + 5000 U/kg Epo (n=12), TBI + 16 mg/kg Pro + 5000 U/kg Epo (n=12). Neurological evaluation was performed using modified Neurological Severity Score on days 1, 2, 7 and 14 post TBI. The results revealed that Prog and Epo individually ameliorated neurological deficit following TBI while the combination of Prog and Epo exacerbated the neurological dysfunction. In conclusion, our study indicates that the combination of Prog and Epo does not improve neurologic outcome after TBI.

## P59

### Triazine Improved Hippocampal Injuries in Animal Model of Alzheimer's Disease

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P59

Triazine derivatives are small synthetic peptides with no apparent toxicity and high target specificity in central nervous system. Hippocampal tissue is the most vulnerable area in the Alzheimer's disease (AD). The aim of this study was to investigate the neuroprotective effect of triazine in AD induced by intra-cerebro-ventricular (i.c.v.) administration of streptozotocine (STZ). Male Wistar, weighting 200-250 grams were bilaterally implanted with chronic cannula in the Lateral ventricle. Animals were divided into seven groups; Control group: animals received no surgery and treatment. Saline group: animals received normal saline after recovery. Sham group: animals received 10% DMSO after recovery. STZ group (Alzheimer's model): animals received STZ in four and six days after recovery. T5, T10 and T15 groups: animals were treated with triazine

derivative, C16H12Cl2N3S, at doses of 5, 10 and 15  $\mu$ M, respectively. All drugs were injected i.c.v. To assess the neuroprotective effect of triazine, we measured the hippocampal CA1 pyramidal layer thickness in all tested groups. The CA1 pyramidal layer thicknesses in STZ group reduced significantly compared to control group. Triazine increased the CA1 pyramidal layer thickness in T15 group compared to STZ group. Our findings suggest that triazine may have protective effect on the hippocampus.

## P60

### Laminin Based Tissue Engineering for Central Nervous System Regeneration

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P60

Central nervous system (CNS) architecture damages, which can be induced by physical injuries during road accidents, often result in the loss of neuronal cell bodies, axons, and associated glia support. But, there is no currently definite treatment for CNS degeneration. Tissue engineering aims to restore the function of living tissues by replacing damaged tissues or organs. Natural or synthetic scaffolds that match the mechanical properties of the native tissue can be used to foster the growth of cells. Cell-cell adhesion and cell-extra cellular matrix (ECM) adhesion are crucial for tissue formation and maintenance of structural integrity. Tissue engineering strategies can involve analyzing the interactions between cells and the ECM, and evaluated changes in cell behavior in various contexts. Identification of binding sites and key motifs in ECM proteins that interact with cellular receptors will allow researchers to generate small peptides that can mimic the function of large ECM proteins. It is crucial that these small peptides are able to interact with the same cell surface receptor(s) as their parent ECM molecule and activate the appropriate signaling pathways that are consistent with the phenotype expected. One of the important ECM proteins is laminins consisting of  $\alpha$ ,  $\beta$ , and  $\gamma$  chains. Laminins are required for basement membrane assembly and they regulate cellular behavior through interactions with cell surface receptors, including integrins, syndecans, and  $\alpha$ -dystroglycan. Recent studies showed that recombinant laminin-511 E8 ( $\alpha 5\beta 1\gamma 1$ ) fragments

are useful matrices for maintaining human embryonic stem cells (hESCs) and human induced pluripotent stem cells (hiPSCs). Using this system, hESCs and hiPSCs can be easily and stably passaged by dissociating the cells into single cells for long periods, without any karyotype abnormalities. The use of laminin-511 may provide permissive microenvironments to enhance cell survival and control neural stem cell fate, both in vitro and in vivo by holding and precisely delivering stem cell based treatments for CNS regeneration.

## P61

### Non-Viral Human ProGDNF Gene Delivery to Rat Bone Marrow Stromal Cells under Ex Vivo Conditions

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P61

Traumatic brain injury (TBI) affects millions worldwide, yet no therapy exists which prevents cell death. One of the options in the treatment of TBI is neurotrophic therapy such as using glial cell line-derived neurotrophic factor (GDNF). It is one of the most important proteins playing a pivotal role in growing and repairing of the nervous system. GDNF therapy is one of the suggested options in the treatment of neurodegenerative diseases. Limitations in the viral gene delivery and its side effects after therapy have encouraged us to use a non-viral method for this purpose. We transfected rat bone marrow stromal cells (BMSCs) in ex vivo conditions using Lipofectamine 2000 reagent with pEGFP-C1 and a constructed vector carrying the human proGDNF (pSecTag2/Hygro B-human proGDNF), transiently and stably; respectively. The rate of transient transfection of rat BMSCs was eight percent and transfected rat BMSCs with pSecTag2/HygroB-human proGDNF stabilized by adding Hygromycin B in cell culture medium at 200  $\mu$ g/ml. Semi-quantitative data analysis from Western-blot technique showed that stable transfected cells secrete GDNF at higher level in comparison with control cells (6.530 fold in the supernatant). The present study supports the utility of liposome-mediated transfection for over-expressing human GDNF in rat BMSCs. For this purpose and in order to get more yield of human GDNF secretion from the stable transfected rat BMSCs, we used a vector containing another signal sequence instead of its own pre-segment of proGDNF protein. This is the

first report in this regard and the data presented will be potentially useful for human gene transfer therapies in a variety of neurodegenerative diseases such as TBI.

## P62

### The Effect of Valproic Acid Therapy on the Glial Scar Formation after Acute Spinal Cord Injury Following by Motor Vehicle Traffic Crashes

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P62

Motor vehicle traffic crashes (MVTCs) are important cause of traumatic spinal cord injury (SCI). SCI is a devastating condition, with loss of sensory, motor, and autonomic function. Inflammatory reaction following a SCI contributes substantially to secondary effects. A biochemical event in that process is gliosis. Valproic acid (VPA) is a histone deacetylase inhibitor and has potent anti-inflammatory properties. The aim of the present study was to examine optimum dose of VPA on gliosis and axonal regeneration sought to functional recovery after acute SCI. Rat models received daily intraperitoneal injections of different doses (150, 200, 300, 400 and 500 mg/kg), at time points (2, 6, 12 and 24 h) after SCI or sham surgery. Spinal cord was examined histologically for glial fibrillary acid protein (GFAP) expression, three month after surgery. Spinal cord sections were stained with silver impregnation to assess demyelination, and axonal regeneration. The injured spinal cord was then examined histologically, including quantification of cavitation. The immunohistochemical evaluation were done with immunofluorescent and immunoperoxidase techniques 12 weeks post-surgery. The expression of GFAP in the untreated group had the highest immunofluorescence while it decreased in the VPA treated group (300 mg/kg delivered at 12 h post-injury,  $P<0.05$ ). The cavity volume in the VPA treated group significantly reduced compared to control (saline-injected) group ( $P<0.05$ ). There were few axons could be noticed in the untreated group while the treated group showed many axons in the regenerating spinal tissues. Quantitative analysis showed that there is a dose dependent decrease in the relative intensity of the GFAP fluorescent at 300 mg/kg (12h). In conclusion, this result suggest VPA reduces inflammatory reaction-induced in SCI.

## P63

### Application of Nanofibrous Scaffolds with Biomolecules as a Promise Approach for Reconstruction of Peripheral Nerve Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P63

Peripheral nerve injuries caused by traffic accidents, resections of tumors or iatrogenic side effects of the surgeries are few of the most common form of trauma occurring with up to 500,000 cases each year in Iran. Conventional strategies including nerve coaptation, and the application of autografts, allografts and xenografts are restricted due to the limited availability of donors, immune-rejections or restrictions such as too big gap length. At the same time, these alternatives do not guarantee full recovery and functionality of the damaged nerves. Due to these reasons, approaches towards the development of biomaterial scaffolds for regeneration of peripheral nerve defects have gained a huge momentum. An ideal scaffold for nerve tissue regeneration requires sufficient biological and physiochemical properties, with major concern on biocompatibility, biodegradability, permeability for oxygen and nutrition, mechanical properties together with appropriate surface characteristics. The design of the engineered scaffold shall focus on mimicking the complex biological nanofibrous structure of the native extracellular matrix allowing the remodeling and repair of the damaged tissue by neighboring cell. Synthetic polymers such as poly-L-lactic acid and poly-ε-caprolactone have been utilized to fabricate electrospun nanofibrous scaffolds and their compatibility towards peripheral nerve tissue regeneration has been investigated. However synthetic polymers alone might not meet all the requirements of an artificial tissue construct since they lack recognition sites for cell adhesion. Incorporating natural polymers, like proteins or peptides might overcome this problem and increase the biocompatibility of the scaffolds. Functionalization of nanofibers is usually performed by electrospinning of synthetic and natural polymer blends or by coating the nanofibrous scaffolds with biomolecules. Core-shell nanofibers prepared by co-axial electrospinning allows for the encapsulation of proteins within the core of the polymeric shell, thus may be preserving the bioactivity of the proteins or biomolecules better than blended or coated structures.

