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ORIGINAL ARTICLE

Confirmation of microevolutionary increase in spina bifida occulta among Swiss birth cohorts

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Abstract Previous studies on the prevalence of spina bifida occulta have indicated a microevolutionary increase in its frequency and possible population differences in the prevalence of the condition. We studied the frequencies of closed and open sacral canals at each sacral level among two birth cohorts in Switzerland. Transverse CT scans and multiplanar reconstruction images of sacra of 95 males and 96 females born in 1940–1950 and 99 males and 94 females born in 1970–1980 in Switzerland were reviewed. We found that individuals born later have significantly more open sacral arches at all sacral levels compared to those born 30–40 years earlier. When results were related to previously published data on Australian cohorts, the trend was the same, but Swiss in both cohorts were less likely to have an open section than Australians at all locations apart from S2. This study confirmed a microevolutionary trend in the opening of sacral canal among two different generations in Switzerland and demonstrated a population difference in the prevalence of spina bifida occulta.

Keywords Sacrum · Opened sacral arches · Secular trend · Anatomical variation

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Introduction

The human neural tube closes during the fourth week of embryonic development. Failure of this process leads to neutral tube defects (NTD). In the cranial vault, this presents as anencephaly or encephalocele. Caudally, it affects fusion of embryonic vertebral arches, resulting in spina bifida. Spina bifida ranges from clinically disabling anomaly such as spina bifida cystica and meningiomyelocele to largely asymptomatic spina bifida occulta. Although regarded as benign, spina bifida occulta has recently been associated with a number of pathologies such as tethered cord syndrome [1, 2], genitourinary dysfunction [3], disc pathology [4], lumbar spondylolysis [5], intraspinal lipoma [2, 6], foot deformities [7] and syringomyelia [8].

Recent evidence suggests that the incidence of spina bifida occulta may be undergoing a change. We observed and reported an increase in opening of sacral canal in Australian individuals born in 1980s as compared to those born 40 years earlier, at all levels, particularly at the S3/S4 level [9]. Such temporal increase in the incidence of spina bifida occulta has also been reported as early as the 1960s by Ferembach and Post [10]. The increasing frequency of

this anomaly and its associated clinical syndromes may have significant implications for the health of the population. The reason behind this phenomenon is unknown. Some propose that there is a continuous closure of canal during life [8, 11]. Indeed under normal conditions, vertebral arches start ossifying at birth and the process is complete by 5–8 years [8], although in certain individuals, this process is delayed and only complete by the age of 15 years [12]. Thus, an apparent vertebral arch defect in children may be filled with new bone as part of the aging process, ossifying a radiologically undetectable connective tissue matrix [8]. Based on the connective tissue theory, Gregerson et al. [8] proposed that defects that persisted past the age of 8 years may represent abnormal ossification rather than a congenital absence of the posterior arch. However, observation on newborn spine at infantile death with spina bifida occulta did not reveal a cartilaginous bridge that could ossify later in life [9]. Following earlier findings contributed by the ongoing evolution of human population [13], a microevolutionary trend in the opening of the sacral canal was proposed in Australia [9]. It is, however, uncertain if this trend occurs in other regions.

A review of migration flow to Switzerland revealed that in comparison to the 1950s, there was an increasing proportion of migrants to the country originating from eastern Europe in the 1990s [14]. However, the predominant ethnicity was Italian among migrants in both 1950s and 1990s [14]. Over the four decades, the majority of Swiss population was still of northwestern and southwestern European origin [14]. Compared with Switzerland, Australia is "genetically a more diversified" country. The Australian ethnic makeup has changed sharply over recent years as a consequence of the new and diverse source countries feeding Australia's migration program [15]. Anglo-Celtic ethnicity has fallen from 90% in the 1940s to 70% in 1999, with a corresponding rise from Asian and western European ethnicity [15]. As much as 60% of Australian people are ethnically mixed and about 20% have at least four distinct ancestries [15]. Such changes promote genetic intermixture among the Australian population.

In this study, we investigated the differences in the closure of the sacral canal among Swiss cohorts born three to four decades apart, and compared the frequencies of closed and open sacral canals at each sacral level between the two, similar to our earlier Australian study [9]. This study also considers populational Swiss–Australian difference in the prevalence of spina bifida occulta.

