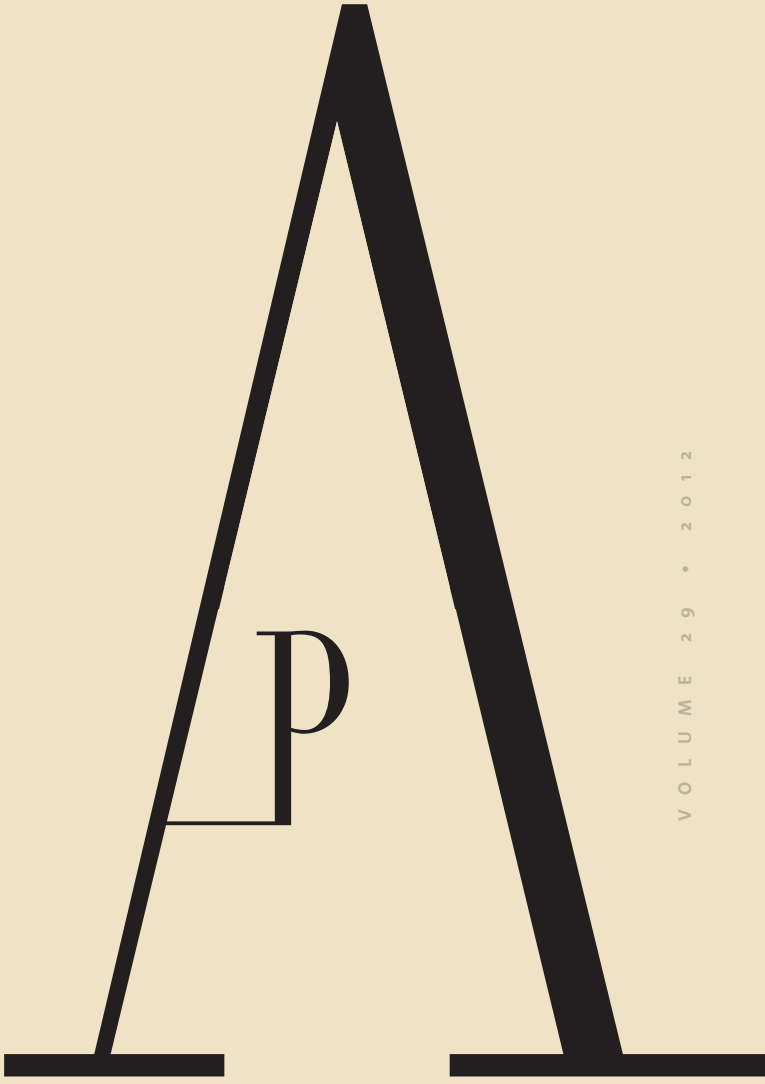
# ANTROPOLOGIA PORTUGUESA



VOLUME 29 • 2012

ANTHROPOLOGY AND HEALTH

CENTRO DE INVESTIGAÇÃO EM ANTROPOLOGIA E SAÚDE UNIVERSIDADE DE COIMBRA

# Assessment of the intake of tryptophan-enriched cereals in the elderly and its influence on the sleep-wake circadian rhythm

**Rafael Bravo[1]; Sergio Matito[2]; Javier Cubero[3]; Lourdes Franco[1]; Cristina Sánchez[1]; Ana B. Rodríguez[1]; Montserrat Rivero[4]; Carmen Barriga[1]**
rbravo@unex.es

**Abstract** Sleep-wake circadian rhythm disturbances are a common problem associated to aging. Although this problem can be caused by several factors, low levels of the indol melatonin are related with these alterations. Our aim was to evaluate if the consumption of cereals enriched with tryptophan, the precursor of both serotonin and melatonin, can enhance sleep problems in elderly people. Participants (n=12; aged 55-67 yr) were selected from Elderly people

**Resumo** Perturbações do ritmo de sono circadiano são um problema comum associado com o envelhecimento. Apesar deste poder ser causado por vários fatores, baixos níveis de melatonina indol estão relacionados com estas alterações. O nosso objetivo foi avaliar se a ingestão de cereais enriquecidos com triptofano, o percursor de serotonina e melatonina, pode melhorar os problemas de sono de pessoas de idade. Os participantes (n=12; com idades entre os 55 e 67 anos) foram selecionados da Univer-