## P64

### Treatment of Spinal Cord Injury Using

## Transplantation of Motoneurons Derived from Adipose Stem Cells Following Histone Deacetylases Inhibitors Therapy in Acute Phase

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P64

The majority of cases of spinal cord injury (SCI) occur during car crashes. SCI damages axons and disrupts sensory and motor neuronal transmission. The replacement of damaged neural cells in the injured CNS is limited. Although various treatment regimens can partially alleviate SCI, the mechanisms responsible for symptomatic improvement remain elusive. In this study, we transplanted motoneurons derived adipose stem cells with Valporic acid in animal model of SCI. Rats were divided into three groups: (1) laminectomy (without SCI) only; (2) laminectomy+SCI+VPA (300 g/kg and 12h post injury); (3) SCI+motoneuron like cells (MNLCs) infused 7 days post injury+VPA (300g/kg and 12h post injury). Contusion injury was performed with a New York University (NYU) weight-drop device. Locomotors function was assessed by the H-reflex and Basso-Beattie-Bresnahan (BBB) test for 12 weeks. Spinal cord was examined histologically, including size of cavitation, expression of glial fibrillary acid protein (GFAP) and axonal regeneration and position of cell replacement, three month after surgery. Open-field test scores of SCI rats which treated with MNLCs+VPA (300 g/kg and 12h post injury) were significantly improved compared to injured group ( $P<0.05$ ). The cavity volume in the VPA+MNLCs group significantly reduced compared to control (saline-injected) group ( $P<0.05$ ). The level of GFAP significantly decreased in the VPA treatment group, while it significantly increased in control ( $P<0.05$ ). Together, our results demonstrated the neuroprotective property of VPA in the SCI model.

### P65

## Treatment of Spinal Cord Injury Using Transplantation of Adipose Mesenchymal Stem Cells Transfected with Poly-L-Lysine/DNA (GDNF)-Super Paramagnetic Iron Oxide Nanoparticles

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P65

For repair of injured nerve fibers after spinal cord injury (SCI), the environment must be appropriate for axonal growth. The delivery of a therapeutic gene, beneficial for axonal regeneration and promote survival neurons, into the central nervous system for repair can be accomplished in many ways. The use of gene therapy to improve of the injured nervous system is a new strategy of treatment. It is based on delivering therapeutic genes to neurons. Direct in vivo gene transfer or gene transfer in combination with transplantation (ex vivo gene transfer) cause promote neuronal survival and axonal re-growth following traumatic injury to the central nervous system. Gene therapy has great potential to treating various diseases and disorders, but the efficient delivery of genes to injury site with the lowest side effects remains a challenge. Moreover, after gene delivery to stem cells, it is also highly desirable to provide screening and post-therapy monitoring. In this study used from Poly-L-lysine coated with super paramagnetic iron oxide nanoparticles (SPIONs) that can deliver nucleic acid-based therapeutic agents (GDNF) and also provide magnetic resonance imaging (MRI). Adipose tissue from rat perinephric fat was digested with collagenase type I, followed by filter and centrifugation; the isolated adipose stromal cells were cultured and then mesencymal stem cells (MSCs) markers were evaluated by RT-PCR and immunocytochemistry; 2 to 5 passage cells were used for ex vivo gene delivery. Poly-L-lysine and Lipofectamine 2000 were compared as transfection vehicles of SPIONs. Labeled adipose MSCs were examined for iron content with Prussian blue staining that was used after differentiation to determine SPIONs localization. Poly-L-lysine transfected up to 20 times more SPIONs into adipose MSCs. SPIONs were disseminated in both the soma and neuritis. Result of real time RT-PCR and SDS page and western blotting techniques showed that transfected cells secrete human GDNF at high level. These findings indicate that Poly-L-lysine is an effective vehicle for SPIONs transfection of adipose MSCs. The intracellular localization of SPIONs distinguished cell migration from axonal or dendritic growth in vivo. The transfected cells with GDNF can be used in clinical applications and treatment of CNS disorders.

### P66

## A Biologically Active Motif of Laminin for Spinal Cord Regeneration

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P66

The majority of spinal cord injuries (SCIs) are happen during road traffic accidents. Injury at any level of the spinal cord will impair respiratory function, through the destruction of motor nuclei and descending motor tracts innervating diaphragmatic, thoracic, intercostal and abdominal accessory muscles. Consequently, the majority of patients die from respiratory complications. Reconstruction and regeneration of the central nervous system following injury is a formidable task. Nerve tissue engineering (NTE) is a promising strategy that has been used to treat neural injury. The biomaterials as a substrate on which cell populations can attach and migrate, play an important role in NTE. These materials can be implanted with a combination of neural progenitor cells as a cell delivery vehicle, and be utilized as a drug carrier to deliver growth factors. Self-assembly nanopeptides can be used in the fabrication of novel biomaterials which are assembled molecule by molecule to produce novel supramolecular architectures. Recently, some of the most promising new synthetic biomaterial scaffolds are composed of self-assembling peptides that can be modified to contain laminin motifs, such as Arg-Gly-Asp-Ser (RGDS), Tyr-Ile-Gly-Ser-Arg (YIGSR) and Ile-Lys-Val-Ala-Val (IKVAV). This Hypothesis suggests that YIGSR is an efficient and safe conduit matrix for nerve regeneration after SCIs.

#### P67

### Efficient Generation of Neurosphere with High Passages (57 Passages) from Adipose Derived Stem Cells (ADSCs) Using Bioactive Substance TNT, a Promising Protocol for Multiple Treatment Modality

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P67

Spinal cord injury (SCI) is a serious condition that affects millions of people worldwide. The most causes for the SCI are motor vehicle accident (43%). Recent advances in stem cell research have brought closer the possibility of repairing the spinal cord. Cell therapy is an option in replacing the lost cells in the injured spinal cord. Adipose derived stem cells (ADSCs) are one of the kinds of stem cells that can be differentiation into neurosphere.

Previous studies used the toxic factors and complicated methods. Here, we apply a nontoxic and efficient method of rat mesenchymal stem cells (MSCs) into neurosphere. As well as, the neurosphere can be differentiated in to glial and neural cells. Primary rat ADSCs were isolated from Wistar rats (200–300 g). Then MSCs derived ADSCs, cultured by DMEM medium supplemented with 10% fetal bovine serum. These cells evaluated by specific markers of MSCs and ADSCs such as; CD49, CD90, CD105. By bioactive substance TNT then MSCs differentiated in to neurosphere in 4 groups that these groups compared with morphology. This differentiation do with nontoxic factor and by dose response of: 1 M, 0.1 M, 0.01 M and 0.25 M and time course at 72 hours. Diameter and number of this neurosphere evaluated every day in 4 groups. MSCs isolated from ADSCs then evaluated by immunocytochemistry that expressed CD90 (80%), CD49 (70%) fibronectin and negative marker CD45. Diameter and number of Neurosphere by 0.1 ng/ml was optimal dose for expansion. Cell therapy is an option in replacing the lost cells in the injured spinal cord. Source of patients need multiple delivery of cells in order to achieve the wanted results.

#### P68

### Combined Treatment of Spinal Cord Injury Using Transplantation of Motoneurons Derived Adipose Stem Cells and Adipose Mesenchymal Stem Cells Transfected with GDNF Following Valproic Acid Treatment

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P68

According to the National Spinal Cord Injury (SCI) Statistic Center, 41.3% of SCIs occur as a result of motor vehicle crashes or motorcycle accidents. SCI is a devastating condition that effects on motor and sensory system. There is no definitive treatment for SCI. Therefore recent studies enhanced approach treatment in order to augmentation of locomotors rating scales. Currently, development in neurotransplantation and gene transfer techniques has introduced a spectrum of promising strategies for treatment of SCI. In this study, we used combined treatment of SCI using transplantation of motoneurons derived from adipose stem cells and adipose mesenchymal stem cell (MSC) transfected with GDNF following Valproic acid treatment. Adipose tissue isolation of perinephric fat in rat and then was digested with collagenase, followed by filter and centrifugation. The isolated adipose stromal cells were cultured and then MSC markers were evaluated by RT-PCR and

immunocytochemistry; 2 to 5 passage cells were used for ex vivo gene delivery. Then adipose derived stem cells (ADSCs) derived into neurospheres which evaluated by immunocytochemistry and RT-PCR assay. The expression of islet-1, oligo-2 and HLXB9 in induced motoneuron like cells (MNLCS) from neurospheres evaluated by RT-PCR and immunocytochemistry. To identify the functional MNLCS, a co-culture preparation of MNLCS and myocytes, Calcium ion imaging and synaptic vesicle release were used. ADSCs treated with a mixture of preinducer (B27, EGF and bFGF) and inducers factors (Shh and RA) adopted a morphology similar to MNLCS. Other group of ADSCs was transfect by vector pLVPT-GDNF-trTR-KRAB-2SM2 and then the two group's cell transplant to contusion model of rat SCI that administrate Valproic acid treatment. Immunocytochemical staining and RT-PCR approved that the treated cells expressed the motoneuron markers islet-1; oligo-2 and HLXB9. The co-cultured with myocytes indicate the formation of neuromuscular connections between MNLCS and myocytes. After two week, MNLCS showed high HLXB9 expression, indicative of full differentiation. Also, the release rate of synaptic vesicles using FM1-43 in the induced MNLCS was 10 fold. Moreover a calcium imaging with fluo-4 results approved that functional excitatory synaptic connections can influence the activity of MNLCS. Result of real time RT-PCR and SDS page and western blotting technique showed that transfect cells secrete human GDNF at high level. Basso-Beattie-Bresnahan (BBB) test scores of spinal cord injured rats treated with adipose MSC transfect with GDNF+MNLCS at 7 days+VPA (300g/kg and 12h post injury) were significantly improved as compared to scores of rats similarly injured ( $P<0.05$ ). The H/M ratio decreased following the treated with adipose MSC transfect with GDNF+MNLCS ( $P<0.05$ ). The cavity volume in this group was significantly reduced compared with the control (saline-injected) group ( $P<0.05$ ). The level of GFAP was significantly decreased in this group, while it was significantly increase in the control rats ( $P<0.05$ ). These findings indicate that neurotransplantation and gene transfer techniques can be used in clinical applications and treatment of CNS disorders.

