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ORIGINAL ARTICLE

Taurine content in different brain structures during ageing: effect on hippocampal synaptic plasticity

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Abstract A reduction in taurine content accompanies the ageing process in many tissues. In fact, the decline of brain taurine levels has been associated with cognitive deficits whereas chronic administration of taurine seems to ameliorate age-related deficits such as memory acquisition and retention. In the present study, using rats of three age groups (young, adult and aged) we determined whether the content of taurine and other amino acids (glutamate, serine, glutamine, glycine, alanine and GABA) was altered during ageing in different brain areas (cerebellum, cortex and hippocampus) as well non-brain tissues (heart, kidney, liver and plasma). Moreover, using hippocampal slices we tested whether ageing affects synaptic function and plasticity. These parameters were also determined in aged rats fed with either taurine-devoid or taurine-supplemented diets.

With age, we found heterogeneous changes in amino acid content depending on the amino acid type and the tissue. In the case of taurine, its content was reduced in the cerebellum of adult and aged rats, but it remained unchanged in the hippocampus, cortex, heart and liver. The synaptic response amplitude decreased in aged rats, although the late phase of long-term synaptic potentiation (late-LTP), a taurine-dependent process, was not altered. Our study highlights the stability of taurine content in the hippocampus during ageing regardless of whether taurine was present in the diet, which is consistent with the lack of changes detected in late-LTP. These results indicate that the beneficial effects of taurine supplementation might be independent of the replenishment of taurine stores.

Keywords Ageing · Nutrition · Synaptic plasticity · LTP · D-Serine · Brain

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Introduction

One consequence of the increase in life expectancy is the deficit in cognitive function during ageing. Some of the complex metabolic changes accompanying the ageing process have been proposed to underlie the cognitive deficit (Gold et al. 2013). This is the case for taurine (2-aminoethane-sulphonic acid), one of the most abundant amino acids in almost all tissues, and especially in excitable ones. Although taurine is not incorporated into proteins, it has been linked with osmoregulation, neuromodulation and detoxification of hypochlorous acid (Huxtable 1992). The concentration of taurine in tissues comes from two sources: biosynthesis and diet. Different pathologies have been associated with taurine deficiency including retinal degeneration, cardiac dysfunction, immune deficiency,

muscle atrophy, premature ageing and impaired reproduction (Schaffer et al. 2014; for review). In fact, chronic administration of taurine was found to ameliorate several age-related deficits such as striated muscle contraction (Pierno et al. 1998), oxidative stress in heart tissue (Parildar et al. 2008), and memory acquisition and retention (El Idrissi 2008). Furthermore, tissue taurine depletion in taurine transporter knockout mice shortens lifespan and accelerates muscle senescence (Ito et al. 2014). The beneficial effects of taurine supplementation on the diet seem to be due to the recomposition of taurine levels lost from tissues during ageing (Pierno et al. 1998; Dawson et al. 1999a; Parildar et al. 2008). Nevertheless, examining the literature related with age-related decline of taurine in the brain it can be seen that not all brain areas behave uniformly (Dawson et al., 1999a; Strolin Benedetti et al. 1991). In addition, it seems that does not exist a linear relationship between taurine concentration and age in several brain areas (Zhang et al. 2009; Paban et al. 2010).

Hippocampal integrity and functionality are essential for correct learning and memory processes. Long-term changes in synaptic efficacy are widely used to gain insight into the cellular basis of learning and memory processes. We found previously that taurine is involved in synaptic plasticity processes like late phase of long-term potentiation (late-LTP) (Galarreta et al. 1996; del Olmo et al. 2003; 2004; Suárez et al. 2014), which is the protein synthesis-dependent phase of LTP. Because taurine participates in late-LTP induction, its reduction could contribute to memory deficit during ageing. Therefore, in the present study we sought to elucidate whether the changes in taurine levels are associated with synaptic plasticity alterations. To this end, we analysed taurine content of several tissues, including some brain areas, and LTP induction in hippocampal slices obtained from rats of different ages (young, adult and aged). In addition, we determined these parameters in two groups of rats long-term fed with either taurine-devoid or taurine-supplemented diets.

Materials and methods

Animals

The care and use of animals was carried out following the European Communities Council Directive (86/609/ECC). Protocols were approved by "Comité Ético de Bienestar Animal" at "Hospital Universitario Ramón y Cajal" (animal facilities ES280790000092). Animals were bred and housed in a special room under pathogen-free conditions at a room temperature of 22 ± 1 °C in a 12 h light/dark cycle with free access to food and water. Male Sprague–Dawley rats were divided into three age groups: young

adult (6–8 weeks old), adult (12–13 months old) and aged (24–25 months old). These rats were fed with a diet containing taurine (0.2 mg/g pellet) from Panlab (Safe A04). Additionally, other group of aged rats were fed with this diet until 12-months old and then they were fed with a diet devoid of taurine (0.002 mg/g pellet) from Harlan (Tekland global 14 % protein rodent maintenance diet). Half of these animals was additionally supplemented with 0.5 % of taurine dissolved in the drinking water (Harlan-TAU group) and the others received normal water (Harlan group) until they turned 24-months old.

