Available online at www.sciencedirect.com

ScienceDirect

C. R. Biologies 332 (2009) 603–612

COMPTES RENDUS BIOLOGIES

Development and reproduction biology / Biologie du développement et de la reproduction

# Progeny's mental aptitudes in man: relationship with parental age at conception and with some environmental factors

Maurice Auroux [a,*], Magali Volteau [b], Béatrice Ducot [c], Thierry Wack [c], Alexia Letierce [b], Laurence Meyer [c], Marie-Jeanne Mayaux [c]

[a] *Andrologie – biologie de la procréation et du développement, Université Paris-Sud, CHU de Bicêtre, 94275 Le Kremlin-Bicêtre cedex, France*
[b] *Unité de recherche clinique, Université Paris-Sud, CHU de Bicêtre, 94275 Le Kremlin-Bicêtre cedex, France*
[c] *Inserm U 822, IFR 69, INED, Université Paris-Sud, AP-HP, CHU de Bicêtre, 94275 Le Kremlin-Bicêtre cedex, France*

Received 16 December 2008; accepted after revision 4 March 2009

Available online 7 April 2009

Presented by Jean Rosa

**Abstract**

Psychometric tests obtained from 6564 young men were studied as a function of the parents' ages at conception and of some characteristics of the subject's postnatal environment. Individual scores, from 0 to 20, were divided into two groups: $n_1 \geqslant 11$ and $n_2 < 11$. In univariate analysis, scores $< 11$ were respectively related to low height, high number of siblings and junior in birth order, subject's and parents' tobacco consumption, parents' alcohol consumption, subject's and parents' low academic standard, parents' youth or ageing at conception. In multivariate analysis, these scores remained related to low height, junior in birth order, subject's and parents' tobacco consumption, parents' low academic standard, parents' youth (both $< 20$). Regarding the respective influences of the environment and of the subject's genome on his cerebral development, one can hypothesize a complementarity between these two factors through the possibility of a genetically determined individual synaptic potential, revealing itself, more or less, according to environmental conditions. ***To cite this article: M. Auroux et al., C. R. Biologies 332 (2009).***


**Résumé**

**Aptitudes mentales de la progeniture chez l'homme : relation avec l'âge parental à la conception et avec certains facteurs environnementaux.** Les tests psychométriques effectués par 6564 jeunes hommes furent analysés en fonction de l'âge des parents à la conception et de certains caractères de l'environnement postnatal. Les scores individuels, de 0 à 20, furent divisés en 2 groupes : $n_1 \geqslant 11$, $n_2 < 11$. Dans l'analyse univariée, les scores $< 11$ sont respectivement associés à une petite taille, à l'importance de la fratrie, au rang de naissance des cadets, au tabagisme du sujet et des parents, à la consommation d'alcool des parents, à un bas niveau académique du sujet et des parents, à la jeunesse ou la vieillesse des parents à la conception. Dans l'analyse multivariée, ces scores restent liés à une petite taille, au rang de naissance des cadets, au tabagisme du sujet et des parents, à un niveau académique parental bas, à la jeunesse des parents (chacun $< 20$ ans). Concernant les rôles respectifs de l'environnement et du génome du sujet dans son développement cérébral, la complémentarité de ces deux facteurs est envisageable dans l'hypothèse d'un potentiel synaptique individuel génétiquement déterminé, se révélant lui-même, plus ou moins, selon les conditions environnementales. ***Pour citer cet article : M. Auroux et al., C. R. Biologies 332 (2009).***

* Corresponding author.
*E-mail address:* auroux.mauriceetmichel@neuf.fr (M. Auroux).

1631-0691/$ – see front matter 
doi:10.1016/j.crvi.2009.02.008

*Keywords:* Male progeny; Psychometric tests; Parental age at conception; Environmental factors; Genetic factors; Synaptic potential

*Mots-clés :* Progéniture mâle ; Tests psychométriques ; Age parental à la conception ; Facteurs environnementaux ; Facteurs génétiques ; Potentiel synaptique

