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RESEARCH COMMUNICATION

Scalp hair loss is not random across follicular units: A new insight into human hair ageing

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Abstract

Objectives: Scalp hair has the greatest number of hairs (typically 1–5) per follicular unit but is also the most susceptible body site to hair loss with age. Hence, we set-out to determine the degree to which scalp hair parameters change with age in women and men, any sex differences thereof and whether hair loss is random across follicular units.

Methods: A retrospective cross-sectional study of 200 Chinese men and 200 Chinese women (30–69 years). Image analysis and manual counting methods were used to measure occipital located hair parameters from 6×8 mm shaved scalp photographs and plucked hair microscopy images.

Results: Of the five hair parameters, the number of hairs per follicular unit had the greatest (negative) correlation with age in both men and women. Men had a greater number of hairs and follicular units than women on average but had a greater decrease in the number of hairs per follicular unit with age, particularly for the loss of multi-hair (3+) follicular units. The loss of hairs with age was significantly different to that expected by a random loss of hairs across follicular units and better described by a model of increased hair loss risk the greater number of hairs per follicular unit.

Conclusions: We have found evidence of hair loss preferentially occurring in multi-hair follicular units, which was more pronounced in men. These data suggest that part of the reason scalp hair is more susceptible to hair loss than on other body sites is due to the greater presence of multi-hair follicular units on the scalp.

KEYWORDS
computer modelling, hair growth, hair treatment

Resume

Objectifs: Le cuir chevelu possède le plus grand nombre de cheveux (généralement de 1 à 5) par unité folliculaire, mais c'est aussi le site le plus sensible à la perte de cheveux avec l'âge. Nous avons donc entrepris de déterminer dans quelle mesure les paramètres des cheveux du cuir chevelu changent avec l'âge chez les femmes et les hommes, quelles sont les différences entre les sexes et si la perte de cheveux est aléatoire entre les unités folliculaires.

Méthodes: Étude transversale rétrospective portant sur 200 hommes et 200 femmes chinois (30-69 ans). Des méthodes d'analyse d'image et de comptage manuel ont été utilisées pour mesurer les paramètres des cheveux situés dans la région occipitale à partir de photographies du cuir chevelu rasé de 6x8 mm et d'images microscopiques de cheveux arrachés.

Résultats: Parmi les 5 paramètres capillaires, le nombre de cheveux par unité folliculaire présentait la corrélation la plus forte (négative) avec l'âge, tant chez les hommes que chez les femmes. Les hommes avaient en moyenne un plus grand nombre de cheveux et d'unités folliculaires que les femmes, mais le nombre de cheveux par unité folliculaire diminuait davantage avec l'âge, en particulier pour la perte d'unités folliculaires à plusieurs cheveux (3+). La perte de cheveux avec l'âge était significativement différente de celle attendue par une perte aléatoire de cheveux dans les unités folliculaires, et mieux décrite par un modèle d'augmentation du risque de perte de cheveux plus le nombre de cheveux par unité folliculaire est élevé.

Conclusions: Nous avons trouvé des preuves que la perte de cheveux se produit préférentiellement dans les unités folliculaires à plusieurs cheveux, ce qui était plus prononcé chez les hommes. Ces données suggèrent qu'une partie de la raison pour laquelle les cheveux du cuir chevelu sont plus sensibles à la perte de cheveux que sur d'autres sites du corps est due à la plus grande présence d'unités folliculaires à cheveux multiples sur le cuir chevelu.

INTRODUCTION

Balding in men follows a notable and specific pattern of hair loss—a receding temporal hairline from the forehead and balding on the vertex/calvaria [1]. In women, scalp hair loss more commonly occurs without hair recession from the forehead or balding at the vertex and is termed female pattern hair loss (FPHL). There is evidence that, although women suffer from a milder version of male pattern baldness (MPB), FPHL is a different phenotype with a stronger environmental influence [2]. However, the underlying physiological differences in the way hair follicles are lost on the scalp between men and women are relatively unknown.