At the appropriate age, the rats were decapitated after applying isoflurane anaesthesia and trunk blood was collected in tubes containing 100 µL of a 5000 I.U./mL heparin solution. One of us quickly removed the brain and prepared hippocampal slices while another dissected heart, kidney and liver. These last three tissues were quickly frozen in dry ice and stored at −80 °C in a freezer until the homogenisation procedure. The cerebellum, cortex and hippocampus were also generally obtained from the same cohort of rats used for electrophysiological experiments. One of the hemispheres was used to isolate the frontal cerebral cortex, cerebellum and hippocampus, which were processed for amino acid determination. The other hemisphere was used to obtain hippocampal slices for electrophysiological experiments.

Hippocampal slice preparation

The brain was dropped into chilled Kreb's–Ringer bicarbonate (KRB) solution containing (in mM): 119 NaCl, 26.2 NaHCO$_3$, 2.5 KCl, 1 KH$_2$PO$_4$, 1.3 MgSO$_4$, 2.5 CaCl$_2$ and 11 glucose. This solution was gassed with 95 % O$_2$ and 5 % CO$_2$. Transverse hippocampal slices of 400 µm thickness were obtained by a manual tissue chopper and placed in an interface holding chamber for at least 3 h at room temperature (22–25 °C). No more than one slice per rat was included in each experimental group.

Recording of evoked synaptic potentials

A single slice was transferred to a submersion-type recording chamber, where it was continuously perfused (2 ml/min) with standard KRB solution. Experiments were carried out at 31–32 °C.

Evoked field excitatory postsynaptic potential (fEPSP) and presynaptic fibre volley (FV) were recorded in CA1 stratum radiatum with tungsten microelectrodes (1 MΩ) connected to an AI-401 preamplifier (Axon Instruments, Foster City, CA) connected to a CyberAmp 320 signal conditioner (Axon Instruments). These field responses were evoked every 30 s by stimulating Schaffer collateral-commissural fibres with biphasic electrical pulses (10–30 µA;

100 μs per polarity) delivered through bipolar tungsten insulated microelectrodes (0.5 MΩ) at CA1 mid-stratum radiatum. The stimulus strength was adjusted to evoke a fEPSP approximately half of its maximal amplitude. Electrical pulses were supplied by a pulse generator A.M.P.I. Mod. Master 8 (Jerusalem, Israel) connected to a biphasic stimulus isolator unit (Cibertec, Madrid, Spain). A stable baseline period was recorded during at least 20 min. To determine whether ageing was accompanied by modifications of release probability of glutamatergic synapses, we used the paired-pulse facilitation (PPF) paradigm (Manabe et al. 1993). Late-LTP was elicited by three trains of high frequency stimulation (HFS; 100 Hz, 1 s, at baseline stimulation strength) at 10-min intervals. Evoked responses were digitised at 20 kHz using a Digidata 1200AE-BD board (Axon Instruments), and stored on a personal computer running Windows™ and using pCLAMP 8.0.2 software (Axon Instruments). The synaptic strength was calculated using the initial falling slope phase of the fEPSP to avoid contamination of the response by the propagated population spike. We also used pCLAMP-8.0.2 software for these calculations. Data were normalised with respect to the mean values of the responses in the last 20 min of the baseline period in standard medium.

Tissue homogenisation

Tissues were homogenised in ten volumes of 5-sulphosalicylic acid (10 %). Final extracts were kept at −20 °C until their amino acid content was determined.

Plasma (1 mL) was deproteinised with 100 μL of 5-sulphosalicylic (35 %) acid and centrifuged at 3000 g for 10 min. The supernatants were stored for amino acid analysis.

Amino acid determination

Amino acids were separated by reverse-phase HPLC after precolumn derivatisation with o-phthaldialdehyde on a C18 column (150 × 4.5 mm particle size 5 μm) using gradient elution at 1 mL/min and quantified by fluorescence detection. Amino acids were identified by their retention times, and their concentrations were calculated by comparison to calibrated amino acid external standard solutions (10 μM). Seven amino acids were regularly identified and separated in the extracts and they were measured with a sensitivity close to 1 pmol (glutamate, serine, glutamine, glycine, taurine, alanine, and GABA).

Statistical analysis

Data are expressed as mean ± SEM. Mean values of the fEPSP slope given throughout the text correspond to averages of 5-min periods. Statistical differences were assessed by two-way analysis of variance followed by a Bonferroni test for multiple comparisons or by two-tailed unpaired t tests as a post hoc evaluation to compare correlative samples. Differences were considered statistically significant when $p < 0.05$.