[1] Chrononutrition Laboratory, Department of Physiology, Faculty of Science, University of Extremadura, Spain
[2] "La Paz" Healthy Center
[3] Health Education Lab. Experimental Science Education Area, Faculty of Education, University of Exremadura, Spain
[4] General Scientific Manager, Grupo Ordesa S.L. Barcelona, Spain

University of The University of Extremadura. During all the assay participants wore a wrist actimeter and they filled every week an STAI anxiety test. Data were collected following this schedule: Control week: participants ingested a control cereal both at breakfast and dinner (22.5 mg tryptophan/ 30g product per dose); Treatment Week: volunteers consumed a tryptophan enriched cereal both at breakfast and dinner (60mg tryptophan/ 30g product per dose); Post-treatment week: participants ingested their habitual diet. We observed a decrease in sleep latency ($p<0.01$), wake bouts ($p>0.05$) and sleep fragmentation ($p<0.001$); on the other hand, an increase in actual sleep time ($p<0.01$), sleep efficiency ($p<0.01$) and immobile time ($p<0.01$) were detected. With respect to the anxiety test, there was an improvement in the state of anxiety. In conclusion, through a tryptophan-enriched diet age related sleep problems can be improved.

**Key words** Chrononutrition; tryptophan; sleep; elderly.

sidade Sénior da Universidade da Extremadura. Durante todos os testes os participantes utilizaram um actómetro de pulso e preencheram semanalmente um teste de ansiedade (STAI). Os dados foram recolhidos com o seguinte horário: semana de controlo, os participantes ingeriram um cereal de controlo ao pequeno-almoço e ao jantar (22,5mg de triptofano/ 30g de produto por dose); semana de tratamento, os voluntários consumiram um cereal enriquecido com triptofano ao pequeno-almoço e ao jantar (60mg de triptofano/ 30g de produto por dose); semana pós-tratamento, os participantes ingeriram a sua habitual dieta. Observámos um decréscimo na latência do sono ($p<0,01$), ataques de vigília ($p>0,05$) e fragmentação do sono ($p<0,001$); por outro lado, foram detetados um aumento no tempo do sono ($p<0,01$), eficiência do sono ($p<0,01$) e tempo imóvel ($p<0,01$). Em relação ao teste de ansiedade, houve uma melhoria no estado de ansiedade. Em conclusão, problemas de sono relacionados com a idade podem ser melhorados através de uma dieta rica em triptofano.

**Palavras-chave** Crononutrição; triptofano; sono; idosos.

## Introduction

Elderly people usually show poor nocturnal sleep (Yong-Lu *et al*., 2002) and about 30% of people over 50 years of age suffer from sleep problems like frequent nocturnal arousals, higher sleep latency and lower assumed sleep than mature people (Zhdanova *et al*., 2009). These alterations are associated with attention or memory difficulties, mood alterations and day-time sleepiness.

Tryptophan is an essential amino acid (Figure 1) which is involved in sleep quality through its metabolites neurotransmitter serotonin and indol melatonin (Garrido *et al*., 2010; Cubero *et al*., 2011). It is well known that melatonin levels decreases in elderly people – it even can be absent – (Baskett *et al*.,