Despite genetic studies linking many genes to balding on the scalp [3], the physiological mechanisms driving hair loss with age are poorly understood as is why the scalp remains an area of particularly high risk of hair loss. Hairs on the scalp occur within follicular units, typically

containing 1–5 hair fibres, with multi-hair follicular units much more prevalent on the scalp than other body sites [4]. Only one study to date, in Japanese women, has investigated hair loss within follicular units with age and found there tends to be a loss of multi-hair follicular units but not single hair follicular units [5]. Whether this pattern of hair loss within follicular units relates to a random loss across the scalp (as loss of hairs in multi-hair follicular units with age creates single hair follicular units) or reflects a bias for increased hair loss within multi-hair follicular units is unknown. In addition, how hair parameters change with age in men and women are lacking, particularly in east Asian populations.

Here, we investigated how hair parameters change with age in both Chinese men and women. In addition, we modelled the rate of hair loss with age to determine whether the observed pattern fitted a random pattern of hair loss.

MATERIALS AND METHODS

Subject selection

Scalp images from 200 female and 200 male subjects were selected from a 2014 collection in the Taizhou Longitudinal Study (TZL) cohort (n = 2964) [6]. All image IDs from the dataset were divided into age groups (30–39, 40–49, 50–69 and 60–69) and sex. We randomly selected IDs from each group and sex, until 50 females and 50 males were selected for each age group. There were eight men with MPB, and no woman were graded as having baldness. All volunteers were Han Chinese and lived in Taizhou, Jiangsu Province, China; the Taizhou economy is at a medium level of affluency among Chinese cities. The volunteers were from different jobs and more details are described in Wang et al. [6]. Ethical approval was given by the Ethics Committee of Fudan University (Ethics Research Approval Number 85), and all subjects were in good health and gave informed written consent.

Measurement of hair parameters

One hair from each subject was plucked from the occipital (mid-back) area of the head. An optical microscope was used to take three 50X photographs of the hair fibre closest to the root (within 3 cm) alongside a measurement scale so that hair thickness could be calculated by a Canny edge detector (also see Figure S1b).

Hair density, follicular unit density and hair density/follicular density ratio were measured from a photograph taken from a 6 by 8 mm shaved area on the occipital part of the scalp (example given in Figure S1). Hair and follicular unit counts were measured by a convolutional neural network (CNN) trained using 2400 sample images, and validated using 565 sample images (Figure S1a); all these images were from a separate collection to the 400 subject test images used for further analyses in this study. First, the 2965 images were manually counted by three persons for hair and follicular unit number, and the average between the three assessors used as the final human measurement. After, a 16-layer CNN (VGG16), written in Python 3.6 and PyTorch 1.0.0 (also see Gallucci et al. [7] for a similar approach), was trained on the training set, and then run on the validation set; the CNN data gave correlations of $r = 0.94$ for hair counts (RMSE 3.9) and 0.86 for follicular units (RMSE 2.6) with the manual counting data. The CNN was then used to automatically estimate hair density, follicular unit density and their ratio on the 400 test images. In addition, we also manually measured the number of follicle units containing 1, 2, 3, 4 or 5 hairs per image/subject on the 400 test images to determine the distribution of hairs per follicle unit for each image, not just the average.

Electronic microscopy was used to take 800X photos to measure the hair scale pattern, which is a marker of damage to the hair cuticle. Due to the labour-intensive nature of this method, we randomly selected hairs from 50 females and 50 males from the different age groups for measurement. The scale pattern was estimated by an algorithm based on the contrast component of Tamura texture features (Figure S1c). Tamura texture was defined to quantify visual patterns of object surfaces based on psychological experiments and has been widely used [8–10]. To evaluate the algorithm, 100 samples (not used in this study) were estimated manually by a classification system for hair damage (Figure S2) [11]. We found a lower contrast value of Tamura texture indicated fewer regular overlaid cuticles and a higher degree of hair damage by comparing it to manual judgement (rho = 0.71).