## 1. Introduction

Many effects of genetic defects on the progeny's quality related to maternal or paternal ageing at conception (indicated by the parents' ages at the time of the child's birth) are well known. Some are evident because they concern the body's morphology, such as trisomy 21 (T 21) or malformations from the mother, dominant autosomal syndromes from the father [1,2], who may present DNA damage in sperm [3]. Others are less conspicuous because they concern functional impairments. For example, paternal ageing could lead to a decrease of girls' longevity [4] or an increase of the proportion of schizophrenic subjects [5–7]. Moreover, a clinical study showed that children born of older parents had lower IQs than children whose parents were younger [8]. Concerning this last point, we developed an experimental model which found that, in the rat, the ageing of males led to a decrease in learning capacity in progeny [9]. We then showed, in man, by means of a psychometric investigation of young adult males entering the French army, that not only was paternal ageing accompanied by similar effects but these could also be related to very young paternal age [10] – and we observed this again in mice [11]. Our results have been recently confirmed by a large study carried out in human male and female adolescents [12]. However, on the whole, these results incited us to take up a new study: (a) in adults, because the relative roles of genetic and environmental factors on cognitive ability, which vary from infancy to adulthood, are then stabilized [13]; (b) using the same method we previously employed, [10], but applied, this time, to a more extensive study involving new army male recruits; (c) studying some environmental factors known to have an effect on progeny's mental aptitudes, including some socio-economic and toxic factors which could be potentially confounding factors; (d) examining parts of the genetic and/or environmental factors possibly involved in the phenomena studied. Indeed, if parental age at conception, particularly paternal age, had an effect on the future IQ of children, it would be possible to envisage a genetic cause of this effect, such as we have already hypothesized [10]. However, it is known that many environmental factors influence the development of IQ – including, in addition to toxic ones as tobacco [14,15], or alcohol [16,17], parents' academic [18,19] and socio-economic status [20,21] or siblings' birth order [18, 22]. Consequently, we wondered if, in the development of mental aptitudes, genetic and environmental factors were independent, complementary or both, and through what possible mechanism.

It was these different points which were considered in our study.

## 2. Materials and methods

In addition to the possible influence of parental ages at conception of a child, our present work compared, using univariate and multivariate analysis, the relative effect of several other factors on the "general mark" (GM) obtained through psychometric tests on young males before entering the army. These factors, for which the influence is known – socio-economic and cultural situations (reflected by subject height and by parents' academic standards, respectively), number of siblings, birth order, child's and parents' tobacco and alcohol consumption – were listed in a questionnaire submitted to each subject. In this way we were able, first, to test the reliability of our method and, secondly, to assess the influence of parental ages at conception, i.e. the influence of possible genetic factors, independently of environmental ones, particularly in the case of the father's age.

### 2.1. Subjects

In France, before the army became a professional activity, all 18-year males, before entering military service, participated in a 2-day preliminary programme, undergoing medical, physical and psychometric testing. For our investigation, a questionnaire regarding the subject and his parents was added. A single military region, that of Ile-de-France, was investigated in March 1990 and January 1991. The population was made up of 10 809 subjects. After removing 1863 unusable questionnaires (refusal to answer, incomplete or contradictory answers, etc.), there remained 8946 subjects. To obtain as much homogeneity as possible, only subjects born to native French parents and born themselves in France, Western Europe, Canada or the United-States were included. Only records with no missing data regarding parents' ages were retained. 6564 subjects then remained. The majority of the population studied were 18- and 21-year olds (the latter being conscripts temporally exempted because of their studies). There were also two extreme limits: one consisting of volunteers who were only 16-years old and the other of late student subjects, whose maximum age was 30.

### 2.2. Psychometric investigation

This Army investigation comprised a series of 187 items, divided in three major types of tests, based on a minimum level of education, i.e. knowing how to read and count. These tests, validated against the Wechsler scales, had been used by the French army since 1981 [23]. They analysed general aptitude for reasoning, so-called "practical intelligence" and the aptitude to use verbal symbols and numbers correctly. The answers were provided as "multiple choice" and tests were marked automatically by machine. These three types of tests have been described previously [10].

Raw scores obtained in each test were combined into a single general mark (GM) with a maximum of 20, referred to as "general intelligence level". Military experts observed that a GM $\geqslant 11$ authorized access to any military occupation, while a GM $< 11$ more or less seriously reduced this possibility.