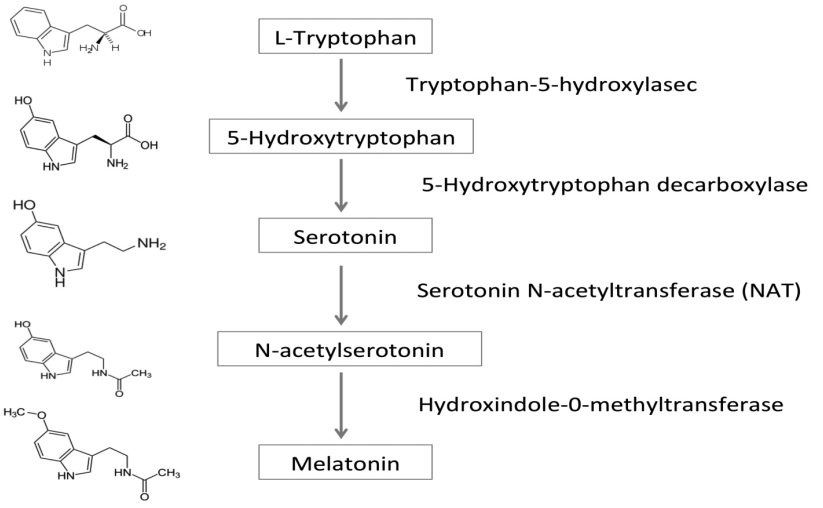



**Figure 1.** Melatonin synthesis pathway from essential amino acid tryptophan.

2003). Sleep problems in old people may be caused by alterations in their tryptophan metabolism. Such alterations produce low levels of the neurotransmitter serotonin – its highest peak is produced at the end of light hours – and the hormone melatonin – which has its peak during dark hours through serotonin N-acetyltransferase activation (Hussain and Mitra, 2000). These molecules are involved in other processes like mood, depression, memory or attention (Silber and Schmitt, 2009).

It has been shown through tryptophan-enriched diets that both serotonin and melatonin levels can be increased, reducing sleep problems (Cubero *et al*., 2005). This may consequently improve sleep in the elderly. Our aim was to evaluate how tryptophan-enriched cereals (ORDESA S.L.) influence old peoples mood and sleep problems.

## Materials and methods

### Sample

Participants (n=12) were volunteers aged between 55 and 67 (Table 1) years who suffered from sleep problems (more than three nocturnal awakenings or more than one hour to fall asleep). All volunteers were retired and women were post-menopausal. They were selected from Elderly People University of the University of Extremadura.

Every volunteer consumed 30 g of tryptophan-enriched cereals (60 mg tryptophan) per dose for breakfast and dinner after a week consuming control cereals (22.5 mg tryptophan per 30 g dose). Finally, there was a post-treatment week with no cereals.

**Table 1.** Characteristics of the participants. Age is expressed in years (mean±SEM). High blood pressure was the only comorbid disease present in this clinical assay. BMI: Body mass index.

| | |
|---|---|
| Males | 3 |
| Females | 9 |
| Age | 62.43±1.43 |
| BMI | 26.11 |
| High Blood Pressure | 2 |

This study was approved by the Ethical Committee of the University of Extremadura (Badajoz, Spain) in accordance with the Declaration of Helsinki, the Council of Europe, and the Universal Declaration of UNESCO on human rights biomedicine, and human genome.

## Measurement of sleep and anxiety

Sleep parameters were recorded by a wrist actimeter (Actiwatch©, Cambridge Neurotechnology Ltd, UK), which participants wore all time, and analyzed with *Sleep Analysis 5*© (Cambridge Neurotechnology Ltd, UK) software.

Before the study and during the study, on the last day of every experimental week at 10.00 a.m; volunteers filled an STAI (Spielberg *et al.*, 2008) anxiety test. STAI results were expressed and related to a Spanish tipification (Urraca, 1981). This assay was carried out in October, 2010.

## Statistics

Data are expressed as mean ± standard error and represented as fold-increase over control levels (expressed as 1).

Statistical analysis were performed with *Graphpad Prism 5*©; sleep parameters were analyzed by ANOVA test and anxiety parameters were analyzed with a Mann-Whitney U test. Significant level was established at p-value<0.05.

## Results

Figures 2, 3, 5 and 6 show that after one week of tryptophan-enriched cereals ingestion both at breakfast and dinner (60 mg tryptophan/ 30 g product per dose) led to an increase in actual sleep time ($p<0.01$), sleep efficiency ($p<0.01$) and immobile time ($p<0.01$). In addition, figures 4, 7, 8 and 9 reveal that sleep efficiency, wake bouts and fragmentation index had lower values than in control week.