Results

Amino acid levels during ageing in different structures

Among the different age groups we did not observe any modification of taurine content in hippocampus, cortex, heart or liver, although there was a reduction in the cerebellum of adult and aged rats compared with young rats. In contrast, taurine concentration increased in the plasma of adult and aged rats, and in kidney of adult animals (Fig. 1).

Glycine exhibited the most uniform change of the amino acids analysed in this study. Its reduction was observed in several brain areas (hippocampus, cerebellum and cortex) and outside the brain (heart, liver and plasma) in adult rats, but also in hippocampus and plasma of aged rats. Serine, a precursor of glycine biosynthesis, was reduced outside the brain (heart, kidney and liver) and in the cerebellum of adult rats but, interestingly, serine concentration increased in the three brain areas analysed in aged rats. This was the clearest change in amino acid content related to ageing in the brain, because modifications of the levels of other amino acids were also detected in 12-month-old rats. Its is noteworthy that other amino acids involved in neurotransmission such as glutamate and GABA did not show significant changes in the brain during ageing, except in the case of the cerebellum of adult rats where a significant reduction in GABA concentration was detected (Fig. 1).

Basal synaptic transmission during ageing in hippocampal slices

In hippocampal slices, we tested for possible changes in basal synaptic transmission during ageing using stimulus–response curves to look at the relationship between the slope of the field excitatory postsynaptic potential (fEPSP) and the fiver volley (FV) amplitude (Fig. 2a1). The FV amplitude is proportional to the number of presynaptic axons recruited by the stimulus and, consequently, related directly to the fEPSP size. To detect a true change of synaptic efficacy, we calculated the ratio FV/fEPSP (Fig. 2a2) at different stimulus intensities. A two-way ANOVA of these ratios yielded no differences in the stimulus factor (the ratios were constant along the whole range of stimulus strengths), but detected significant differences in the age factor ($F_{2,136} = 27.195$; $p < 0.0001$). Post-hoc analysis