### 2.3. Questionnaire about subjects (current status) and parents

In our earlier investigation [10], we were restricted by military conditions to subjects' date of birth and parents' ages (and the latter were not normally required). In the present work, on the contrary, numerous questions were authorized. We could therefore employ multivariate analysis and, so, make this investigation more secure than the first. Factors studied were:

- subject's and parents' places of birth;
- subject's date of birth, height and weight; however, two of these factors were not maintained: (a) subject's age, because this variable was closely related to academic standard ($p < .0001$) and to GM ($p < .0001$); (b) weight, because this variable was closely related to height ($p < .0001$) which, being known to reflect the socio-economic status [24–26], was chosen as socio-economic indicator;
- number of brother(s) and sister(s) (6 classes);
- birth order (5 classes);
- subject's and parents' current tobacco consumption before and at time of interview (at least 5 cigarettes or 2 pipes a day) (answer: yes or no); no question about pregnancy period;
- subject's and parents' current alcohol consumption before and at time of interview (at least 1 litre of wine or equivalent a day) (yes or no); no question about pregnancy period;
- subject's and parents' academic standard reflecting cultural status and comprising 4 classes: non-schooled or primary standard; secondary or technical school, 1st cycle; secondary or technical school, 2nd cycle; A level and more; parents' academic standards, though closely related ($p < .0001$), were, nevertheless, separately studied because of a possible difference between mother's and father's influences;
- parents' socio-economic status (10 classes); this factor was not analysed because the ten classes proposed in our questionnaire proved insufficiently descriptive of actual occupations;
- parents' dates of birth and ages at the date of the investigation; this enabled us to verify the consistency of answers and calculate parents' ages at the time of the subject's birth (father: 7 classes; mother: 6 classes). Though closely related ($p < .0001$), father's and mother's ages at this time were also separately studied, because of a possible difference between father's and mother's influences.

The study received the authorization of the "Service de Santé des Armées". The investigation was anonymous.

### 2.4. Statistical analysis

The two GM populations were compared in the various situations presented in the questionnaire. Quantitative results expressed as means were compared using Student's $t$ test. Qualitative results were compared using Chi-2 test. Multivariate logistic regression (SAS program, SAS Institute, version 8.2) was used to assess the independent role of selected factors and to search for possible effect modifications between some variables.

## 3. Results

### 3.1. General characteristics of the studied population

The mean GM $\pm$ sd was $12.6 \pm 5.6$ ( min.: 1.0, max.: 20); the mean subjects' age was $19.8 \pm 1.7$ (min.: 16.0, max.: 30.0); the mean father's age at the subjects' birth

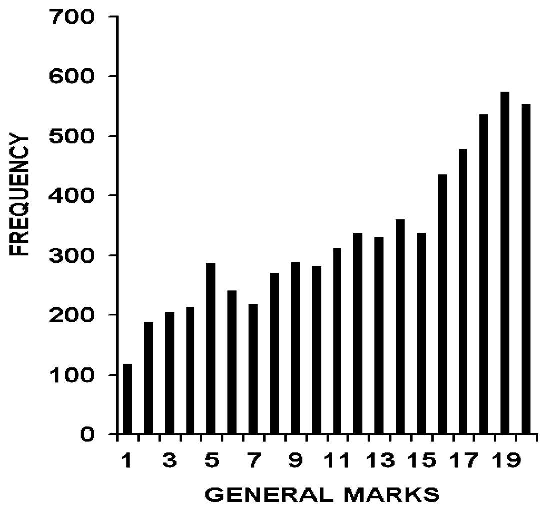


Fig. 1. Distribution of general marks.

was $28.5 \pm 6.1$ (min.: 15.0, max.: 62.0); the mean mother's age at the subjects' birth was $26.0 \pm 5.5$ (min.: 14.0, max.: 45.0). The distribution of GMs is shown in Fig. 1. Since this distribution was not normal, we chose to split GM into two groups according to the gradation established by military experts: $\geqslant 11$ ($n_1 = 4257$, 64.9%), $<11$ ($n_2 = 2307$, 35.1%).

### 3.2. Univariate analysis (Table 1)

We compared the two groups according to the different variables of the questionnaire. Except for "subject's alcohol consumption" in which these groups did not differ, they were significantly different for the other variables. In these, the GM < 11 group was respectively related to low height, high number of siblings and junior birth order, subject's and parents' tobacco consumption, parents' alcohol consumption, subject's and parents' low academic standard, parents' youth/aging at conception.