Materials and methods

Ethics committee approval was obtained from Ethics Committee of Canton Zürich to review abdominal CT examinations from the Institute of Diagnostic Radiology, University Hospital Zürich, Switzerland. Transverse CT scans, multiplanar reformations and volume-rendered 3D images of sacra of 100 males and 100 females born in 1940–1950 and 100 males and 100 females born in 1980–1990, were examined. The samples were constructed by taking the first 100 CT scans for each birth cohort of males and females according to the order of the examination date, starting from the commencement of the study (November 2006 backwards). All examinations were performed using a dual-source CT scanner (Somatom Definition, Siemens Healthcare). Images were reconstructed with a slice thickness of 2 mm and an increment of 1.5 mm. The software tool Voxar 3D (Toshiba Medical Visualization Systems) integrated into the hospital's picture archiving and communication system (PACS, IMPAX, AGFA Healthcare) was used for post-processing. Images taken for symptoms possibly related to spina bifida occulta were excluded, as were trauma cases with pelvic ring disruptions that interfered with the assessment of the sacral canal opening or the location of the opening. As a result of these exclusions, the final sample sizes were 95 males and 96 females born between 1940 and 1950, and 99 males and 94 females born between 1970 and 1980. The CT images from the total of 384 subjects included in this study were taken for the following clinical indications not associated with symptoms that were linked with spina bifida occulta: suspicion of abdominal malignancy or abdominal infection, surveillance of known malignancy under chemotherapy or radiotherapy, postoperative control after surgery, e.g. of the liver (carcinoma, metastases or abscesses) or bowels (mainly inflammatory disorders or malignancy) and urolithasis. These indications were similar in the age and sex groups investigated.

Closure of the sacral canal was scored separately at five sacral levels: S1–S5 as previously reported [9]. The canal was considered open if there was no bone bridging of the right and left sacral vertebral arches. Sacral canal opening was graded as: canal closed or canal opened.

Frequencies of non-closure at each level were compared between the sexes and the two birth cohorts. Differences in non-closure frequencies across the vertebral levels were assessed using logistic GEE regression models. Interaction effects involving vertebral level were included in the models to investigate whether differences between sexes, birth cohorts and populations changed across the vertebral levels. Results of the models are expressed using odds ratios and associated p values. A two-tailed p value of 0.05 was taken as indicating statistical significance.

Results

The numbers of sacral canal opening among cohorts of Swiss males and females (both age groups combined) and

among older (born in 1940–1950) and younger cohorts (born in 1970–1980) are presented in Table 1. Frequencies of open sacral canals at each vertebral level in males and females are presented in Fig. 1, while those individuals born between 1940 and 1950, and 1970 and 1980, are presented in Fig. 2.

Swiss females were less likely to have open sacral arches than Swiss males independently of vertebral level (OR = 0.72, $p = 0.11$), although the difference was not statistically significant. Swiss individuals born between 1970 and 1980 had significantly more open sacral arches than those born between 1940 and 1950 independently of vertebral level (OR = 0.50, $p < 0.01$).

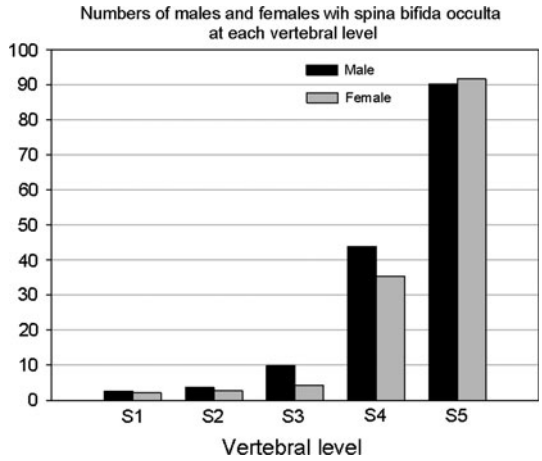

Fig. 1 Frequency of open sacral canals at specified levels in Swiss males and females

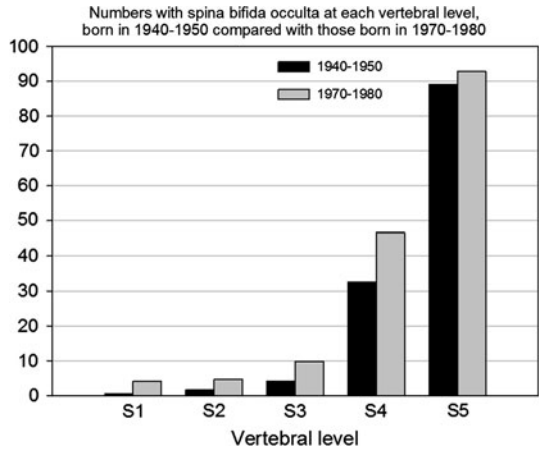

Fig. 2 Frequency of open sacral canals at specified levels in Swiss individuals born 1940–1950, and 1970–1980