Data analyses

Hair parameters

Hair fibre thickness and hair density were transformed to more normal distributions by using the square root of the measures. A log transformation was used for hair-follicular unit density (base-e log). Correlation analysis was used to investigate the relationship between different parameters. Shapiro–Wilk normality tests were used to determine if parameters were normally distributed or not, and the Wilcoxon rank-sum test to estimate differences between

sexes. Correlation analysis was used to investigate the relationship between different parameters and age.

Modelling loss of hair fibres

To assess the credibility of two hair fibre loss models, 1000 bootstrap samples were simulated from the original data for each age and gender group in each case. The models applied were: Hair loss at random from 30- to 39-year-olds to 60 to 69-year-olds was computed separately for both males and females but at a constant rate irrespective of hairs per follicular unit (probability of a hair being lost between the two age groups ~0.17 and ~0.13 males and females, respectively). The higher rate of hair loss the more hairs per follicular unit, but different rates for each gender: Rate of loss $= 1 - p\hat{}n$, where n is the number of hairs in the follicle and p is increased hair-loss risk effect within a follicular unit, estimated as 0.09 for males and 0.05 for females.

The percentage of follicles with three or more hairs was determined for each 60–69 subject, and then the average equivalent percentage was computed for each simulated set. Follicles with 0 hairs were excluded from the calculation as no such observations were possible. To test the null hypothesis that hair loss reflected the approach being assessed, the proportion of these bootstrap statistics (percentages) that was more extreme than the actual percentage was used, that is in this case, the p-value is the proportion of simulated values that are lower than the observed value. This test was performed once to assess each approach.

RESULTS

Hair parameters and sex differences

Table 1 shows the distributions of hair parameter values across sexes and additionally with low, average and high representative values. Males had a significantly higher hair density and follicular unit density than females, but similar fibre thickness and number of hairs per follicular unit (i.e. ratio of hair density/follicular unit density).

Hair parameter changes with age

The hair number per follicular unit had the greatest negative correlation with age ($r = -0.58$ and -0.48 in males and females, respectively), whereas the density of follicular units more weakly changed with age ($r = 0.24$ and -0.26 for males and females, respectively); see Figure S4 for visualizations and relationships with age for the parameters.

Hairs per follicle unit and their change with age

There was a small decrease in two hair follicular units and a marked decrease in three or more hairs per follicular unit with age; in contrast, there was an increase with age in one hair follicular unit, Figure 1a,b, and was more notable in the men. Indeed, there was a greater difference in the ratio of 3+ hair follicular units over one hair follicular units between men and women at 60–69 than at 30–39-year-olds although the sex difference in the 60–69 group was outside significance, Table 1 $p = 0.08$.

Finally, we modelled the likelihood of losing the number of hairs per follicular unit based on random loss as well as an increased likelihood of hair loss the more hairs per follicular unit. When examining the change in the proportion of three or more hair follicular units with age, the observed data was significantly different to the random model, but not significant difference was evident between the observed data and the model predicting increased risk of loss for every extra hair per follicle unit, Figure 2a–d.

DISCUSSION/CONCLUSION

Here, we found that men have a greater density of hairs as well as follicular units than women. However, the loss of multi-hair follicle units with age was greater for men leading to less 3+ hair follicle units on average for men than women in their 60s. Furthermore, the loss of hairs per follicular unit in men and women was more similar to a model of increased risk of hair loss the more hairs per follicular unit, which was particularly the case in men.

Recent advances in genomic studies, particularly the genome-wide association study (GWAS), have helped identify genes underlying MPB [3]. FPHL is less well explored with data indicating it has, at least in part, a different aetiology [2]. Although the change with age in the hair parameters found here was generally similar between men and women, men did lose more hairs per follicular unit with age faster than women giving a lower number of multi-hair follicular units relative to single hair follicular units by age 60–69. This effect could be the result of the greater genetic susceptibility to MPB in men. Investigations into how MPB linked DNA sequence variants drive loss of hairs within follicular units could give

TABLE 1 Hair parameter characteristics by sex.