### 3.3. Multivariate analysis (Table 2)

Only variables with significant results in the univariate analysis were retained in the multivariate analysis. Nevertheless, subject's academic standard was excluded because the correlation between GMs and academic levels was so strong that it could be considered that these two parameters measured the same thing – mental aptitudes – by two different means. Through multivariate analysis, Table 2 showed that subject's low height, parents' low academic standard, junior birth order, subject's and parents' tobacco consumption, father's and mother's youth at conception, taking those aged below 20, were significantly related to GM < 11. However, such a relationship did not appear with the parents' aging.

In accordance with the Turkheimer and al.'s results [21], the parents' cultural and socio-economic status, measured in our study by the parents' academic standard and the subject's height, were found to be the most important factors for having GM $\geqslant$ 11 or < 11. The role of the father's age was overall not significant ($p = .12$), even if the OR associated with the 15–19 year class was significantly different from one compared to the 25–29 year class as the reference. No effect modification between father's age and these variables was found.

## 4. Discussion

Multivariate analysis confirmed the role of socio-economic and cultural factors, of birth order, of toxic factors such as family tobacco consumption and showed the influence of father's and mother's youth at conception on young adult males' mental performances.

### 4.1. Cultural and socio-economic factors

The probability for the subject to have a GM < 11 was inversely related to:

(a) *the parents' educational level*. In children, some studies showed this negative correlation concerned the mother [18], and others concerned the father [19], but via a related factor – the father's social class. Indeed, if the parents' academic standard can directly influence the progeny's cultural environment, their socio-economic status, part also of his environment, plays an analogous and important role [20,21]. However that may be, the academic achievement and higher social classes seem often associated [20,21].

(b) *the subject's height*. This negative correlation has previously been described [27]. The subject's height, reflecting the socio-economic status, could involve an early undernutrition of children in low socio-economic classes [18–20,26–28] – undernutrition of which deleterious effects are known in the rat [29]. However, genetic [24,26] or psychological [30] factors could interact with socio-economic ones.

On the other hand, the probability for the subject to have a GM < 11 was positively related to the birth order and that as soon as the 2nd child. These results were in harmony with previous studies [18,22]. Nevertheless, according to some authors [31,32], only a

Table 1
Univariate analysis. Comparison of the studied variables according to GM levels.

| | | GM ⩾ 11 | GM < 11 | *p* value |
|---|---|---|---|---|
| **Subject's height (cm)** | | | | |
| m ± sd [%] (frequency) | | 177 ± 6.4 [64.9] (4257) | 174 ± 6.7 [35.1] (2307) | *< .0001* |
| **Number of brother(s) and sister(s)*** | | | | *< .0001* |
| 0 | %(frequency) | 14.2 (605) | 12.5 (287) | |
| 1 | | 41.7 (1771) | 34.5 (792) | |
| 2 | | 26.0 (1104) | 25.7 (591) | |
| 3 | | 10.9 (463) | 12.3 (281) | |
| 4 | | 4.2 (180) | 6.9 (158) | |
| 5+ | | 3.0 (126) | 8.1 (187) | |
| **Birth order*** | | | | *< .0001* |
| 1 | | 49.3 (2048) | 42.6 (965) | |
| 2 | | 31.5 (1307) | 29.6 (671) | |
| 3 | | 12.0 (500) | 14.2 (323) | |
| 4 | | 4.4 (181) | 6.4 (144) | |
| 5+ | | 2.8 (118) | 7.2 (163) | |
| **Subject's and parents' tobacco consumption*** | | | | |
| Subject | yes | 41.0 (1745) | 56.6 (1304) | *< .0001* |
| Father | yes | 35.4 (1493) | 49.6 (1130) | *< .0001* |
| Mother | yes | 15.4 (651) | 21.8 (501) | *< .0001* |
| **Subject's and parents' alcohol consumption*** | | | | |
| Subject | yes | 1.8 (75) | 2.0 (46) | *= .50* |
| Father | yes | 8.1 (341) | 14.6 (332) | *< .0001* |
| Mother | yes | 1.7 (74) | 2.5 (58) | *< .033* |
| **Subject's and parents' academic standard*** | | | | |
| Subject | a | 0.2 (11) | 4.5 (103) | *< .0001* |
| | b | 15.6 (662) | 69.9 (1609) | |
| | c | 18.5 (785) | 15.7 (362) | |
| | d | 65.7 (2791) | 9.9 (227) | |
| Father | a | 18.4 (701) | 35.0 (643) | *< .0001* |
| | b | 31.2 (1189) | 43.4 (797) | |
| | c | 12.0 (457) | 8.8 (162) | |
| | d | 38.4 (1468) | 12.8 (234) | |
| Mother | a | 22.6 (866) | 39.8 (736) | *< .0001* |
| | b | 32.1 (1232) | 39.3 (726) | |
| | c | 12.0 (462) | 9.7 (180) | |
| | d | 33.3 (1280) | 11.2 (206) | |
| **Parents' ages at the subject's birth** | | | | |
| Father | 15–19 | 1.4 (60) | 3.6 (84) | *< .0001* |
| | 20–24 | 25.2 (1072) | 32.0 (739) | |
| | 25–29 | 33.5 (1425) | 29.7 (685) | |
| | 30–34 | 23.1 (981) | 20.0 (462) | |
| | 35–39 | 11.3 (483) | 8.8 (203) | |
| | 40–44 | 4.4 (188) | 4.3 (98) | |
| | 45–70 | 1.1 (48) | 1.6 (36) | |
| Mother | 14–19 | 5.8 (248) | 13.3 (307) | *< .0001* |
| | 20–24 | 36.5 (1554) | 40.8 (942) | |
| | 25–29 | 31.5 (1339) | 24.2 (558) | |
| | 30–34 | 17.7 (753) | 13.3 (306) | |
| | 35–39 | 6.7 (285) | 6.3 (146) | |
| | 40–50 | 1.8 (78) | 2.1 (48) | |