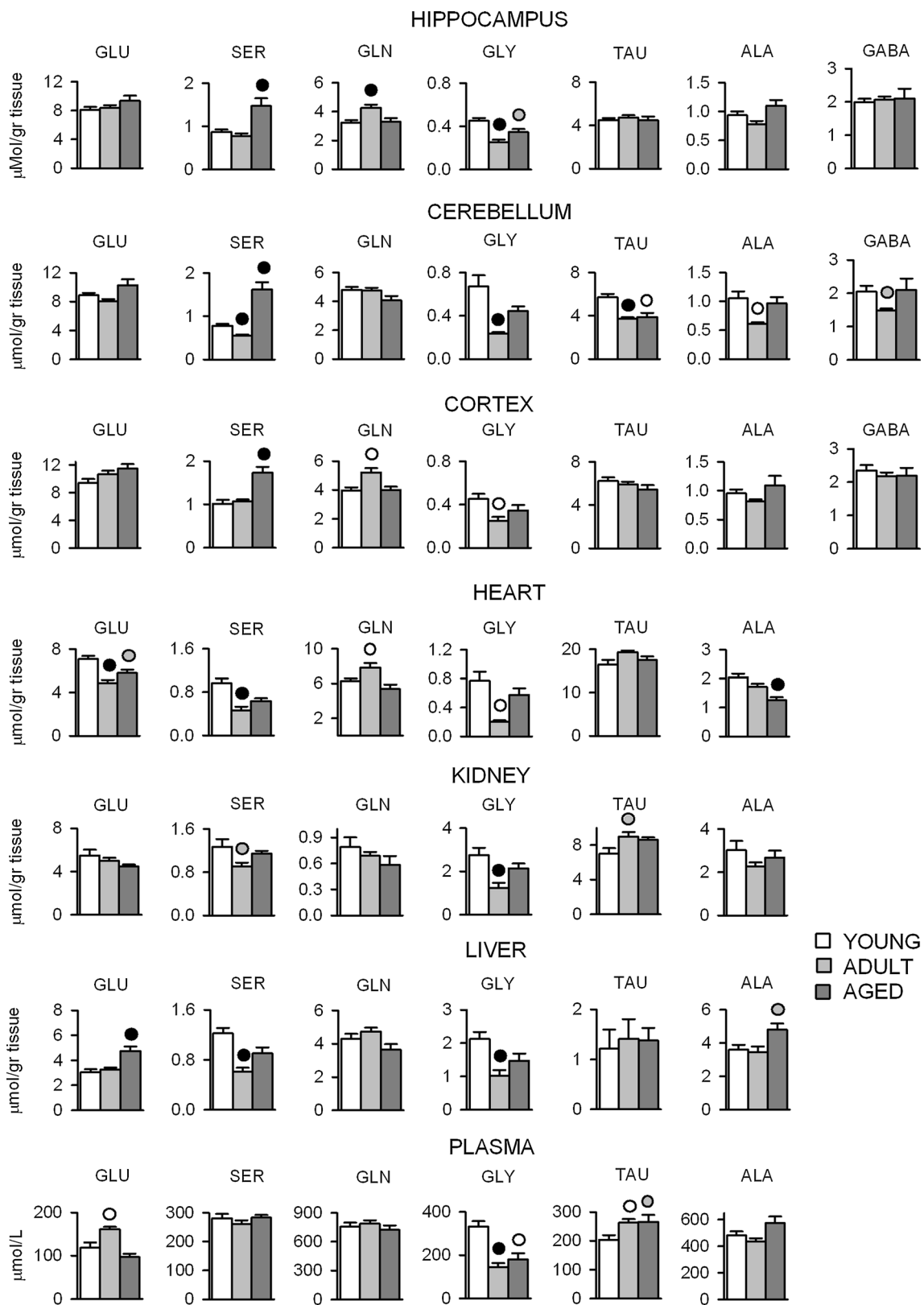
Fig. 1 Amino acid levels in different structures of young, adult and aged rats. *Histograms* represent the content of Glu, Ser, Gln, Gly, Tau, Ala, and GABA in brain areas (hippocampus, cerebellum and cortex), heart, kidney, liver and plasma obtained from young ($n = 9$–23), adult ($n = 11$) and aged ($n = 6$) rats. Statistical differences obtained when comparing with the young group were placed on the *bars* corresponding to adult and aged groups: *white circles* $p < 0.05$; *grey circles* $p < 0.01$; *black circles* $p < 0.001$
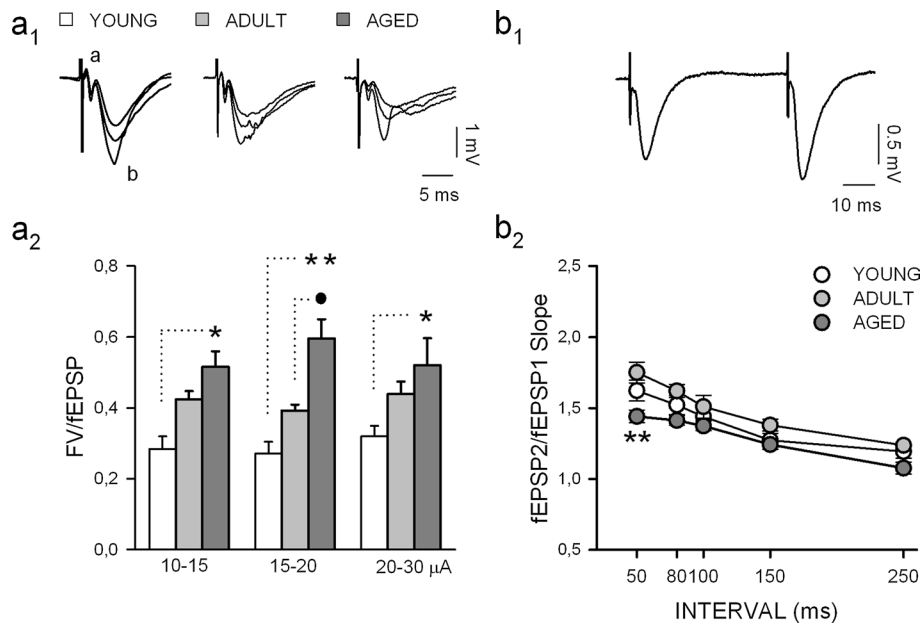
Fig. 2 Basal synaptic transmission in hippocampal slices obtained from young, adult and aged rats. **a1** Superposition of field potentials (*a* indicates FV and *b* indicates fEPSP) evoked by increasing stimulus strength and recorded in a representative hippocampal slice from each group. **a2** FV/fEPSP ratios for different ranges of stimulus strengths (young, $n = 5$; adult, $n = 7$; and aged, $n = 7$ rats). Statistical differences comparing young vs. aged (*$p < 0.05$; **$p < 0.01$) and adult vs. aged ($\bullet p < 0.05$). **b1** Paired-pulse facilitation induced by a pair of identical stimuli separated with a 50 ms interval. Note that the fEPSP evoked by the second stimulus is higher than that obtained with the first. **b2** Average of paired-pulse facilitation ratios (second fEPSP/first fEPSP) obtained at different pulse intervals. Statistical differences comparing adult vs. aged (**$p < 0.01$)

revealed that FV/fEPSP ratios in young and adults rats were indistinguishable ($p > 0.05$; Bonferroni t test). However, statistically significant differences were found between young and aged rats at all stimulus intensities ($p < 0.05$; Bonferroni t test). These results indicate that aged rats display a reduction in synaptic efficacy in CA3-CA1 synapses with respect to young group, under basal conditions.