Parameters	Gender	Sample size	First tertile/17th percentile	Median/50th percentile	Third tertile/83rd percentile	Shapiro test (*p*-value) for normality	Sex differences (Wilcoxon rank-sum test *p*-value)
Tamura texture (contrast)	Female	50	14.13	21.06	26.22	0.94	0.7
	Male	50	14.5	19.88	27.27	0.01	
	Combined	100	14.46	20.35	26.52	0.36	
Hair fibre thickness (μm)	Female	200	74.75	86.22	100.15	1.5×10^{-3}	0.69
	Male	200	72.43	85.69	100.45	0.7	
	Combined	400	73.47	86.04	100.23	9.8×10^{-3}	
Hair density (number/cm^2)	Female	200	80.95	97.62	118.39	0.01	3.21×10^{-4}
	Male	200	87.3	104.76	126.16	0.43	
	Combined	400	82.54	100.99	123.02	0.01	
Follicular unit density (number/cm^2)	Female	200	38.1	44.44	54.24	4.1×10^{-4}	1.82×10^{-4}
	Male	200	42.06	46.83	55.56	4.4×10^{-6}	
	Combined	400	39.68	46.03	55.56	1.9×10^{-7}	
Hair density/follicular unit density ratio	Female	200	1.87	2.18	2.54	0.98	0.87
	Male	200	1.91	2.21	2.49	3.7×10^{-3}	
	Combined	400	1.9	2.19	2.51	0.07	
Number of one hair follicular units	Female	200	4	9	14.17	4.9×10^{-4}	0.13
	Male	200	5	10	15	1.8×10^{-6}	
	Combined	400	5	9	15	6.1×10^{-8}	
Number of two hair follicular units	Female	200	10	14	17	0.15	0.37
	Male	200	10	14	18.17	1.8×10^{-2}	
	Combined	400	10	14	18	3.4×10^{-3}	
Number of 3+ hair follicular units	Female	200	2	4	8	4.1×10^{-8}	7.8×10^{-2}
	Male	200	2	5	9	1.7×10^{-4}	
	Combined	400	2	5	8	8.1×10^{-10}	
Ratio of 3+ hair follicular units over one hair follicular unit in 30–39-year-olds.	Female	50	0.21	0.73	1.7	3.9×10^{-11}	0.33
	Male	50	0.36	0.83	1.39	2.3×10^{-7}	
	Combined	100	0.27	0.8	1.51	1.8×10^{-15}	
Ratio of 3+ hair follicular units over one hair follicular unit in 60–69-year-olds	Female	50	0.1	0.41	1.32	2.3×10^{-12}	0.08
	Male	50	0.02	0.21	1	5.0×10^{-9}	
	Combined	100	0.06	0.3	1.02	$<2.2\times10^{-16}$	

Note: A Shapiro test for data normality and Wilcoxon rank-sum test for sex differences were performed on the data. Males had greater hair density and follicular unit density but tended to have less multi-hair follicular units at 60–69 years. Example images of the differences between low (17th) and high (83rd percentile) values for hair thickness and hair density/follicular unit density ratio are given in Figure S3.