Discussion

Previous studies of spina bifida occulta were mainly concerned with opening of sacral canal at the S1 level, which corresponded to the classical definition of this anomaly. Saluja reported an incidence of opening of sacral canal at the S1 level in Londoners born in the eighteenth to nineteenth century and modern Londoners to be 11.6 and 10%, respectively [10]. Post reported an incidence of 16% of opening of the S1 sacral canal in a study on ancient Egyptians [16]. An Australian sample [9] revealed an opening of 13.5% at this level. Our current findings of S1 canal opening among Swiss samples differed from the above-mentioned three populations. We found a surprisingly low S1 canal opening of 2.34%. In fact, when compared with this Swiss cohort, the Australian cohort [9] has an odds of S1 sacral canal opening of 6.50 ($p < 0.01$). When comparison was made between the Swiss and Australian samples, Australians were more likely to have an open section than Swiss. The differences observed between populations, however, depended on the vertebral level (interaction $p < 0.01$). Post hoc tests revealed that the odds of sacral canal opening were significantly higher at all vertebral levels other than S2. The odds of sacral canal opening between the two populations are presented in Table 2. Such population differences in sacral canal opening have also been previously observed. When the sacral opening of the S1 level in the ancient Egyptians was compared with other ancient populations (Peruvians, American Indians, Aluetians) of roughly the same era, Post observed a significantly higher incidence of opening at this

Table 1 Frequencies of open sacral arches at various sacral levels in cohorts of Swiss males and females, as well as those born earlier (1940–1950) and later (1970–1980)

Group	S1		S2		S3		S4		S5	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Overall ($n = 384$)	9	2.34	12	3.13	27	7.03	152	39.58	349	90.89
Female ($n = 190$)	4	2.11	5	2.63	8	4.21	67	35.26	174	91.58
Male ($n = 194$)	5	2.58	7	3.61	19	9.79	85	43.81	175	90.21
Older cohorts born in 1940–1950 ($n = 191$)	1	0.52	3	1.57	8	4.19	62	32.46	170	89.01
Younger cohorts born in 1970–1980 ($n = 193$)	8	4.15	9	4.66	19	9.84	90	46.63	179	92.75

Table 2 Frequency (%) and odds ratio of open sacral arches at various sacral levels among Australian and Swiss cohorts

Location	Frequency (%)	Odds ratio	*p* value
S1: Australian vs. Swiss	13.50 vs. 2.34	6.5029	<0.0001
S2: Australian vs. Swiss	4.25 vs. 3.13	1.3760	0.4059
S3: Australian vs. Swiss	12.25 vs. 7.03	1.8458	0.0147
S4: Australian vs. Swiss	61.75 vs. 39.58	2.4641	<0.0001
S5: Australian vs. Swiss	99.25 vs. 90.89	13.2713	<0.0001

level (16 vs. 1–4%) [16]. Causes of population differences in sacral canal opening can be possibly explained by genetic differences among populations, or by epigenetic factors resulting in anatomical variations.

This study also demonstrates a higher prevalence of spina bifida occulta among the younger cohort when compared with those born 30–40 years earlier. This finding was consistent with previous findings: the study on two Australian population groups that also indicated a trend toward opening of sacral canal in the younger population [9]. When prevalence of spina bifida occulta among people born early in the twentieth century is compared with that among people born later, an approximate doubling in incidence has been noted [13]. It was hypothesized that such changes were brought about by the ongoing evolution of human population as a consequence of relaxed natural selection and increasing mutations and gene flow [9, 13].

The use of peri-conceptional folic acid, 4 mg daily for women with family history of NTD and 400mcg daily for women with no family history of NTD, had been shown to reduce both the recurrence of NTD or the first occurrence of NTD. A meta-analysis by Lumley et al. [17] estimated a 70% reduction in neural tube defects with peri-conceptional supplementation with folic acid. Although the benefits of folic acid had been reported as early as 1980 [17], the use of folic acid supplementation was not popularized until 1992 in Australia [18] and 1996 in Switzerland [19]. This meant that older cohorts (born 1940–1950) from both populations would not have received folic acid supplementation, while some of the younger cohorts (born 1970–1980) would have received folic acid supplementation. Despite this, younger cohorts in both Swiss and Australian population have a higher incidence of sacral canal opening compared to the older cohorts. Future studies will aim to study the frequency of sacral canal opening among cohorts born in the twenty-first century to determine if there is a reversal in trend considering that most would have received supplementary folic acid.

This paper compares the occurrence of spina bifida occulta between two multiethnic populations with similar levels of technological advancement and medical care. Both countries are geographically very distant, but share similar living conditions, and have gene pools based on European stock, but with admixtures. As far as we know, there are no more recent data organized in a similar way. Interestingly, although prevalence is different, the trend is similar, demonstrating a microevolutionary increase in spina bifida occulta among two populations. Clinical implications of the differences in prevalence of spina bifida occulta among various populations have not yet been established. It is, however, reasonable to hypothesize that clinical syndromes associated with spina bifida occulta would be higher in certain populations with higher prevalence of spina bifida occulta. Despite being relatively small, the sample sizes in this preliminary study on the prevalence of spina bifida occulta among two Swiss generations were sufficient to demonstrate the interesting phenomenon. We will however continue this study into the future not only to test the trend over time, but also, by increasing the sample size, to obtain a more accurate figure of the prevalence of spina bifida occulta. Such future studies will be useful in planning future health-care requirements.

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