We also examined whether ageing was accompanied by changes in release probability using the paired-pulse facilitation (PPF) paradigm. To this end, we measured the ratio between the second and first fEPSP slopes at different inter-stimulation intervals (50, 80, 100, 150 and 250 ms). Figure 2b shows that PPF ratios were statistically indistinguishable among the three age groups, except at the 50 ms interval in aged rats compared with adult rats ($p < 0.01$).

Hippocampal LTP during ageing

We also explored whether late-LTP was modified in hippocampal slices obtained from aged rats. We induced late-LTP by applying three-HFS trains. Although we obtained a smaller potentiation immediately after HFS trains in adult and aged slices with respect to young slices, the magnitude of synaptic potentiation measured at 1 h (young 171.8 ± 7.1 %; adult: 165.9 ± 8.6 %;
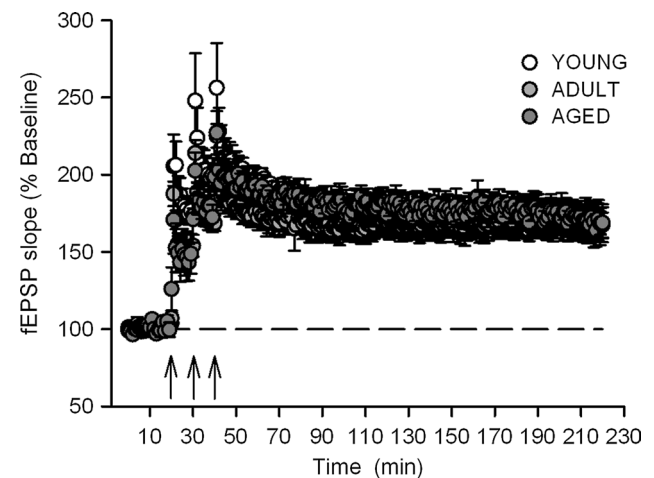

Fig. 3 Time course of fEPSP changes obtained after inducing late-LTP in hippocampal slices from young, adult and aged rats with three HFS trains (100 Hz, 1 s) at the time indicated by *arrows*. Young, $n = 10$; adult, $n = 8$ and aged, $n = 4$ rats

aged: 182.6 ± 8.0 %), 2 h (young: 168.8 ± 7.9 %; adult: 168.7 ± 11.5 %; aged: 175.76 ± 8.8 %) and 3 h (young: 167.9 ± 7.0 %; adult: 167.9 ± 12.2 %; aged: 168.8 ± 10.0 %) after tetanisation was indistinguishable among the three slice groups ($F_{2,57} = 0.5324$; $p = 0.5901$; two way ANOVA; Fig. 3).

Effect of different diets with or without taurine on amino acid levels in aged rats

In the next set of experiments we tried to alter taurine content of aged rats by feeding them with a diet without taurine (Harlan) or supplemented with taurine (0.5 %) in the drinking water (Harlan-TAU).

Amino acid analysis in brain areas of these animals revealed a significant reduction of taurine concentration only in the cerebellum of rats fed with Harlan diet when compared with aged rats fed with Panlab diet, which was not observed in rats supplemented with taurine (Fig. 4). Similar changes in taurine concentration occurred in the kidney. In contrast, taurine concentration increased in plasma and liver of rat receiving taurine supplementation in the drinking water. Furthermore, no differences in taurine were detected among the three groups of diets in hippocampus, cortex and heart.

We found that long-term feeding with Harlan diet also reduced the concentration of other amino acids such as serine, alanine, glutamate and GABA in brain structures and outside the brain, but increased glutamine concentration in the liver (Fig. 4). These changes were not generally affected by taurine supplementation. Interestingly, Harlan diet only modify the concentration of glutamate in the plasma.

Effect of different diets on LTP induction

In hippocampal slices obtained from rats belonging to each group of diet that were used for amino acid analysis, we performed electrophysiological recordings, like those commented above, to determine whether taurine content in the diet affect L-LTP induction. In Fig. 5 it is shown that the application of three trains of HFS induced perdurable synaptic potentiation that was statistically indistinguishable among the different types of diets ($F_{2,32} = 0.1548$, $p = 0.8573$).

Discussion

Age-related decline of brain taurine has been associated with cognitive deficit in old rodents (El Idrissi 2008; El Idrissi et al. 2013). In fact, taurine supplementation recovered learning and memory in a mouse model of Alzheimer´s disease (Kim et al. 2014). However, taurine did not affect learning and memory in cognitively intact adult rodents (Ito et al. 2009; Kim et al. 2014). Notably, in Alzheimer's patients significant correlation exists between low concentration of taurine in cerebrospinal fluid and decrements in performance of a learning test (Csernansky et al. 1996). These data incentive the investigation of mechanisms linking taurine levels with memory processes.

