‘Bomb fuse’ DNA linked to health problems in Cushing’s

Cushing’s syndrome patients may suffer from persistent health problems even after treatment because their DNA is unstable, according to a study presented today at the European Congress of Endocrinology in Wroclaw, Poland. The findings could eventually lead to a new treatment for Cushing’s syndrome, as well as contributing to a wider understanding of the role of DNA maintenance in a range of common health conditions.

Each year, two out of every million adults is diagnosed with Cushing’s syndrome. The rare disease is caused by a tumour in the pituitary or the adrenal glands that produces too much of the stress hormone cortisol. High levels of cortisol can lead to health problems such as premature aging, diabetes, osteoporosis and cognitive difficulties. The condition can be managed by reducing cortisol levels through surgery, medication, or radiotherapy. In spite of this, most health complications of Cushing’s syndrome are not completely reversible even when cortisol levels are managed.

Patients with chronic stress or depression exhibit high levels of cortisol and are known to have shortened DNA sequences on the ends of their chromosomes. These sequences, known as telomeres, are like a bomb fuse – they become shorter every time a cell divides. Eventually they become so short that the cell is unable to divide and subsequently dies. This shortening process is associated with aging.

In this study, researchers from the Hospital Sant Pau and CIBERER Unit 747 of the Universitat Autònoma de Barcelona compared the telomere length of 77 Cushing’s patients with 77 healthy individuals. As expected, the researchers found that older patients had shorter telomeres. No differences were observed between both Cushing’s syndrome and control patients. However, three years after being cured, researchers noticed that in a small group of Cushing’s syndrome patients telomere length had actually increased, even though they normally get shorter with time.

The findings open up an exciting new avenue for research. “We’ve seen that the cells of Cushing’s patients struggle to maintain their DNA stability,” said Dr Anna Aulinas, endocrinologist and lead author of the study. “We don’t know why this happens, but this DNA instability could be implicated in the health complications suffered by Cushing’s patients after treatment. We believe that telomere biology might play a role in the origin of these complications. This study is an important step in helping us identify new therapeutic targets.”

The researchers now plan on recruiting more patients to test whether their findings are also observed in larger groups. They will also look more closely at the role of the enzymes responsible for maintaining telomeres in Cushing’s patients, which could also have wider significance. “Telomere biology is a really exciting area of research as it affects so many fundamental biological processes. In other diseases, such as certain cancers and cardiovascular disease, research is devoted to look for new drugs and therapies to maintain and repair the telomere machinery and dynamics. Our work could therefore be an additional piece of the puzzle.”

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Notes for editors

1. For further information about the study, please contact:

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2. The study *Does hypercortilism of Cushing’s syndrome affect telomere length?* will be presented at the European Congress of Endocrinology at 15:18 on Tuesday 6 May 2014.

3. For all other press enquiries, please contact the European Society of Endocrinology press office

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4. The 16th European Congress of Endocrinology is taking place in Wroclaw, Poland, from 3-7 May 2014. For a full programme, visit [www.ece2014.org](http://www.ece2014.org).

5. The European Society of Endocrinology aims to promote research, education and clinical practice in endocrinology for the public benefit, [www.ese-hormones.org](http://www.ese-hormones.org).

   The European Society of Endocrinology has produced a series of educational videos to help patients make sense of the wealth of information currently online regarding hormone-related conditions and enable them to make informed decisions about their health. You can view the videos by visiting: [http://www.ese-hormones.org/education/patientvideos.aspx](http://www.ese-hormones.org/education/patientvideos.aspx).

ABSTRACT

**Does hypercortisolism of Cushing’s syndrome affect telomere length?**

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**Introduction:** Hypercortisolism in Cushing’s syndrome (CS) determines increased mortality and morbidity. Hypercortisolism is also present in chronic depressive disorders and stress, where
telomere length (TL) is shorter than in controls. We hypothesized that telomere shortening may occur and contribute to premature morbidity in CS.

**Aim:** Investigate TL in CS compared to matched controls, and longitudinally in a subset of CS patients evaluated both with active disease and after endocrine cure.

**Methods:** Seventy-seven CS patients (14 males, 59 of pituitary and 17 of adrenal origin; 21 with active disease) and 77 matched controls (for age, gender, smoking) were compared. Mean age was 48±12 in CS vs 48±12 years in controls. In 15 active patients, a second analysis was also performed once they were in remission (mean age 43±12 vs 46±11 years, respectively, p <0.05). Leukocyte TL was measured by TRF-Southern technique (kit-telo TTAGGG Telomere length Assay, Roche).

**Results:** A negative correlation between TL and age was found (r =-0.341, p <0.001). CS patients had more hypertension, diabetes, dyslipidemia, osteoporosis, a greater BMI and total leukocyte count in CS than controls (p < 0.05). Globally, mean TL did not differ in CS and controls (7667 vs 7483 base pairs-bp). TL shortening was observed in both CS and controls with dyslipidemia (controls 7213 vs 7700 bp and CS 7328 vs 7957, p < 0.05). After adjustment for age, TL was shorter in active disease than in remission (7271 vs 7870, p <0.05).

**Conclusions:** As previously described, aging and dyslipidemia were associated with TL shortening in both CS and controls, but did not differ globally. However, we show for the first time that when patients are followed longitudinally, active CS is associated to TL shortening compared to remission, suggesting a negative impact of hypercortisolism on the telomere maintenance system.