## P69

### The Potential Use of In Vitro Transfection of Neural Stem Cells by Psectag2a-NT4 for Spinal Cord Injury Therapy

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P69

In our country, motor vehicle accident is known as the important cause of spinal cord injury (SCI). The cell therapy in some SCI could be more powerful using

gene therapy. One of the approaches to gene therapy is cell based gene delivery. Neurotrophin 4.5 promotes the survival of sympathetic and peripheral sensory neurons and can induce differentiation of the PC12 cells. It activates two related tyrosine kinase receptors and shares these receptors with other neurotrophins. Primers were designed to amplify NT4 by addition of Xho I and EcoR V restriction sites on PCR product from pCMV-SPORT6 vector as a template. This product was purified and subcloned into the pSecTag2A to construct pSecTag2A-NT4 vector. Neural stem cells (NSCs) were cultured and evaluated for expression of stemness markers. NSCs transfect by lipofectamine reagent contained pSecTag2A-NT4 vector. Real time PCR and western blotting assessment showed that transfect cells secrete NT4 permanently in high level. Cell based gene therapy is a sustained gene delivery method. The NT4 protein can be used in treatment of SCI.

## P70

### Produce Neural Stem Cell from Neurosphere of Rat Adipose Derived Stem Cell

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P70

Spinal cord injury (SCI) is frequent after traffic accident in worldwide. Research performed over the last decade revealed that cells surrounding the central canal of the adult spinal cord acquire stem cell properties either in vitro or in response to injury. Adipose-derived stem cells (ADSCs) are an easily available source of Mesenchymal stem cells (MSCs). ADSCs can transdifferentiate into cells of other lineages such as neural stem cells. ADSCs have potential applications for the repair and regeneration of acute and chronically damaged tissues. In this study, ADSCs were isolated from rat adipose tissue cultured in DMEM supplement penestrep. ADSCs at passage 3 were identified by immunocytochemistry with antibodies analysis against with CD44, CD90, CD105, as well as CD34, CD45, CD106. We could induce rat ADSCs into floating neurospheres. Then neurospheres evaluated by immunocytochemistry for NF68 and nestin. Diameter and number of this neurosphere were measured. Neurosphere can be converted into neural stem cell (NSCs). NSCs were confirmed by NF68 and nestin expression using immunocytochemistry assay. The isolated ADSCs expressed CD44, CD90 and CD105 while CD34, CD45 and CD106 didn't express. Immunocytochemistry technique was used for NF68 and nestin expression in neurospheres. We observed that diameter of neurospheres increased and the number of neurosphere decreased. Our immunocytochemical assessment of nestin and NF68 in NSCs showed that

these markers expressed. In the present study, we have demonstrated that MSCs can be efficiently induced into neurospheres under appropriate conditions. Moreover, these neurospheres were expanded and converted into NSCs that can be used for SCI treatment.

#### P71

### **Toward Treatment of Post-Traumatic Spinal Cord Injury: Differentiation of Oligodendrocytes from Adipose Stem Cells**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P71

Traumatic spinal cord injuries (SCIs) lead to severe and permanent neurological deficits. Although no effective therapeutic option is currently available, recent other studies have shown that cell transplantation strategies hold promise to enhance functional recovery after SCI. Adipose stem cells (ADSCs) obtained from pararenal and inguinal region of rats. ADSCs were cultured and then differentiated to the neural stem cells (NSCs). Directed differentiation of stem/progenitor cells to oligodendrocytes (OLCs) lineage was done and the cell viability was assessed by trypan blue. Immunocytochemistry was carried out by NF68, NF160, fibronectin and nestin for NSCs. Also, it was done by O4, O1, and oligo2 for OLCs. Results showed that fibronectin, CD44, CD90 and CD45 expressed  $94.32 \pm 0.45\%$ ,  $95.48 \pm 0.24\%$  and  $97.16 \pm 0.82\%$  respectively. Expression of O1, O4 and oligo2 showed that combination of HRG, PDGF, bFGF and T3 (25 ng/ml) have an effective role in transdifferentiation of ADSCs into OLCs. ADSCs can differentiate to mature OLCs. Our suggestion is that oligodendrocytes can be used as a therapeutic strategy for treatment of SCI in future.

#### P72

### **Bioactive Substance ATC Can Generate Neurosphere from Adipose-Derived Stem Cells (ADSCs)**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P72

Generation neural stem cells from neurosphere-derived adipose tissue using bioactive substance ATC. Adipose tissue from rat hypodermal and pararenal fat was digested with collagenase, followed by filter and centrifugation; the isolated adipose stromal cells were cultured in dishes. These cells evaluated by specific markers of adipose-derived stem cells (ADSCs) such as bioactive substance

ATC and then ADSCs differentiation into neurosphere in four groups that compared morphologically. Diameter and number of this neurosphere evaluated every day in four groups. ADSCs are mesenchymal stem cells that can be extracted from adipose tissue and obtained by a less invasive method. ADSCs markers were measured by immunocytochemistry that expressed CD90 (80%), CD44 (70%) and fibronectin while CD45 didn't express. Diameter and number of Neurosphere by (0.1 ng/ml) was optimal dose for expansion. Then these cells evaluated by neuroectodermal markers such as nestin and NF 68 that expressed >80% and this data approved by RT-PCR technique. This study develops a simplified, efficient, and nontoxic approach by lowest factors which derives a large number of neurospheres from Adipose-derived stem cells (ADSCs). With our newly devised approach 10 to 15 passage cells were used for in vitro differentiation. Neuronal differentiation was induced by incubation of the ADSCs with bioactive substance (ATC) induction media.

#### P73

### **The Immunological and Neuroimmunological Mechanisms of Traumatic Brain Injury**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P73

Cortical spreading depression (CSD) are associated with dramatic failure of brain ion homeostasis, efflux of excitatory amino acids from nerve cells, increased energy metabolism and changes in cerebral blood flow. There is strong clinical and experimental evidence to suggest that CSD is involved in the mechanism of migraine, stroke, subarachnoid hemorrhage and traumatic brain injury. Therefore, in the present study, we used the spreading depression model to investigate the effects of repeated spreading depression on peripheral and central adaptive immune responses. Moreover, we studied the effect of repetitive spreading depression on dark neuron density and expression of GABAA  $\alpha$  and  $\beta$  receptors. The results of the present study demonstrate that repeated spreading depression in rats induced elevated lymphocyte proliferation, IFN- $\gamma$ , pro and anti-inflammatory cytokines in peripheral and central levels. Brain assays also demonstrated reduced alterations in GABAA  $\alpha$  and  $\beta$ , GAD and HSP70 expression and enhanced the number of dark neurons. The findings could help to explain the interrelatedness of adaptive immunity, peripheral inflammation, and traumatic brain injury.

## P74

### Differentiation of Bone Marrow Stem Cells (BMSC) to Neurosphere Using Bioactive Substance ATC

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P74

Generation neural stem cells from neurosphere-derived bone marrow stem cells using bioactive substance ATC. Bone marrow cells (BMSCs) were isolated from rat. BMSCs cultured by DMEM/F12 medium supplemented with 10% fetal bovine serum. These cells evaluated by specific markers of BMSCs such as bioactive substance ATC, B27. Then BMSCs differentiated in to neurosphere and divided in two groups which were evaluated morphologically. Diameter and number of this neurosphere evaluated daily. BMSCs markers were measured by immunocytochemistry that expressed, CD 90 (75%) CD 44 (60%) fibronectin. Diameter and number of Neurosphere by 0.1 ng/ml was optimal dose for expansion. Then these cells evaluated by neuroectodermal markers such as nestin and NF 68, NF 200 and NF160, that expressed >80 % and this data approved by RT-PCR assay. This study develops a simplified, efficient, and nontoxic approach by lowest factors which derives a large number of neurospheres from BMSCs. With our newly devised approach 10 to 15 passage cells were used for in vitro differentiation. Neuronal differentiation was induced by incubation of the BMSCs with bioactive substance (ATC) induction media.