Figure 2

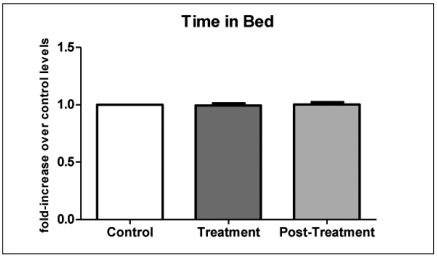



Figure 3

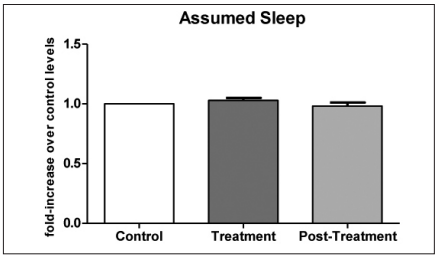



Figure 4

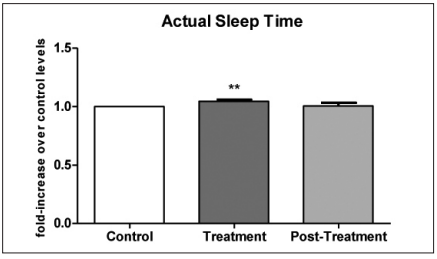



Figure 5

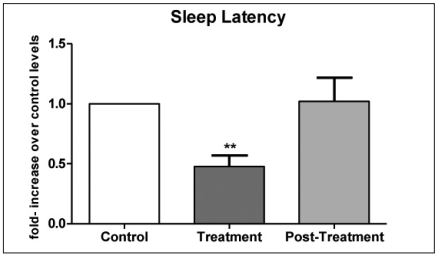



Figure 6

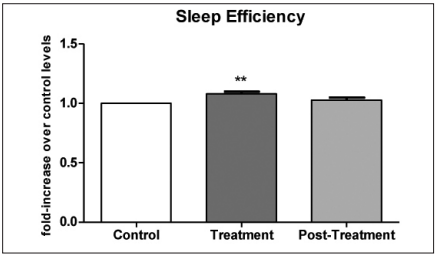



Figure 7

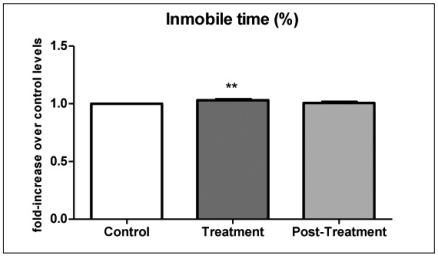



Figure 8

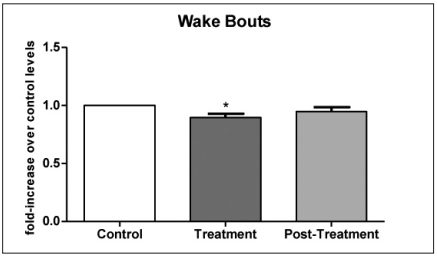



Figure 9

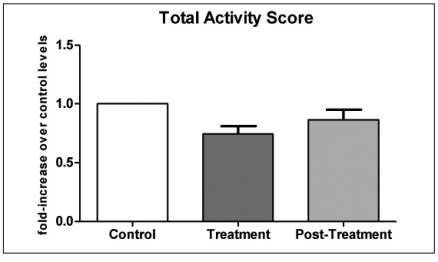
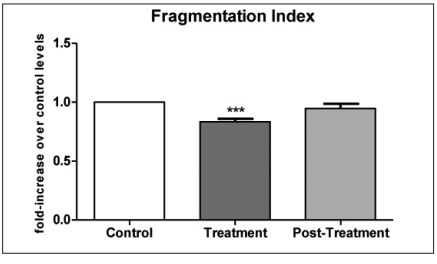



Figure 10




**Figures 2 to 10.** Tryptophan enriched-cereal influence on several sleep parameters. Results are expressed as fold-increase over control levels. Each value represents mean ± SEM. *p<0.05; **p<0.01; ***p< 0.001 with respect to control.

After participants ingested tryptophan-enriched cereals for one week there was a decrease in state of anxiety (Figure 10; $p<0.05$). However there were no changes in trait anxiety (Figure 11).