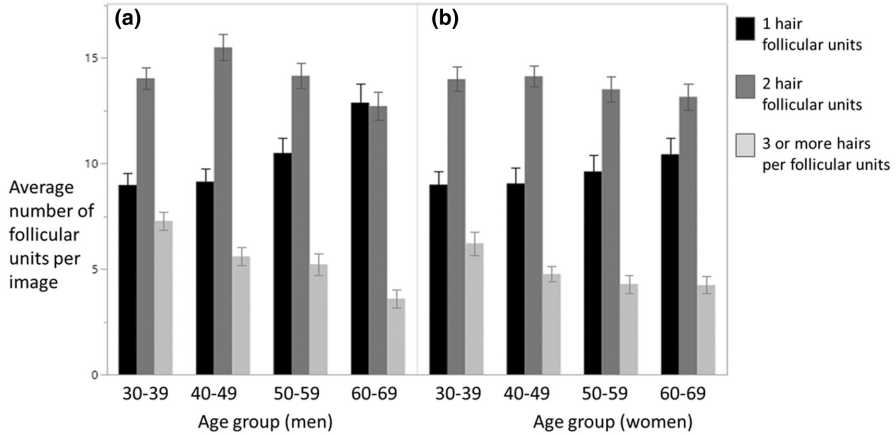

FIGURE 1 The number of hairs per follicular unit across age groups. (a) The average number of follicular units containing one (dark grey bars), two (medium grey bars) and three or more hairs (light grey bars) per subject image for each age group in men. (b) The average number of follicular units containing one (dark grey bars), two (medium grey bars) and three or more hairs (light grey bars) per subject image for each age group in women. Errors bars depict standard error for each age group, with 50 men and 50 women per age group.