## P75

### Toward Treatment of Post-Traumatic Spinal Cord Injury: Differentiation of Oligodendrocytes from Bone Marrow Stem Cells

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P75

Traumatic central nervous system injuries lead to a severe and permanent neurological deficit. Oligodendrocytes (OLCs) are vulnerable to damage in a variety of neurologic diseases. Although no effective therapeutic option is currently available, recent other studies have shown that cell therapeutic strategies hold promise to enhance functional recovery after injury. The aim of this study is to analyze transplantation of OLCs which differentiated from bone marrow stem cells (BMSCs) in rat models of spinal cord injury. BMSCs were

isolated from twenty-day old rat and were plated for differentiation to neurosphere. BMSCs were evaluated by different immunocytochemistry markers such as fibronectin, CD106, CD44, CD90 and CD45. Cell viability was assessed by trypan blue method. OLCs were assessed by immunocytochemistry for O4, oligo2 and O1 markers. Our results showed that the fibronectin, CD44, CD90 and CD45 expressed  $94.32 \pm 0.45\%$ ,  $95.48 \pm 0.24\%$  and  $97.16 \pm 0.82\%$  respectively. Expression of O1, O4 and oligo2 showed that combination of HRG, PDGF, bFGF and T3 (25ng/ml) have an effective role in transdifferentiation of BMSCs into OLCs. BMSCs can differentiate mature OLCs. Our suggestion is that oligodendrocytes can be used as a therapeutic strategy for treatment of spinal injuries in future.

## P76

### The Neuroprotective Roles of NMDA Receptors Antagonist Against with Lesion in Central Nucleus of Amygdala

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P76

The N-Methyl-D-aspartic acid (NMDA) receptor is one of the specific types of ionotropic receptors which lied to glutaminergic system. It has been widely accepted that NMDA receptor neurons promote anxiety, in humans as well as in animal models. However, in the previous study seems inhibiting of this receptors decreased the protective role in neural cell. Demonstration of NMDA receptor activity had neurodegeneration effect. The hypothesis of this study based on evaluated neuroprotectivity effect of NMDA receptor inhibition in the central nucleus of the amygdala (CeA) which have role in anxiety. In this study, we confirm that NMDA antagonist (MK801) is neuroprotective when CeA had confronted regional electrical lesion. Kindling of amygdala by electrical lesion which presented by stimulation of the CeA area after microinjection of MK801 (0.5 and 0.75µg/kg) in the kindling area is may indicate neuroprotection from secondary injury. It seems the rats were confronted electrical lesion indicated specific decreases in the percentage of open arm time and percentage of open arm entries in elevated plus maze. However, in histopathological study, the mean of dark neurons of CeA in the MK801 group was less than lesion group.

We concluded that inhibited of NMDA receptors in CeA neurons may contribute to induced neuroprotection by electrical lesion.

#### P77

### Cell Therapy Approaches to Enhancing Neuro-Regeneration after Spinal Cord Injury: Generation Neural Stem Cells from Neurosphere-Derived Adipose Stem Cells Using Bioactive Substance TNT

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P77

In the last few years, a lot of preclinical studies showed the therapeutic potential of stem cells in spinal cord injury (SCI). Neural stem cells (NSCs) can be differentiated into all cell types of spinal cord. NSCs are cells that maintain the capacity to differentiate into brain-specific cell types, and may also replace or repair of injury in central nervous system. Here in, we describe the efficient conversion of Adipose derived stem cells (ADSCs) into a neural stem cell-like under the influence of a factor inducing non-toxic bioactive substance TNT. ADSCs were isolated from adipose tissue of Wistar rat and were cultured. ADSCs were treated with bioactive substance TNT. These cells grew in neurosphere-like structures and differentiated to neural stem cells. Immunocytochemistry and RT-PCR techniques were performed to evaluate early neuroectodermal markers including SOX2, OCT4, NANOG, NeuroD and nestin. Our results showed that these markers expressed in high level. Also, NSCs were immunoreactive to NF68, NF200 and nestin. In addition, we confirmed the expression of SOX2, OCT4, NANOG and NeuroD genes by RT-PCR assay. The findings of this study provide a new method to generate NSCs from ADSCs by using non-toxic bioactive substance TNT, which can be helpful in cell therapy of SCI and degenerative diseases.

#### P78

### Depakine Improve Axonal Growth In Vitro and In Vivo after Spinal Cord Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P78

Central nervous system axons fail to regenerate after spinal cord injury (SCI), partially due to the accumulation of extracellular matrix molecules in the lesion and formation of the glial scar. Depakine, as known as histone deacetylase inhibitor, has neuroprotective effects. This study evaluated the histological changes (cavitation and axon regeneration) after SCI associated with (following administration of Depakine in rat model) Depakine treatment in a rat model. Sections were stained with silver impregnation to assess demyelination, and axonal regeneration. The injured spinal cord was then examined histologically, including quantification of cavitation. The cavity volume in the Depakine group was significantly reduced compared to the control (saline-injected) group ( $P<0.05$ ). There were few axons could be noticed in the untreated group while the treated showed many axons in the regenerating spinal tissues. Depakine reduce inflammation after SCI, and is effective for histology and higher axonal regeneration.

#### P79

### The Repair Effects of Histone Deacetylases Inhibitors on Improves Locomotion: In Vivo Evaluation with Electromyography (EMG) after Spinal Cord Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P79

Spinal cord injury (SCI), a common result of car accidents, high-altitude falls and crashes, and other violent injuries is increasing yearly. Histone deacetylases (HDAC) inhibitors including Depakine the main characteristics of the use of anti-inflammatory. The purpose of this investigation is to evaluate the effect of Depakine intervention on the acute SCI at the chronic phase using functional parameters to access the outcome. Locomotors function was assessed by the H-reflex and Basso-Beattie-Bresnahan (BBB) test for 12 weeks. The ratio of the maximum H to M reflexes (H/M ratio) was used the plantar muscle of rats. The stimulator electrodes were inserted around the sciatic nerve. To elicit the H-reflex, the sciatic nerve was stimulated with increasing stimulus intensity for 0.2 ms at 0.1 to 10 Hz, so that the first H-wave appears. Recordings were made before and at first week, 6th week, 12th week intervals after drug administration. H-reflex and BBB scores in rats receiving Depakine were significantly higher than in the saline group ( $P<0.05$ ). BBB test showed the highest score was achieved by 300 mg/kg at 12 hr and the results of the electromyography (H/M ratio) were consistent with behavioral test. The quantitative assessment of

the cavitation in the Depakine group was significantly reduced compared to the control (saline-injected) group ( $P<0.05$ ). The percentage of decrease in the H/M ratio was 25.8 % (relative to the corresponding delivery time at the same dose in the first week post-injury), accordingly, 26.8, 29.1 and 27.3% at 200, 300 and 400 mg/kg. The data demonstrated that there was an improvement of the contusion rat model treated at the acute phase of injury with optimal dose of Valproic acid which is characterized by an increase BBB score.

## P80

### Imaging Action Potentials with Calcium Indicators Fura-4 in Motor Neuron Like Cells Derived Adipose Stem Cells

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P80

Cell replacement therapy has provided the basis for future clinical applications to treat central nervous system injury, a common result of car accidents. Induced functional motoneurons are an option for replacing the lost motoneurons. Adipose derived stem cells (ADSCs) are an appropriate source of cells for autologous cell therapy with the ability of neural differentiation. In this study, ADSCs were induced to neurospheres using B27 and bFGF as pre-inducer, and then neurospheres were induced to motoneuron-like cells (MNLCs) by Sonic hedgehog (SHH) and retinoic acid (RA) as inducers. ADSCs markers such as CD90, CD44, CD49d, CD106, CD31 and CD45 were measured by immunocytochemistry analysis and their multipotency were evaluated by incubation of the ADSCs with adipogenic, chondrogenic and osteogenic induction media. Then neurospheres derived ADSCs were evaluated by immunocytochemistry and RT-PCR assay. The expression of islet-1, oligo-2 and HLXB9 in induced MNLCs from neurospheres evaluated by RT-PCR and immunocytochemistry assay. To identify the functional MNLCs, a co-culture preparation of MNLCs and myocytes, calcium ion imaging and synaptic vesicle release was used. ADSCs treated with a mixture of pre-inducer (B27 and bFGF) and inducers factors (SHH and RA) adopted a morphology similar to motoneuron cells. Immunocytochemical staining and RT-PCR approved that the treated cells expressed the motoneuron markers islet-1; oligo-2 and HLXB9. The co-cultured with myocytes indicate the formation of neuromuscular connections between MNLCs and myocytes. After two week, MNLCs showed high HLXB9 expression, indicative of full differentiation. Also, the release rate of synaptic vesicles using FM1-43 in the induced MNLCs was 10 fold. Moreover a calcium imaging with fluo-4

results approved those functional excitatory synaptic connections can influence the activity of MNLCs. These results indicate ADSCs can be differentiated to a functional MNLCs phenotype and may be benefit for treatment of motoneuron diseases.

## P81

### Evaluating the Function of Motoneuron-Like Cells Differentiated from Rat Adipose Derived Stem Cells through Voltage-Sensitive Dyes (Rh 795) and Investigating the Synaptic Vesicle Recycling

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P81

Cell replacement therapy has provided the basis for future clinical applications to treat central nervous system injuries following by car accidents. Induced functional neurons are an option for replacing the lost neurons. The ability to monitor changes in membrane potential is a useful tool for studying neuronal function, but there are only limited options available at present. Here, investigated the potential of voltage-sensitive dyes, RH 795, for imaging the membrane potential of motoneurons like cells (MNLCs) differentiated from adipose derived stem cells (ADSCs) using an epifluorescence-based cell imaging system. In this study described a novel method for the detection of action potential-capable MNLCs differentiated from ADSCs using voltage-sensitive dyes (VSDs). We compared the results of extracellular applied VSDs in a more detailed labeling of cellular processes with calcium indicators. MNLCs were maintained in culture medium and then loaded with the VSDs RH795. For the RH795 loading, cultures were maintained in a artificial cerebrospinal fluid (ACSF) buffer and incubated at 37°C in the dark. The cells were then washed 3 times and incubated for 60 minutes in ACSF buffer in the dark. With RH-795, a fluorescence change was observed in the frame immediately following the stimulation onset, reaching a maximum at 10–20 ms after stimulation onset and then decaying during the subsequent frames. This method allows for a repeatable fast and accurate stimulation of neurons derived from stem cell cultures to assess their differentiation state, which is capable of monitoring large amounts of cells.