Figure 11

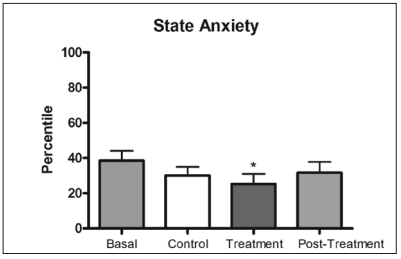
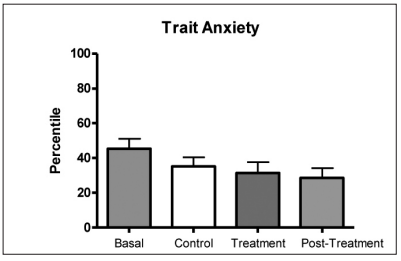



Figure 12




**Figures 11 and 12.** Tryptophan enriched-cereal influence on State Trait Anxiety Inventory (STAI). Results are expressed related to a Spanish tipification. Each value represents mean ± SEM. *$p<0.05$ with respect to basal.

## Discussion

The essential amino acid tryptophan has been reported as a molecule with sleep-enhancing properties which can improve sleep/wake cycle through its conversion into melatonin, which has a strong natural hypnotic effect (Garrido *et al*., 2009; Garrido *et al*., 2010; Bubenik and Konturek, 2011). It has been reported that some populations who suffer from sleep problems can improve their sleep through a tryptophan-enriched diet both animals or humans (Cubero *et al*., 2007; Cubero *et al*., 2009; Paredes *et al*., 2009).

After tryptophan administration serotonin and melatonin levels become higher (Sánchez *et al*., 2008). In this way, populations which present low melatonin or serotonin levels – like babies and elderly people – can have better levels of these molecules to improve their sleep/wake cycle (Riemersma *et al*., 2005; Cubero *et al*., 2005).

It is well accepted that sleep problems have negative effects on mood, in fact, it has been extensively investigated with experimental models by tryptophan acute depletion (Silber and Schmitt, 2009). On the other hand, it has been reported that melatonin has a possible anti-depressive, anxiolytic, analgesic or sedative effects, among others, probably based on its effect on the circadian functions regulation (Hansen *et al*., 2011).

## Conclusion

Tryptophan-enriched cereals improved actual sleep time, sleep efficiency, immobile time, sleep latency, wake bouts and fragmentation index in the

volunteers of this sample. Also, this kind of diet improved aspects of anxiety-like trait or state during the treatment week, enhancing the volunteers' mood.

These findings suggest that the intake of tryptophan-enriched cereals exert positive effects on the sleep of elderly with sleep problems and they may, therefore, represent an alternative to treatments based on pharmacological drugs.

## Bibliographic references


Baskett, J. J.; Broad, J. B.; Wood, P. C.; Duncan, J. R.; Pledger, M. J.; English, J.; Arendt, J. 2003. Does melatonin improve sleep in older people? A randomized crossover trial. *Age and Ageing*, 32:164-170.

Bubenik, G. A.; Konturek, S. J. 2011. Melatonin and aging: prospects for human treatment. *Journal of Physiology and Pharmacology*, 62(1): 13-19.

Cubero, J.; Valero, V.; Sánchez, J.; Rivero, M.; Párvez, H.; Rodríguez, A. B.; Barriga, C. 2005. The circadian rhythm of tryptophan in breast milk affects the rhythms of 6-sultatoxymelatonin and sleep in newborn. *Neuroendocrinology Letter*, 26(6): 657-661.

Cubero, J.; Narciso, D.; Terrón, M. P.; Rial, R.; Esteban, S.; Rivero, M.; Parvez, H.; Rodriguez, A. B.; Barriga, C. 2007. Chrononutrition applied to formula milks to consolidate infants´sleep/wake cycle. *Neuroendocrinology Letters,* 28(4): 360-366.

Cubero, J.; Chanclón, B.; Sánchez, S.; Rivero, M.; Rodríguez, A. B.; Barriga, C. 2009. Improving the quality of infant sleep trough the inclusion at supper of cereals enriched with tryptophan, adenosine 5' - phosphate, and uridine-5'-phosphate. *Nutritional Neuroscience*, 12(6): 272-280.