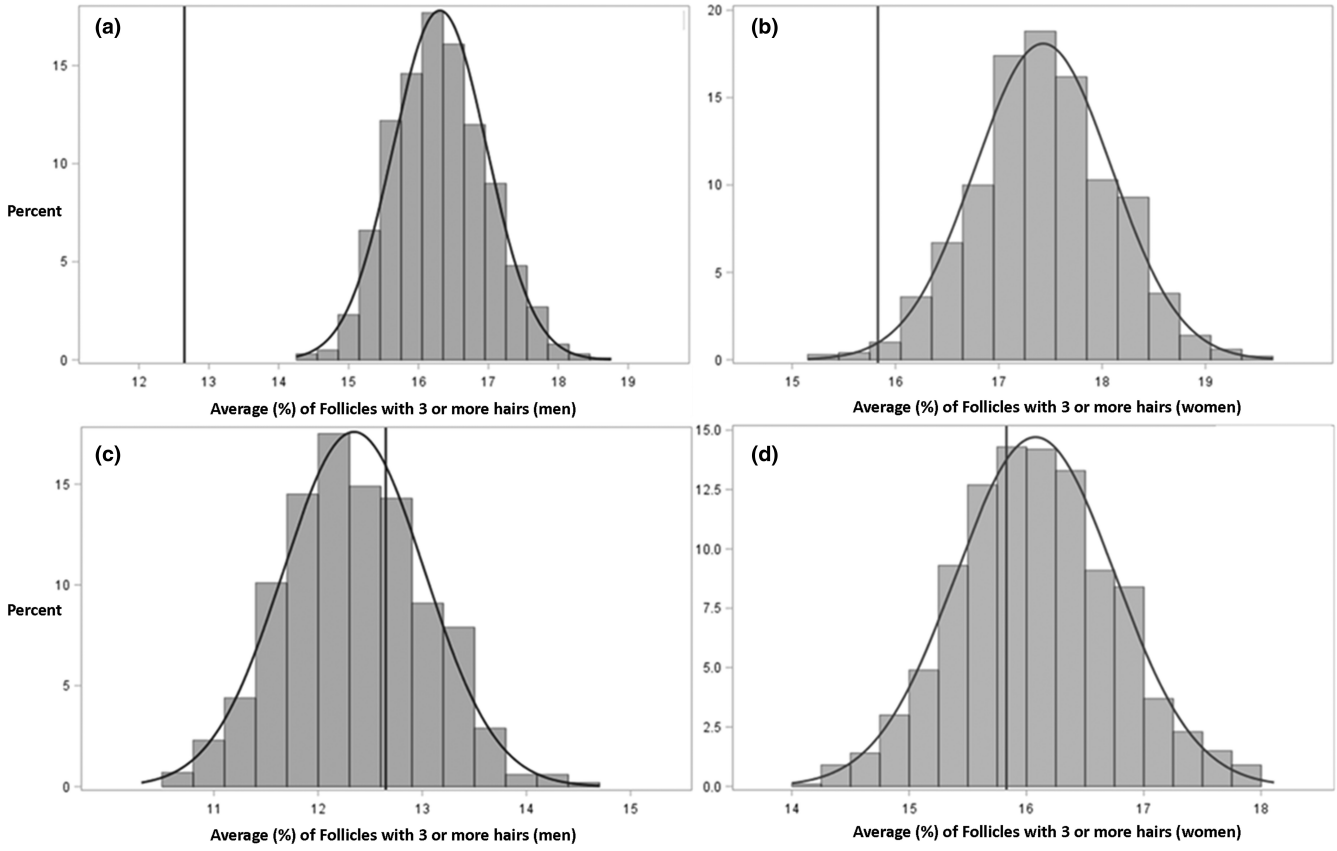

FIGURE 2 (a–d) Depiction of the distribution of 1000 simulated hair loss iterations for the percent of follicles with three or more hairs. Simulations used the 30–39 age group hair numbers per follicular unit and simulated hair loss via two different methods to generate new counts of hairs per follicular unit, with a new reduced total hair count as found in the 60–69 age group. (a) In men, random loss of hairs across follicular units (b) In women, random loss of hairs across follicular units, (c) In men, hair loss as per a higher chance of hair loss for every extra hair per follicle unit & (d) In women, hair loss as per a higher chance of hair loss for every extra hair per follicle unit. The vertical line in each chart depicts actual percentage of follicular units in the 60–69 age group with three or more hairs. Same statistics was used to determine fit of simulations with observed and was $p < 0.001$ for (a), $p = 0.008$ for (b), $p = 0.673$ for (c), and $p = 0.363$ for (d). In other words, it is unlikely hair loss follows a random loss across follicular units and more likely it preferentially occurs in follicular units with greater numbers of hairs.

further insights into this phenomenon, such as if androgen receptor signalling interacts with and exacerbates such loss.

Only one study to date has examined hair loss per follicular unit and found that one hair follicle unit increased with age, whereas there was a decrease in three or more hair follicular units [5]. Here, we also observe a similar pattern and also demonstrate that hair loss is unlikely due to random loss of hairs across follicular units. One explanation for this non-random pattern of hair loss is that there is a competition between hair bulbs within follicular units; for example, vascular supply of nutrients could diminish with age as capillaries that associate with vellus hairs (the precursors to hair loss) are smaller and less numerous [12]. In support of this, minoxidil, which prevents hair loss, could be stimulating hair regrowth via improved blood supply to the hair follicle [13]. However, it is not known if the reduced capillary supply is pre- or post-vellus hair formation, and minoxidil's exact mode of action is unclear [13]. These data do, however, indicate that interventions that slow the loss of hairs within multi-hair follicular units should help reduce the amount of hair loss with age.

As a weakness of this study, the counting of hairs per follicular unit can be challenging if hairs overlap one another, although as the counting was done blind to age or sex of the subject this should have had an equal influence across images. In addition, the analysis assumes that the older groups are representative of what will happen to the younger groups when they age, which might not necessarily be the case. However, as there are 100 subjects per each 10-year age group, the results should be generally representative of the ageing effects on hair and are supported by a separate study showing a similar pattern of hair loss per follicular unit with age [5]. Notwithstanding this, replication of these data is warranted, to determine whether such non-random loss of hairs is generalizable across populations.

In conclusion, we find evidence of preferential loss of hairs in multi-hair follicular units more than that expected by chance. As multi-hair follicular units are much more dominant on the scalp these findings could explain, at least in part, the notable susceptibility of the scalp to hair loss.

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CONFLICT OF INTEREST STATEMENT

Authors I.A., R.B., P.M., M.R., X.G. and D.A.G. are Unilever employees and had a role in data analysis and the manuscript. Although no products were tested, this manuscript could promote the use of anti-ageing products and services leading to financial gain for Unilever.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy restrictions and regulations in China.

ETHICS STATEMENT

All participants provided written informed consent, and all study protocols were approved by the institutional review boards of the pertinent research institutions. The research was approved by the Ethics Committee of Human Genetic Resources at the Shanghai institute of life Sciences, Chinese Academy of Sciences.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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