## P82

### Beneficial Effect of 5-HT Receptor Agonist Administration on Memory Rehabilitation after Closed Head Injury

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P82

The serotonin (5-HT) receptors are a group of G protein-coupled receptors (GPCRs) and ligand-gated ion channels that found in the central and peripheral nervous systems. 5HT receptor can substantially influence brain functions such as learning and memory, perception of the environment, mood states, and responses to alcohol and other drugs of abuse. Lysergic acid diethylamide (LSD) as a 5HT receptor agonist causes expansion and an altered experience of senses, emotions, memories, time, and awareness. As we know closed head injuries are usually caused by blows to the head and frequently occur in traffic accidents, falls and assaults and leads to some disorders like spatial memory dysfunctions. Acute treatments of Adult 8-week-old male Wistar rats with agonists of 5-HT receptor subtypes were followed by a single injection of 5'-bromodeoxyuridine (200 mg/kg, i.p.) 2 h before killing to examine the effect of these drugs specifically on spatial memory rehabilitation. Our data showed that LSD can promote rehabilitation of spatial memory dysfunction after closed head injury.

**P83**

**Enhancement of Seizure Incidence after Traumatic Brain Injury**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P83

Traumatic brain injury (TBI) is an important clinical problem in the worldwide and especially due to breaking driving rules in IRAN, but undesirable consequences of trauma can persist for the rest of patient's life. We investigated the effect of a novel weight drop model of TBI on incidence of seizure 2 weeks after TBI. In this regard, 21 male Wistar rat weighted 250-300 gr randomly were divided into 3 groups: 1) Sham (n=7) 2) Pentylentetrazole (PTZ) (n=7) 3) TBI+PTZ (n=7). Firstly, TBI was induced in the middle of right parietal bone by releasing of 500 gr weight after removing of skin and exposure of skull. Seizure susceptibility was evaluated by injection of a subconvulsant dose of a GABA inhibitor drug, PTZ. Animals were observed during 1 hour after drug administrations and score of seizure was determined according to Racine's scale. Our finding show TBI remarkably increase the rate of tonic-clonic seizure incidence in compared to other groups. In the sham group 0%, PTZ 20 % and 80% in TBI group showed tonic-clonic seizure, respectively. In TBI-PTZ group both the rate and score of seizure

were significantly higher than sham and PTZ groups. According to our results induction of TBI (by our newly described weight drop model) increases the seizure susceptibility in the male wistar rats.

**P84**

**Intractable Post-Traumatic Epilepsy: Clinical Analysis of Patients with Blunt and Penetrating Head Injuries Sustained in War**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P84

Post-traumatic epileptic seizure is a common complication of brain trauma including military injuries. We present clinical characteristics and correlates of post-traumatic epilepsy in 163 head-injured veterans suffering from intractable epilepsy due to blunt or penetrating head injuries sustained during the Iraq-Iran war. The medical records of 163 war veterans who were admitted by the Epilepsy Department of the Shefa Neuroscience Center between 2005 and 2009 were retrospectively reviewed. The mean follow-up period after developing epilepsy was 17.2 years. The time interval between the trauma and the first seizure was shorter and the seizure frequency was higher in epileptic patients suffering from penetrating head trauma. There was no difference in seizure type between epileptic patients traumatised by blunt or penetrating injury. Patients with seizure frequency of more than 30 per month mostly had simple partial seizure. Frontal and parietal semiologies were observed more frequently in patients with penetrating trauma, whereas patients with blunt trauma showed a higher temporal semiology. The most common brain lesion observed by CT scan was encephalomalacia followed by porencephaly and focal atrophy. There was no association between intracerebral retained fragments and different characteristic features of epilepsy. Patients with military brain injury carry a high risk of intractable post-traumatic epilepsy decades after their injury, and thus require a long-term medical follow-up.

**P85**

**Spreading Depression in the Brain Cortex and Spinal Cord**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P85

Cortical spreading depression (CSD) has been suggested to underlie some neurological disorders such as migraine.

Despite the intensity with which many investigators have studied SD in the brain, only a few studies have aimed to identify SD in the spinal cord. Here we described the main characteristic features of SD in the spinal cord induced by different methods including various spinal cord injury models and demonstrated that SD enhances the spinal cord activity following a transient suppressive period. These findings suggest that SD may play a role in the mechanisms of spinal neurogenic shock, spinal cord injury, and pain. Furthermore, we studied the effect of CSD on the neuronal activity of the spinal cord. CSD was induced via cortical pinprick injury or KCl injection in the somatosensory cortex. CSD did not propagate into the cervical spinal cord. However, intracellular recordings of the neurons in the dorsal horn of C2 segment, ipsilateral to the hemisphere in which CSD was evoked, showed a transient suppression of spontaneous burst discharges, followed by a significant enhancement of the neuronal activity. This indicates a link between a putative cause of the neurological symptoms and the subsequent pain of migraine.

## P86

### **Effect of Concomitant Use of Erythropoietin and Progesterone in Traumatic Brain Injury**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P86

Traumatic brain injuries may cause some neurological deficits, such as altered level of consciousness or coma, sensory-motor dysfunction, and seizure attacks. The neuroprotective effect of progesterone and erythropoietin has been shown in different types of brain injuries and cerebral ischemia. This study aims to evaluate the probable additional neuroprotective effects of progesterone and erythropoietin after brain injury. The effects of progesterone, erythropoietin or the combination of these substances were investigated in 54 male Wistar rats suffering from traumatic brain injury. The effects of drugs were investigated using modified neurological severity scores as well as counting the number of dark neurons (injured cells) in the hippocampal CA1 and CA3 areas. Our data revealed that the scale of neurological deficits increased by co-application of progesterone and erythropoietin in brain-injured rats. Assessment of dark neurons did not show a significant decrease in the number of dark neurons after combined treatment compared to control groups. Our study showed that the combination therapy did not exhibit any synergistic effect and may worsen the outcome of traumatic brain injury.

## P87

### **Closed Traumatic Brain Injury Model in Sheep Mimicking High-Velocity, Closed Head Trauma in Humans**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P87

There are only a few, non-evidence based, neuroprotective strategies for treatment and prevention of brain injuries after closed head trauma. To establish new therapy strategies, a novel animal model is needed. The aim of our investigation was to link standardized small animal models and actual patient medical care. Data of experimental small animal studies often cannot be transferred to CNS injury in humans. For standardization of high-velocity brain trauma, novel devices for initiating closed traumatic brain injury in sheep were established. The following new devices were tested: A) an anatomically shaped rubber bolt with an integrated oscillation absorber; B) stationary mounting of the bolt to guarantee stable experimental conditions; C) different degrees of trauma severity, and D) trauma analysis via high-speed video recording. Measurements of intracranial pressure, pH, brain tissue oxygen, and carbon dioxide pressure were performed. Brain injuries were documented with MRI and compared to pathological findings. Skull fractures were prevented by the new devices. Enhancement of extracellular glutamate, aspartate, and GABA concentrations began sixty min after the trauma. MRI and pathological findings showed characteristic patterns of mild and severe brain trauma. The severe closed traumatic brain injury exhibited axonal injuries, subarachnoid hemorrhage, and contusions with bleeding. The model presented here achieves a gain in standardization of severe- closed traumatic brain injury. This model seems to close the gap between experimental small animal models and clinical studies. Comparing of this model with human findings showed several similarities and suggest that this model is reliable for clinically oriented experimental studies. Details of this study were published (Grimmelt et al., 2011).

## P88

### **The Incidence of Traumatic Brain Injury: a Meta-Analysis**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P88

In western countries such as United States data from 2002-2006 showed that at least 1.7 million people sustain a traumatic brain injury (TBI) each year. Of those individuals, about 52,000 die, 275,000 are hospitalized, and 1.365 million are treated and released from an emergency department. In 2000, direct medical costs and indirect costs such as lost productivity of totaled an estimated \$76.5 billion. Children aged 0 to 4 years, older adolescents aged 15 to 19 years, and adults aged 65 years and older are most likely to sustain a TBI. Almost half a million (473, 947) emergency department visits for TBI are made annually by children aged 0 to 14 years. Adults aged 75 years and older have the highest rates of TBI-related hospitalization and death. In twenty three European reports from Denmark, Sweden, Finland, Portugal, Germany, and from regions within Norway, Sweden, Italy, Switzerland, Spain, Denmark, Ireland, the U.K. and France an aggregate hospitalized plus fatal TBI incidence rate of about 235 per 100,000 was recorded but prevalence rate data were not reported from any European country. An average mortality rate of about 15 per 100,000 and case fatality rate of about 11 per 100 have been reported as well. The TBI severity ratio of hospitalized patients was about 22:1.5:1 for mild vs. moderate vs. severe cases, respectively. The percentages of TBI from external causes varied considerably and several reports reported an association of alcohol use with TBI. In eastern countries such as China, a total of 14,948 of cases of TBI were identified from 77 hospitals in eastern China. In Iran, TBI-patients in Motahhari hospital in Urmia during 2005 to 2006 years were recorded. From the total of 1796 hospitalized patients for TBI, 721 patients (40.1%) have acute TBI that 1392 (77.5%) of them were males. The findings of this study demonstrated that the lack of a system to road-user safety was the main cause of injury; therefore the focus of all activities should take place in this field.