In the present work we found that hippocampal taurine levels were not modified during ageing as reported by other authors in rats (Strolin Benedetti et al. 1991; Dawson et al. 1999a; Zhang et al. 2009; but see Banay-Schwartz et al. 1989) and mice (Duarte et al. 2014). We neither observed any modification of hippocampal taurine concentration when aged rats were fed with a diet without taurine or supplemented with taurine. Moreover, we did not detect any alteration in late-LTP induction and maintenance in aged rats. This observation is similar to that reported by other groups inducing LTP with high intensity stimulation parameters (see Rosenzweig and Barnes 2003, for review) and it is consistent with the lack of changes in hippocampal taurine content during ageing, because our previous studies showed that taurine participates in the induction of hippocampal late-LTP (del Olmo et al. 2004; Suárez et al. 2014). Nevertheless, our present results show alterations in some basal synaptic parameters such as reduction of synaptic efficacy, which has been also reported by other authors in aged hippocampal slices (Hsu et al. 2002; Rosenzweig and Barnes 2003). Moreover, our results with PPF ratio indicate that presynaptic release of glutamate was partially enhanced in aged rats with respect to adult rats but was not enhanced compared to young rats. Obviously, this synaptic modification does not seem to be caused by changes in the hippocampal taurine content.

It has been reported that taurine supplementation (0.05 %) in drinking water for 8 months significantly increased the performance (passive avoidance paradigm) of aged mice as compared to untreated controls (El Idrissi 2008; El Idrissi et al. 2009). However, these findings can not be unequivocally attributed to the recomposition of taurine stores in brain areas because taurine was not analysed in the aforementioned studies. In fact, our present results show that taurine concentration in the hippocampus, a brain area essential for memory processes, was steady and it did not change with either rat ageing or taurine presence in the diet. Similarly, taurine administration to rats did not change taurine concentration in the brain structures (Sved et al. 2007; Murakami and Furuse 2010). In contrast, other authors (Dawson et al. 1999a) using much higher doses of taurine supplementation in aged rats (1.5 % instead of 0.5 % used in our study) were able to enhance taurine content in both peripheral and central nervous system.

