Faculty of Medicine,
Beni-Suief University Postgraduate Research Program Template

1. Proposed Study Title;

Effect of Melatonin Supplemented at the Light or Dark Period on Recovery of Sciatic Nerve Injury in Rats

2.Candidate Name;

Enas Ezzat Mohammed Rateb.

3. Date of Registration; January 2014

a. Occupation: Demonstrator (معيد), Physiology Department, Beni-Suief University.

b. Full mailing address : enas_omyahya@yahoo.com

c. Phone number	01004545601
d. Fax number	No.
f. E-mail addresses	enas_omyahya@yahoo.com

4. Investigators Contact Information;

a. Principal Investigator	. **Prof.Dr. Samah Elattar** Professor of Physiology Faculty of Medicine – Cairo University
b. Other Investigators	**Prof.Dr..Nashwa Saeed Eltablawy** **Professor of Physiology** **Faculty of Medicine – Cairo University** **Dr. Shaimaa Nasr Amin** **Lecturer of Physiology** **Faculty of Medicine-Cairo University**

c. Department name	**Physiology**
d. Full mailing address	No.
e. Phone number	23624747
f. Fax number	no
g. E-mail addresses	no

5. Background and Rationale;

Peripheral nerve injuries are commonly encountered in clinical practice due to several causes such as accidental trauma, acute compression, or surgery. All of these traumas can cause temporary or life-long disabilities that can subsequently lead to social or economic problems. Despite recent advances in microsurgical techniques and equipments, functional recovery following repair of transected nerves often remains suboptimal. Following injury, dramatic changes occur in the axon, cell body, and the Schwann cell covering of the nerve to help prepare for regeneration. Besides, changes in the intracellular environment, including molecular composition in lesioned neurons, resulting in overproduction of reactive oxygen species have also been occurred **(1).**

Melatonin is synthesized by the pineal gland predominately in a circadian manner; however, there is also non-circadian production in other organs.

Melatonin plays an important role in the regulation of many metabolic processes and acts as a signal for certain physiological events which may act as an antioxidant molecule showing effects on neurogenesis, intervening in lipid metabolism**(2).**

Melatonin concentrations in the body are typically lower during the day and reach to maximal levels at night in the dark **(3).**

6. Objectives;

The present work aims to study the effect of exogenous melatonin treatment on crush injuries of the sciatic nerve in rats and documents if that melatonin treatment has significant beneficial effect on sciatic nerve injury if it is given in the light or the dark.

7. Study Design; e.g. randomized controlled trial

Case control study.

8. List of Correlative Studies; (maximum five references if applicable)

1- Stoll, G., Muller, H.W., 1999. Nerve injury axonal degeneration and neural regeneration: basic

insights. Brain Pathol. 9, 313–325.

2- Maldonado, M.D., Siu, A.W., Sanchez-Hidalgo, M., Acuna-Castroviejo, D., Escames, G., 2006. Melatonin and lipid uptake by murine fibroblasts: clinical implications. Neuro Endocrinol. Lett. 27, 601–608

3- Waldhauser, F., Waldhauser, M., Lieberman, H.R., Deng, M.H., Lynch, H.J., Wurtman, R.J., 1984. Bioavailability of oral melatonin in humans. Neuroendocrinology 39, 307–313.

4- Genovese T, Mazzon E, Muia C, Bramanti P, De Sarro Cuzzocrea S (2005) Attenuation in the evolution of experimental spinal cord trauma by treatment with melatonin. J Pineal Res38:198–208

5- Kaya, Y., Sarikcioglu, L., Aslan, M., Kencebay, C., Demir, N., Derin, N., Angelov, D.N., Yildirim, F.B., 2013. Comparison of the beneficial effect of melatonin on recovery after cut and crush sciatic nerve injury: a combined study using functional electrophysiological, biochemical, and electron microscopic analyses. Childs Nerv. Syst. 29, 389–401.

9. Study Methods;

Population of study & disease condition (e.g women with hepatitis, ……)

Adult male rats with the SNI only rats underwent a nerve injury procedure..

Background and Demographic Characteristics (e.g. weight, age ……)

Adult rats100-150 gm

Inclusion criteria:

1. Adult male albino rats.
2. Age 4-6 weeks.
3. Body weight 100-150gm

Exclusion criteria:

1. Female rats
2. Young age (younger than 4 weeks)
3. Small body weight (less than 100 gm)

Interventions: (in details) .

Forty adult male albino rats will be included in this study. Rats will be acclimatized to nomal environmental conditions. All rats had access to food and water and were housed in standard cages in an animal room with controlled environmental temperature and relative humidity.

Rats were randomly divided into 4 groups and they were synchronized to a 12 h light \12 h dark schedule.

SNI was induced by clamping the sciatic nerve at the upper border of the quadratus femoris for 2 min for all groups except the control one**(4)**.

The groups are:

1-**Group 1(**n=10**)**: control group.

2-Group 2 (n=10**):** SNI was induced and the rats will be injected intraperitoneally with vehicle**.**

3-Group 3(n=10**):** SNI was induced and the rats will be injected intraperitoneally by 50 mg/ kg of melatonin in light period**(5)**.

4-Group 4(n=1**0):** SNI was induced and the rats will be injected intraperitoneally by 50 mg/ kg of melatonin in dark period.

Six weeks after melatonin administration, the following parameters will be measured:

1-Superoxide dismutase.

2-Inflammatory marker(IL-1B).

3-NGF.

4-Bcl-2.

5-Nerve conduction velocity.

6-Muscle contraction.

Possible Risk:

none

Primary outcome parameter (maximum two)

1- Nerve conduction velocity

2- Superoxide dismutase and NGF

Secondary outcome parameters

1- Inflammatory marker(IL-1B)

2- Apoptosis (Bcl-2)

3- Muscle contraction

Sample size (number of participants included)

40 rats

Statistical analysis

Data was summarized using mean, standard deviation for the quantitative variable. Comparisons between groups were done using analysis of variance (ANOVA) with multiple comparisons post hoc test in quantitative variables. P-values less than 0.05 were considered as statistically significant**.**

10.Source of funding;

None

11. Time plan; (when to start/ when expected to finish/ when to publish)

Start: February2015

End: : August 2016

Publish: September 2016

12. Ethical committee approval;

Approved by the Institutional Ethics Committee. All rats will be provided with standard laboratory chow and water and will be housed in accordance with institutional animal care policies.

13. Cooperation with other departments;

Name of department Biochemistry

Name of investigators

14. Other notes;