## P89

### Traumatic Brain Injury and Genes

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P89

Traumatic brain injury (TBI) is one of the serious neurodisorders commonly caused by car accidents and sports. Preventive measures are highly recommended to reduce the risk and number of TBI cases. After TBI, the primary injury to the brain initiates a secondary injury process that spreads via multiple molecular mechanisms in the pathogenesis of TBI. Many studies in animals using cDNA microarray hybridization

technique have shown differential regulation of 86 genes (mainly transcription factors, signal transduction genes and inflammatory proteins) which take part in the physiological and pathological response to TBI. Genetic polymorphisms which involve interleukin-6 (such as -174G>C and -572G>C) and haemoxygenase -1 may influence the inflammatory effects seen after TBI. In addition, genes regulating the vascular responses including the hypoxia-inducible factor-1 and 2 (HIF1&2) genes activate following cerebral ischemia. Moreover, Apolipoprotein epsilon and P53 genes regulate the neuronal response to TBI. Also, there are three isoforms of the enzyme catechol-o-methyl transferase (COMT) encoded by 3 genetic polymorphisms (COMT Val/Val, COMT Val/Met, and COMT Met/Met) which regulate catecholamines activity following TBI. A greater understanding of the genetics could aid in the prediction of outcomes and could be targeted for treatment strategies.

## P90

### Methamphetamine and Traffic Accidents

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P90

Methamphetamine hydrochloride is a white to light brown crystalline powder, or clear chunky crystals resembling ice. The majority of street methamphetamine is produced in clandestine laboratories. The drug manufacturer states that patients should be informed that methamphetamine and amphetamine may impair the ability to engage in potentially hazardous activities such as driving a motor vehicle. In epidemiology studies drive-off-the-road type accidents, high speed, failing to stop, diminished divided attention, inattentive driving, impatience, and high risk driving have been reported. Significant impairment of driving performance would also be expected during drug withdrawal. In a recent review of 101 driving under the influence cases, where methamphetamine was the only drug detected, blood concentrations ranged from <0.05-2.36 mg/lit (mean 0.35 mg/lit, median 0.23 mg/lit). Driving and driver behaviors included speeding, lane travel, erratic driving, accidents, nervousness, rapid and non-stop speech, unintelligible speech, disorientation, agitation, staggering and awkward movements, irrational or violent behavior, and unconsciousness. Impairment was attributed to distraction, disorientation, motor excitation, hyperactive reflexes, general cognitive impairment, or withdrawal, fatigue and hyper somnolence.

## P91

## Epilepsy and Road Accidents

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P91

Epilepsy is one of the most prevalent serious neurologic conditions, affect 1% of the population worldwide. People with epilepsy may feel it's safe to drive when their seizures seem to be under control, but patients with epilepsy were seven times more likely to have a driving accident leading to emergency room care than those without epilepsy. People with seizures had 2.3 times the rate of fatal driver crashes as people with cardiovascular disease or high blood pressure and 4.6 times the rate for patients with diabetes. From results of a survey of 72 epileptic car drivers who had a mean driving history of 8.6 years, 18 (25%) had experienced one or more automobile accidents ascribed to a seizure while driving, with the total number of accidents of the surveyed group amounting to 35. All the drivers were known to have partial epilepsy, 13 of them having temporal lobe epilepsy. Most accidents caused damage to only the driver's car and/or mild physical injury; and fifty-four percent of the accidents were not reported to the police, and many that were reported were ascribed to driving while asleep, to careless driving or to similar behavior.

### P92

## Importance of Adequate Sleep Time in Safe Driving

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P92

Sleep deprivation (SD) increases the risk of human-error related accidents and a major cause of motor vehicle accidents. The overall prevalence of insufficient sleep in adults has been estimated at 20%. According to a comprehensive study prevalence of daytime sleepiness, among young adults (age 21 to 30 years), the average nocturnal sleep time during weekdays was 6.7 hours and on weekends was 7.4 hours. Studies in young adults indicate that 8 to 9 hours of extended nocturnal sleep are needed to resolve sleepiness caused by decreased sleep time. Driving is a complex task, which can be broken down into specific cognitive processes. Sleep-deprived driving is the operation of a motor vehicle while being cognitively impaired by a lack of sleep. Results

of a 1998 survey showed, 23% of adults have fallen asleep while driving. There is not accurate statistical document of sleep deprivation related events in Iran. Total SD impairs attention and working memory, but it also affects other functions, such as long-term memory and decision-making. Partial SD is found to influence attention, especially vigilance. Thus, by attention to frequent incidence of sleep deprivation and extensive effects of SD on cognitive functions during driving, modification of sleep time in order to prevention of insufficient time, could be valuable way to increase safe driving and prevent motor vehicle accidents.

### P93

## Comparison Effect of Aggressive Behavior on Road Traffic Accidents between Iranian and British Drivers

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P93

Frustrating situations that impede or prevent some form of ongoing goal-directed behavior are believed to act as a catalyst for aggressive behavior. From social learning approaches aggression is a learned response through observation or imitation of socially relevant others. Many psychological factors are at play in aggressive driving and many may prove difficult to control. Human beings are naturally prone to territoriality and have the tendency to view their vehicle as an extension of their personal domain. They feel threatened by other vehicles and respond aggressively or out of an instinct of self-protection. Nowadays, aggressive responses are common among Iranian people specially drivers. Road traffic accidents (RTAs) are leading causes of death and serious injury in military organizations. It has been estimated that annually one million people die in road traffic accidents worldwide. According to accident statistics, 9.1 Finns, 8.9 Dutch, and 7.5 Britons per one billion vehicle kilometers were killed in traffic accidents in 2002 whereas the corresponding figure for Greeks and Turks were 26.7 and 73, respectively. Based on statistics of 1390 in Iran, 38.28/100 persons died during last decade. Most road traffic accidents can be directly attributed to human factors as a sole or a contributory factor such as mood. In this review study, we compared relation between RTA and aggressive characteristics of drivers in Iran and UK. Previously published results indicated Iranian drivers behave more aggressively in anger situation than the British drivers. Finally, it can be concluded that the high rate of motor vehicle accidents in Iranian population may be caused from more aggressive temper of Iranians. Whereas, a broad range of risky

driving behaviors contribute to RTAs, preventing or changing these offers promise for accident prevention.

#### P94

### Music While Driving; the Impact of Music on Driving Performance

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P94

Music has been used as mood modulator by humans for many years. Nowadays music is mostly play as one of the switch in a car. Although music listening is common at during driving. Its impact on driving performance has developed debates and controversies. Studies have shown that self-selected in-car music listening can improve driver's mood and behavior. However other studies have reported that background music can be a risk factor for distraction. Spending of time could be increased by performing music search that eventually, driver eyes off the roadway, therefore, suggests that searching music could be problematic at driving. The results of this study demonstrate music as a mood regulator which could decrease anxiety and impulsive behavior in drivers. They also suggest that preparation a self-preferred classic music selection before deriving could reduce distractions due to music search tasks.

#### P95

### Sleep Apnea and Traffic Accidents; A Brief Review

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P95

Sleep apnea syndrome (SAS) is a potentially serious sleep disorder in which breathing repeatedly stops and starts. SAS can cause drowsiness and lack of concentration during driving due to sleep deprivation. Patients with clinical features of SAS and self-reported sleep attacks at the wheel do poorly in simulated monotonous driving. The goal of this investigation was to review the different views about the relationship between SAS and traffic accidents. We performed a systematic literature search, using Pub Med with the following entry: "Accidents, Traffic"[Mesh] and "Sleep Apnea Syndromes"[Mesh]. The search resulted in identifying 216 studies. Full texts of articles which met the inclusion criteria and their finding are discussed in this study.

#### P96

### Childhood Condition and Risky Behavior in Adulthood

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P96

Behavior refers to the actions made by organisms in conjunction with their environment, which includes the other systems or organisms around as well as the physical environment. Lots of types of behavior exist such as conscious or unconscious, voluntary or involuntary and overt or covert. Childhood has a remarkable role on formation of human behavior in his later life which already has been proven. Lots of risky behaviors origin from childhood imbalances, habits, wishes, playing and factors which affect children's life such as living place cultural level, lack of education, family problems, and social deficits. One of the most obvious risky behaviors is traffic violation whether derived from childhood or from other risky behaviors like smoking, drinking or using illegal drugs. This review aimed at having an overview on relations between some risky behaviors and their effectiveness from childhood with a particular focus on the driving impairment.