Thus, the benefits of taurine supplementation in aged rats reported by some authors (El Idrissi 2008; El Idrissi et al. 2013), might come from the replenishment of other areas, distinct from hippocampus, where taurine suffered depletion during ageing. The cerebellum and the striatum are the most consistently brain areas where a reduction of taurine has been demonstrated during the ageing process (Banay-Schwartz et al. 1989; Strolin Benedetti et al. 1991; Eppler and Dawson 1998; Dawson et al. 1999a, b;
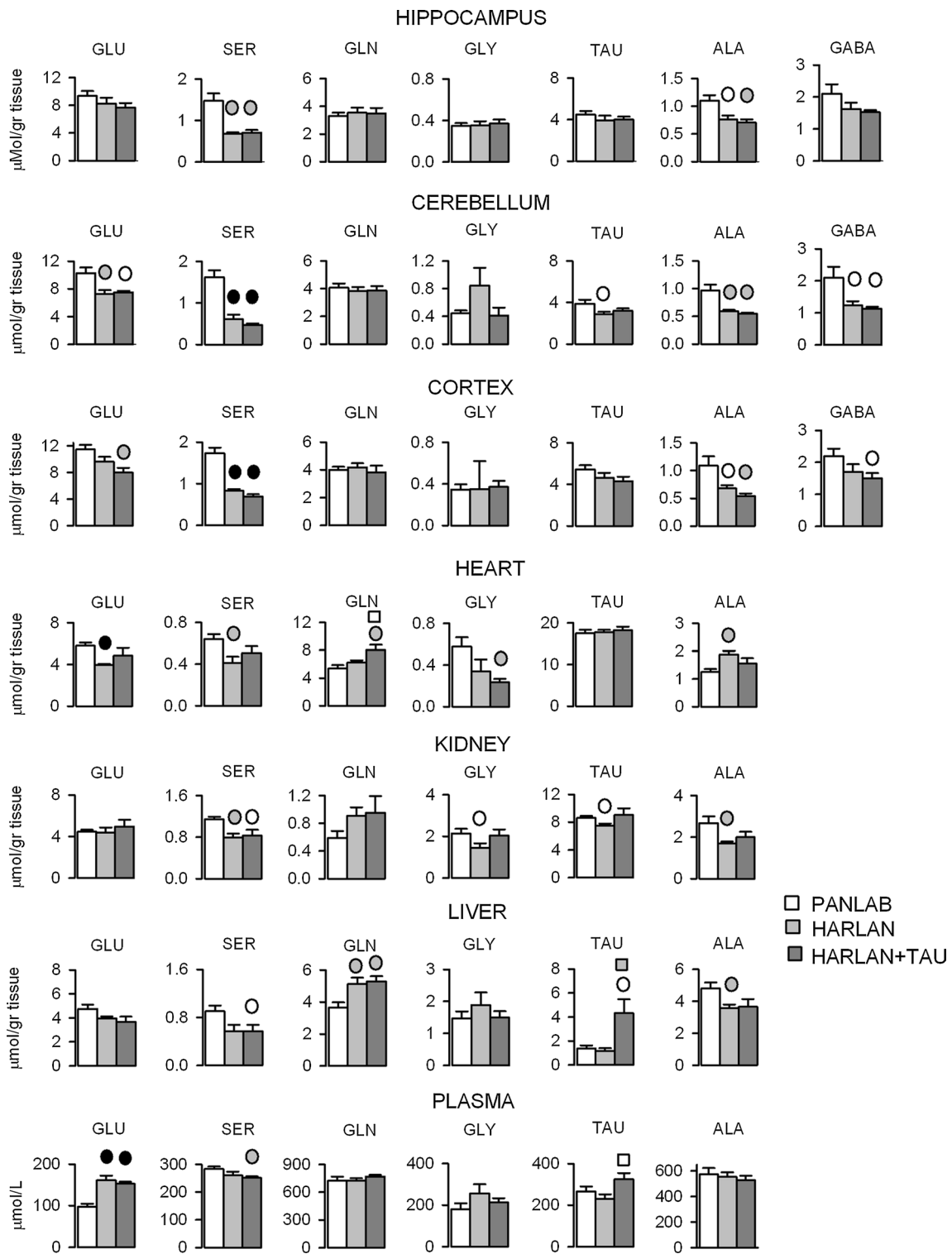
Fig. 4 Amino acid levels in aged rats fed with different diets with or without taurine. *Histograms* represent the content of Glu, Ser, Gln, Gly, Tau, Ala, and GABA in brain areas (hippocampus, cerebellum and cortex), heart, kidney, liver and plasma obtained from aged rats fed with either a diet with taurine (Panlab; $n = 6$), a taurine-devoid diet (Harlan; $n = 6$) or this diet supplemented with taurine (0.5 %) in the drinking water (Harlan-Tau; $n = 5$). Statistical differences obtained when comparing with the Panlab group were placed on the *bars* corresponding to Harlan and Harlan-Tau groups and are indicated by: *white circles* $p < 0.05$; *grey circles* $p < 0.01$; *black circles* $p < 0.001$. Statistical differences obtained when comparing Harlan group with Harlan-Tau group are indicated on Harlan-Tau bars by: *white squares* $p < 0.05$; *grey squares* $p < 0.01$; *black squares* $p < 0.001$
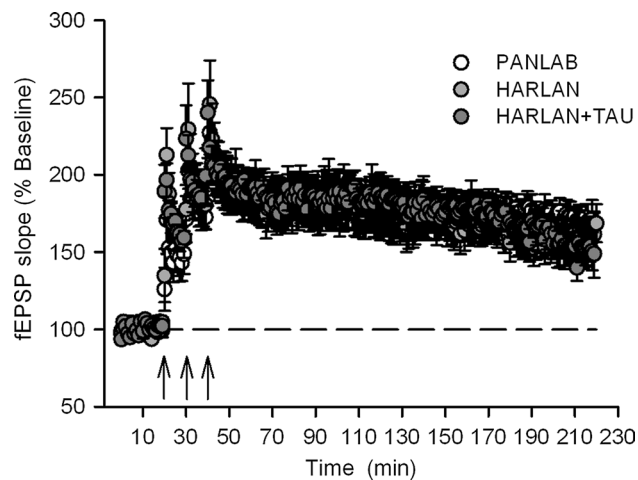
Fig. 5 Late-LTP induction in hippocampal slices obtained from aged rats fed with different diets with or without taurine. No differences were observed in the magnitude of fEPSP potentiation induced in slices obtained from rats fed with Panlab ($n = 4$), Harlan ($n = 5$) or Harlan-Tau ($n = 5$)

Zhang et al. 2013; Duarte et al. 2014). Our results in rats under dietary taurine deficit also demonstrate that cerebellum is especially prone to lose its taurine content. However, this taurine reduction was not related with ageing process because taurine reduction was similar in adult rats than aged ones. Therefore, the beneficial effects of taurine supplementation on the passive avoidance test (El Idrissi 2008; El Idrissi et al. 2009) a learning task not only related to hippocampal functioning (Tinsley et al. 2004; Arias et al. 2015) might be due to restitution of taurine content in brain areas other than the hippocampus.

Another possibility is that taurine supplementation might have a pharmacological effect independent of the replenishment of tissue stores, as in the case of the hippocampus where taurine content did not change during ageing. In this context, it has been reported that chronic supplementation of taurine to aged mice significantly ameliorated the age-dependent decline in memory acquisition and retention, through a mechanism involving GABAergic neurotransmission (El Idrissi et al. 2013).