Cubero, J.; Otalora, B. B.; Bravo, R.; Sánchez, C. L.; Franco, L.; Uguz, A. C.; Rodríguez, A. B.; Barriga, C. 2011. Distribution of 5-HT receptors in the mammalian brain. *Trends in Cell & Molecular Biology*, 6: 41-46.

Garrido, M.; Espino, J.; González-Gómez, D.; Lozano, M.; Cubero, J.; Toribio-Delgado, A. F.; Maynar-Mariño, J. I.; Terrón, M. P.; Muñoz, J. L.; Pariente, J. A.; Barriga, C.; Paredes, S. D.; Rodríguez, A. B. 2009. *e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism* [Online], 4(2009): e321-e323. DOI: 10.1016/j.eclnm.2009.09.003.

Garrido, M.; Paredes, S. D.; Cubero, J.; Lozano, M.; Toribio-Delgado, A. F.; Muñoz, J. L.; Reiter, R. J.; Barriga, C.; Rodríguez, A. B. 2010. Jerte Valley Cherry-Enriched Diets Improve Nocturnal Rest and Increase 6-Sulfatoxymelatonin and Total Antioxidant Capacity in the Urine of Middle-Aged and Elderly Humans. *Journal of Gerontology*, 65a(9): 909-914. [Published Online: 14-6-2010]. DOI:10.1093/Gerona/glq099.

Hansen, M. V.; Madsen, M. T.; Hageman, I.; Rasmussen, L. S.; Bokmand S.; Rosenberg, J.; Gögenur, I. 2011. The effect of melatonin on depression, anxiety, cognitive function and sleep disturbances in pa-

tients with breast cancer. The melody trial: protocol for a randomized, placebo-controlled, double-blinded trial. *BMJ open* [Online], 2(1): e000647. DOI: 10.1136/bmjopen-2011-000647.

Hussain, A. M.; Mitra, A. K. 2000. Effects of aging on tryptophan hydroxylase in rat brain: implications on serotonin levels. *Drug Metabolism and Disposition*, 28: 1038-1042.

Paredes, S. D.; Marchena, A. M.; Bejarano, I.; Espino, J.; Barriga, C.; Rial, R.; Reiter, R. J.; Rodríguez, A. B. 2009. Melatonin and tryptophan affect the activity-rest rhtyhm, core and peripheral temperatures, and interleukin levels in the ringdove: Changes with age. *Journal of Gerontology*, 64(3): 340-350.

Sánchez, S.; Sánchez, C. L.; Paredes, S. D.; Barriga, C.; Rodríguez, A. B. 2008. Circadian levels of serotonin inplasma and brain after oral administration of tryptophan in rats. *Basic & Clinical Pharmacology & Toxicology*, 104: 52-59.

Silber, B. Y.; Schmitt, J. A. J. 2009. Effects of tryptophan loading on human cognition, mood and sleep. *Neuroscience and Biobehavioral Review,* 34(3): 387-407.

Spielberger, C. D.; Gorsuch, R. L.; Lushene, R. E. 2008. *Cuestionario de Ansiedad Estado/ Rasgo.* Madrid, TEA ediciones.

Urraca, S. 1981. *Actitudes ante la muerte (preocupación, ansiedad, temor) y religiosidad*. Madrid, Facultad de Psicología, Universidad Complutense de Madrid.

Riemersma, R. F.; Mattheij, C. A. M.; Swaab D. F.; Van Someren E. J. W. 2005. Melatonin rhythms, melatonin supplementation and sleep in old age. *The Neuroendocrine Immune Network in Ageing,* 4: 199-211.

Yong-Lu, H.; Rong-Lu, L.; Quing-Song, W.; Van Someren, E. J. W.; Xu, H.; Jiang-Ning, Z. 2002. Age-associated difference in circadian sleep-wake and rest-activity rhythms. *Phisiology & Behaviour*, 76: 597-603.

Zhdanova, I. V.; Wurtman, R. J.; Regan, M. M.; Taylor, J. P. S.; Leclair, O. U. 2009. Melatonin treatment for age-related insomnia. *The Journal of Clinical Endocrinology & Metabolism*, 86(10): 4727-4730.

Artigo recebido a 28 de Fevereiro de 2011 e aceite a 27 de Janeiro de 2012.