#### P97

### Motor Vehicle Accident During the Pregnancy

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P97

Trauma during pregnancy is remarkably common, motor vehicle crashes are cause of hospitalized trauma during pregnancy. Trauma occurs in 5% of pregnancies that appropriate high proportion of maternal and fetal mortality. Motor vehicle crashes, falls, assaults, including domestic violence, are all important mechanisms of injury. Motor vehicle accidents account for more than 50% of all traumas during pregnancy and 82% of fetal deaths occurring during these automobile accidents. The most common injuries seen in pregnant women, such as: blood loss, abruption placenta and the presence of disseminated intravascular coagulation was the most significant predictor of fetal mortality. Following blunt trauma, abruption of the placenta is the most common cause of fetus loss. The use of seat belts decrease rate of maternal and fetal mortality. Despite current recommendations and laws regarding seat belt use

during pregnancy, one-third of pregnant women didn't use seat belts or use improperly. In conclusion, pregnant women should be counseled to wear seatbelts throughout pregnancy to reduce motor vehicle crashes risk.

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## P98

### Road Traffic Collisions and Spinal Cord Injuries

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P98

A spinal cord injury (SCI) refers to any injury to the spinal cord or nerves at the end of the spinal canal that is caused by trauma instead of disease often causes permanent changes in strength, sensation and other body functions below the site of the injury. Road traffic collision (RTC) or car crash occurs when a vehicle collides with another vehicle, pedestrian, animal, road debris, or other stationary obstruction, such as a tree or utility pole. Motor vehicle related events were the most common event leading to spinal cord injury in this sample. In RTCs, occupants made up approximately 60% of all spinal injuries, pedestrians accounted for 17%, and bicycle and motor cycle riders approximately 8% and 15% respectively. Through these statistics this paper has a review on the causes of SCIs specially derived from RTCs and its consequences and prevalence.

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## P99

### The Whole History of Shefa Research Center's Activities on Road Safety During the Last Year

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P99

Iran and neighboring countries have a very high rate of road accidents with thousands of victims per year. In last 20 years, more than half million Iranian were killed in road accidents; millions suffering from injuries. As you know unintentional injuries are a leading cause of death among children and young adult. "Shefa" Neuroscience Research Center is working on different scientific researches on neuroscience as well as working on the treatment of the related diseases. Furthermore, it is planned to have a comprehensive program on the prevention of road accidents and neurotrauma. Road safety publicity can be used to achieve various aims and objectives. In general, the aims of such publicity are to change the road user's behavior, attitude or knowledge in order to increase road safety. Mass media campaigns

can achieve the following: increase awareness of a behavior, raise the level of information about a topic or issue, help form beliefs, especially where they are not firmly held, make a topic more salient and sensitize the audience to other forms of communication, stimulate interpersonal influences via conversations with others (e.g. Police, teachers, or parents), generate information seeking by individuals, and reinforce existing beliefs and behaviors.

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## P100

### Potential Effect of Drinking before Driving in Crash Production; a Cultural Problem

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P100

Driving is a complex psychomotor task involving distinct cognitive, perceptual and decision making skills. It needs to more concentration and alertness to driving safe. Several studies have shown the potential effects of alcohol in crash production by epidemiological and laboratory analysis. Alcohol is obviously the most common single cause of traffic accidents in America. A review of the relation of alcohol to fatal accidents showed that nearly half of the drivers fatally injured in an accident had an alcohol concentration in the blood of 0.05 g/l or more. Driving is therefore a divided attention task involving speed and lane control as well as monitoring. To do this in a safe manner requires careful attention and alertness which can be problematic for people who consume alcohol before driving. Generally alcohol could be effect on reaction time, tracking, concentrated attention, divided attention performance, information processing capabilities, visual function, perception, psychomotor performance, and also on driver performance measures. It has been reported that if the blood alcohol gets to 3g/l, hallucination starts and hazardous behavior appear, because driver doesn't have a real evaluation for distinguish of distances. The results of many studies show that alcohol remains one of the main contributing factors of traffic accidents in many countries. So, prevention of alcohol consumption among drivers must be improved.

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## P101

### Reduction of Driving Skills by Fatigue Related Sleep Deprivation; a Brief Review

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P101

Sleep deprivation is a condition of not having enough sleep; it can be either chronic or acute. A chronic sleep-restricted state can cause fatigue. Fatigue is a subjective state related to sleep deprivation, the more someone is deprived of sleep the more likely that person is to be fatigued. Several studies indicated that drowsiness/fatigue can affect steering performance and speed control. Researchers showed that fatigue had more effect on the steering performance of drivers when they drove on straight road segments than when they were driving on curved road segments, they suggested it is more difficult for fatigued drivers to pay attention when the task demands are low, than this task demands are higher. Driver fatigue is an important causal factor in many highway crashes. It has been estimated that 1,200 deaths and 76,000 injuries annually could be attributed to fatigue-related factors and that the cost of these crashes at \$12.4 billion per year. Accidents due to driver sleepiness, caused by sleep deprivation or drug effects, are often assumed to be the result of the driver falling asleep behind the wheel. Reducing the extent of the drowsy driver problem is critical to improving the safety of roads. Accident rates showed a small increase after a moderate reduction in the previous night's sleep (4h vs. 8h), and a marked increase with progressive sleep deprivation. The driving data provide confirmation that sleepiness is a significant factor leading to off road accidents. In this way the main point is that the steering performance of drivers is impaired when they stayed awake for an extended period. Our review brings us one step closer to the development of highway engineering and in vehicle drowsy driver warning systems and devices to prevent the sleepy driver from endangering themselves and others.

## P102

### A Brief Review; the Importance of Visual Ability and Driving Performance

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P102

The eyes are organs that detect light and convert it into electro-chemical impulses in neurons. Visual perception is the ability to interpret information and surroundings from the effects of visible light reaching the eye. Medicine recognizes that altitudes above 1500 meters start to affect humans so that, the eye is very sensitive to restriction of its supply of oxygen. A dimming of vision accompanied by loss of peripheral perception may result from low blood pressure, shock and loss of consciousness. Generalized hypoxia occurs in healthy people when they ascend to high altitude, where it causes altitude sickness leading to potentially fatal complication. On the other

hand, consuming alcohol can have short-term negative effects on vision. Brain functions can be impaired by alcohol within minutes of consumption since alcohol is absorbed in the blood. Depth perception and night vision are affected by high level alcohol in blood. It becomes impossible to accurately judge how far away objects are when depth perception deteriorates. Vision becomes blurred or you may see double since and eye muscles lose their precision causing them to be unable to focus on the same object. After drinking alcohol, drivers tend to focus on the road straight ahead and avoid what is happening in their side vision. In this manner age is important in eyesight too. In Causes of visual aging, although there are neural losses, the major decline is due to changes in the eye's optics. First, the lens becomes yellower, making discrimination of blue colors more difficult. More importantly, less light entering the eye reaches the photoreceptors. Further, the pupil shrinks, allowing less light to enter the eye. In results of this factors indicate older driver's demands quicker reaction times in response to more complex situations. Finally, visual acuity and driving performance change gradually, and older drivers may not be aware of changes.

## P103

### Driving-Related Risks in Attention Deficit Hyperactivity Disorder (ADHD) of Teens and Adults

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P103

To determine whether teenagers and young adults with attention deficit hyperactivity disorder (ADHD) have more motor vehicle citations and crashes and are more careless drivers than their normal peers. In fact, studies have found that teenagers and adults with attention deficit disorder are nearly twice as likely as the general population to have had their licenses suspended. People with ADHD have serious difficulties planning ahead, following through, and staying on task things you need to do to drive safely. Parent ratings of current symptoms of ADHD, oppositional defiant disorder, and conduct disorder, a survey of various negative driving outcomes, and a rating scale of driving behavior. ADHD, and especially its association with oppositional defiant disorder/conduct disorder, is associated with substantially increased risks for driving among teenagers and young adults and worthy of attention when clinicians counsel such patients and their parents.

## P104

### Survey on Cell Phone Usage on Driving Performance; Handheld Vs. Hard Free

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P104

Reviews in many countries indicate that drivers often talk on mobile (cell) phones. Studies have been done on possible effects of concurrent mobile phone use on driving performance. Previous studies have found that phone talking could impair performance on simulated or instrumented driving tasks, using such measures as reaction time, following distance, and situational awareness. Most of these impairments have resulted from cognitive distractions. Furthermore, some other suggested that neither gender nor driving skill level had any effect on such hazards. So a person using a mobile phone when driving is four times more likely to have a crash. Numerous governments have introduced regulations governing the use of mobile (cellular) telephones while driving. Data indicated a significant effect of telephoning while driving as opposed to normal driving internationally, drivers report usually using hand held phones. Due to worries about risks of a potential crash, use of hand held phones is illegal in most countries. There also was some evidence that the use of a hand-held mobile phone (when compared to a hands-free system) was associated with poorer driving performance. We concluded that simply conversing over a hands-free telephone while driving does not in itself impair performance. Driving performance was rated better for hands free than for handheld mode. Interestingly research shows so few effects from hand free mobile phone as it may not be illegal. However, a difficult conversation may affect the driving adversely, and any prolonged manipulation of the telephone is liable to produce a performance decrement, particularly under conditions that put heavy demands on the driver's attention and skill. Put this together result showed higher risk of car crash by using cell phone.