The mechanism by which taurine content in some tissues declines with ageing while in others remains unaltered is currently unknown. The release of taurine seems not be affected by ageing at least in hippocampal slices (Saransaari and Oja 1997). Taurine content in different tissues is derived from two sources: biosynthesis and diet. Taurine biosynthesis is mainly localised in the liver and is very active in rodents. The presence of taurine in cells devoid of the biosynthetic machinery to produce taurine is due to the existence of a specific taurine transporter, TauT (Liu et al. 1992). Decline of taurine during ageing may be partially caused by a deficit in biosynthesis, at least in

Fischer 344 rats (Eppler and Dawson 2001). However, we demonstrated that although taurine supplementation was able to increase plasma levels of taurine in aged animals, it did not modify taurine content in most tissues, indicating that taurine uptake is altered or saturated during ageing. In fact, knocking out TauT reduces taurine content between 70 and 99 % depending on the type of tissue (Ito et al. 2008; Heller-Stilb et al. 2002). In TauTKO mice, the lifespan is shortened and muscular senescence accelerated (Ito et al. 2014). Considering all these data, it might be hypothesised that the severity of taurine depletion during ageing in some tissues (e.g., cerebellum) is closely related with the reduction of TauT expression or function, which would not be uniform in all tissues.

Outside the brain, we did not observe marked alterations in taurine content in heart, kidney and liver obtained from aged rats. Dawson et al. (1999a) also did not find any significant variation in taurine content of heart in aged Fischer 344 rats, but a small reduction (16.6 %) of taurine levels in the heart of aged Wistar rats was reported by Parildar et al. (2008). Interestingly, a marked increase of taurine was observed in the liver of aged rats supplemented with taurine. Other authors have reported that liver specifically accumulates taurine orally administrated (Sved et al. 2007). Taurine accumulation in the liver may be explained by the recently reported uptake of taurine in hepatocytes throughout the GABA transporter 2 (GAT2), which transports taurine with smaller affinity than TAUT (Zhou et al. 2012). This implies that at the elevated taurine levels attained in plasma during taurine supplementation, GAT2 can transport more taurine whereas TAUT is saturated. Taurine accumulation in hepatocytes might be required to produce its hepato-protective action (Miyazaki and Matsuzaki 2014).

Taurine concentration in the plasma of our aged rats increased compared with young rats, although it was indistinguishable from the values obtained in the adult group, similar to that obtained in the blood of aged Wistar rats (Pierno et al. 1998).

With ageing, amino acids other than taurine presented modifications in several brain areas. Notably, L-serine content increased in the aged group in hippocampus, cerebellum and cortex, whereas glycine concentration decreased in these three areas, but with statistically significance only in the hippocampus. L-serine is the precursor of both glycine and D-serine, two amino acids involved in neurotransmission. Glycine is the endogenous ligand of ionotropic glycine receptors (Betz and Laube 2006) and also is a co-agonist of glutamate receptors of the N-methyl-D-aspartate (NMDA) type (Paoletti et al. 2013). D-Serine also plays this co-agonist role at NMDA receptors. Endogenous levels of D-serine are dramatically reduced during ageing (Potier et al. 2010) which seems to impair NMDA-R activation and therefore to negatively affect LTP-induction. This

deficit in LTP was alleviated by exogenous application of D-serine (Potier et al. 2010). Our data reveal a decrease of glycine and an increase of L-serine in the hippocampus of aged rats, which might be related with the age-associated decline of the LTP type induced by weak stimulation paradigms (Rosenzweig and Barnes 2003). The enhanced content of L-serine in brain areas of aged rats may be due to the reduced expression of serine racemase, the enzyme responsible for D-serine biosynthesis. In fact, the D/L-serine ratio was lowered by 85 % in old rats compared with young rats (Potier et al. 2010).

It is also remarkable, although out of the scope of our present work, the effect that different conventional rodent diets have on amino acid profile in several tissues. In particular, the reduction of glutamate, serine and GABA, amino acids participating in neurotransmission, was clearly seen in several brain areas of aged rats fed with Harlan diet when compared with those fed with Panlab diet.

In summary, we have provided experimental evidence that the ageing process produces heterogeneous changes in the amino acid profile (mainly in L-serine and glycine contents) depending on the type of tissue analysed. Specifically, our study highlights the stability of taurine content in the hippocampus during ageing, which is consistent with the lack of changes detected in late-LTP, a taurine-dependent synaptic plasticity event. This work also call the attention on the fact that the effects obtained with taurine supplementation might be due to taurine actions on molecular mechanisms other than taurine-replenishment of cellular stores.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The care and use of animals was carried out following the European Communities Council Directive (86/609/ECC). Protocols were approved by "Comité Ético de Bienestar Animal" at Hospital Universitario Ramón y Cajal (animal facilities ES280790000092).This article does not contain any studies with human participants performed by any of the authors.

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