## P105

### Geographic Information Systems on Accident Risk Assessment and Management

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P105

The paper discusses the use of modern information technologies, and in particular geographic information systems (GIS), in the management and control of major accident risk. For this purpose, the regulatory framework of the recent "Seveso II" Directive is briefly described. The referencing in space of the phenomena may be defined in terms of a geometrically exact or a relative location. The former uses local or world coordinate systems defined using a standard system of spheroids, projections, and coordinates which give an approximation of the form of the earth (a spheroid) onto a flat surface. The coordinate system may be purely local, measured in tens of meters, or it may be a national grid or an internationally accepted projection that uses geometrical coordinates of latitude and longitude. This paper places the concept of transportation GIS in the broader perspective of research in GIS and Geographic Information Science. The emphasis is placed on the requirements specific of the transportation domain of application of this emerging information technology as well as on core research challenges.

## P106

### Review on Strategy Road Safety Improving in Developing Country

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P106

Car accidents are documented as a growing public health problem in Iran as well as other developing countries. Generally growing number of population and vehicles are not accompanied by extending road construction programs. These could be result in high death, disability, and economic loss in such country compare to develop one. This mainly affected young person who are economically more active. In this line, World Health Organization (WHO) has stressed some strategy and proposed guidelines to reduced car accident in developing countries. Including; adequate epidemiological data on traffic injuries should be collect. In some country with low level of car crash vehicle ownership is limited, which lead to less crowded traffic. In such places, improvement and expanding of public transport could reduce road traffics. Surveys also find that improving medical services and education could significantly reduce car accidents. Also research has found that driver's errors could be accompanied by law violations. In some cases driver observations of police station is so weak, should be more in some date of year and during vacation times. Importantly analysis of accident data should be done for identification of locations problems and detect most dangerous areas. Road and vehicle engineering measures

have been well proven effective in reducing accidents. Further investigation is essential and will require close intersectorial collaboration between, traffic police, health, law and transport authorities.

#### P107

##### **Weather-Related Road Accident: A Brief Review**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P107

Road accident severity may be influenced by a number of various systematic causal factors. The Weather and road accidents have a close relationship with each other and a number of methods have been proposed for measuring the risk of a road accident with rainy, foggy, and snowy weather and high winds. Recent studies indicate that road collision rates increase during precipitation. The weather was found to be a major factor affecting accident number. While other studies believe that the weather might be a contributing factor in accidents, though not necessarily the principal one. The important thing is to understand the link between different climates and travel risk. On very wet days the number of accidents was often double that of corresponding dry days. Also, Single-vehicle accidents were affected more by wet weather than were most other types of accident. Statistical testing shows that the average frequency of accidents, during periods of rainfall, is significantly different from the average frequency at other times. On the other hand, data suggest that accident risk returns to normal, despite the lingering effects of wet road conditions. We conclude that traffic weather forecast could be considered as a lowering weather-related road accident factor.

#### P108

##### **Memory of Accident in Children**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P108

Road traffic accidents represent the important health threat to children in developing countries. Post-traumatic stress disorder (PTSD) can occur as result of road traffic accidents. In this regard, people under 30 years old are the main victims of road traffic accidents. During previous decades road accident consequences for mental state or other aspects of life was neglected. Survey proposed that psychiatric problems are common during respondents. Almost twenty percent of subjects described psychiatric complications at one year. Nature

and severity of physical injuries showed no significant correlation with psychiatric disorders. Studies have shown PTSD is common among who have experienced road accident and associated with disability especially for travel. PTSD found in the 35 percent of children, which were involved in the road traffic accidents. Children with PTSD were more likely to have social withdrawal, emotional regulation and blaming others. Moreover, some data have suggested that the reactions of children to accident may be temporary. Providing children with opportunities to talk about their accident may be helpful in preventing or reducing psychological distress. In conclusion, setting some to reduced emotional stress of road accident could help children to recover from PTSD.

#### P109

##### **Decreased Driving Performance in People with Parkinson's Disease Due to Cognitive Overloading**

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P109

Cognitive deficits such as impairments in attention, memory, information processing and executive functioning can be found in some Parkinson's disease (PD) patients. Recent studies suggested that PD drivers generally performed poorer than their healthy age-matched controls with regards to their cognitive and motor abilities during the psychometric testing. According to Michon's model of car driving three major levels of driving behavior exist include strategic level, tactical level and operational level. These three levels of driving behaviors may be influenced by cognitive deficits in drivers with PD resulting in the inability to dual task and handle the cognitively demanding driving environment. The participants with PD performed poorer in the operational level where they have to exhibit behaviors such as performing second to second driving and alter their behavior while multitasking. In addition, PD drivers are at risk of compromising their operational level strategies of driving under the presence of cognitive overloading. People with PD also had a significant increased response time to the cognitive overloading task when compared to the age-matched controls. Drivers' training may incorporate cognitive strategies for people with Parkinson's disease who decides to continue driving. In conclusion, the driving

performances of people with PD are significantly more affected under the presence of cognitive overloading compared to their age-matched control.

## P110

### Driving and Neurodegenerative Diseases

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P110

The proportion of elderly in the general population is rising, resulting in greater numbers of drivers with neurodegenerative disorders such as Alzheimer's disease (AD) and Parkinson's disease (PD). AD is a progressive neurodegenerative disorder typified by memory impairment with executive dysfunction, motor problems, and/or language difficulties. Parkinson's disease is a progressive neurodegenerative disease that impairs ability to execute conscious physical movement in addition to other motor functions. What is more, mood disturbances may occur as well. However, PD appears to be associated with decreased driving and increased crashes, especially in those with worse motor and cognitive dysfunction. A review panel found that drivers with mild cognitive impairment (MCI)-very mild AD (Clinical Dementia Rating Scale [CDR]=0.5) -have impairments similar to drivers aged 16-21 or those driving under the influence of alcohol at a blood alcohol concentration <0.08%. They were also recommended to reassess dementia severity and driving fitness every 6 months, but quit driving in mild AD (CDR=1) due to history of increased crashes and poor driving performance. In conclusion, Medical diagnosis or a clinician's assessments alone are not accurate enough to determine driving competence in those with dementia. Although neuropsychological tests help them to understand associations of driver performance with cognitive impairment, a general lack of validated cut off scores makes it impossible to employ these tests in a standardized fashion to advice patients. Furthermore, there are no established guidelines on driver's follow-up timing with mild dementia; recommendations range from 6 months or less than a year. Thus, medical diagnosis or age alone is not reliable enough to predict driver safety, crashes, or revoke the driving privileges of these drivers. In addition, outlining the evolution of driving safety, understanding the mechanisms of driving impairment, and developing a reliable and

efficient standardized test battery for prediction of driver safety in neurodegenerative disorder informed healthcare providers to advise their patients about neurodegenerative disorders with more certainty, affected policy, and develop rehabilitative measures for driving.

## P111

### Road Safety and Children's Education

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P111

Road safety must be shared responsibility between the school, the parents/caregivers, the children, territorial authority, transport agencies, and police. Children need to learn to use the roads safely, to walk and cycle in safety, and also to use their common sense when crossing a road or getting into a car. Road safety is essential for children's freedom, development, and exercise and of course the roads need to be used with respect. Road safety should be taught by example and guidance with a trusted adult, from an early age. Parents need to teach awareness of the roads from the moment a child can understand. In addition for primary age children basic road safety is in the PSHE (personal, social and health education) curriculum and more is being done to increase the time spent on teaching road safety in schools. However the best training for children is practical pedestrian training at the roadside. Furthermore older children are at further risk because of the longer journeys to and from school with friends and often on their own. In school, children are taught to recognize and manage risk and make safer choices about healthy lifestyles, different environments and travel. In conclusion, the Government will have ambitious targets to reduce the number of children who die or are injured by 50%, but parents and child carers have a duty to inform, educate and train our children and to maximize child safety on our roads.

## P112

### Safe Driving and Alzheimer's Disease

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The Neuroscience Journal of Shefaye Khatam, 2015; 2(S3): P112

People with Alzheimer disease (AD) have decreases in brain cell function that may increase their risks as drivers. The changes in brain cells affect memory (at first, short-term memory and then much later, long-term memory) and other thinking functions. In addition, people with early AD, though often very functional in many areas of life, may not be as competent behind the wheel of a car as those without the memory-damaging disease. Furthermore, many people with AD and their families are not aware how dementia affects a person's driving abilities, often until there has been an incident involving an accident, getting lost while driving or other driving crisis. The need for overall education around this issue is critical. In addition, the declining cognitive abilities of a person with AD will ultimately lead to the need for the individual to stop driving. It is difficult to determine when restrictions are needed because little solid evidence exists linking various stages of dementia with driving behavior. However, at some point in the progression of the disease, driving performance errors will present a safety risk to both the individual and the public. In conclusion, the person with AD should participate in the planning and decision making regarding the cessation of driving. Furthermore, driving demands quick reaction time and fast decision making; because of this, a person with AD will eventually become unable to drive. However, driving privileges must be withheld when the individual poses a serious risk to self or others.

***Publisher:*** Shefa Neuroscience Research Center


***Layout Designing & Publication:***

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Imam Ali: "Do act according to the clear signs, because the way is straight and leads to the house of safety".

امام علی (ع) می فرمایند: "راه صحیح شما را به خانه امن می رساند".

قال الامام علی (عليه السلام): "فالطريق نهج، يدعوا الى دار السلام".

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