* The sum of frequencies recorded was sometimes below 6564 because some answers lacked in questionnaires. a: non-schooled or primary standard; b: secondary or technical school, 1st cycle; c: secondary or technical school, 2nd cycle; d: A level and more.

Table 2
Multivariate analysis. Risk factors for having GM < 11.

| | Adjusted Odds Ratio | 95% Cl* | *p* value |
|---|---|---|---|
| **Subject's height (cm)** | | | *< .0001* |
| 152–171 | 2.01 | 1.67–2.42 | |
| 172–175 | 1.55 | 1.28–1.87 | |
| 176–179 | 1.25 | 1.04–1.51 | |
| 180–199 | 1 | | |
| **Father's academic standard** | | | *< .0001* |
| a | 2.78 | 2.21–3.50 | |
| b | 2.47 | 2.01–3.04 | |
| c | 1.42 | 1.10–1.85 | |
| d | 1 | | |
| **Mother's academic standard** | | | *< .0001* |
| a | 2.42 | 1.91–3.06 | |
| b | 1.96 | 1.58–2.45 | |
| c | 1.75 | 1.34–2.29 | |
| d | 1 | | |
| **Birth order** | | | *< .0036* |
| 1 | 1 | | |
| 2 | 1.25 | 1.05–1.48 | |
| 3 | 1.50 | 1.16–1.94 | |
| 4 | 1.82 | 1.24–2.67 | |
| 5+ | 1.95 | 1.20–3.17 | |
| **Number of brother(s) and sister(s)** | | | ns† |
| **Subject's tobacco consumption** | | | *< .0001* |
| No | 1 | | |
| Yes | 1.59 | 1.40–1.81 | |
| **Father's tobacco consumption** | | | *< .0001* |
| No | 1 | | |
| Yes | 1.35 | 1.18–1.54 | |
| **Mother's tobacco consumption** | | | *< .0035* |
| No | 1 | | |
| Yes | 1.29 | 1.09–1.53 | |
| **Father's alcohol consumption** | | | *< .1095* |
| No | 1 | | |
| Yes | 1.18 | 0.96–1.46 | |
| **Mother's alcohol consumption** | | | ns† |
| **Father's age at the subject's birth** | | | *< .1212* |
| 15–19 | 1.62 | 1.04–2.52 | |
| 20–24 | 1.20 | 1.00–1.44 | |
| 25–29 | 1 | | |
| 30–34 | 0.92 | 0.75–1.12 | |
| 35–39 | 0.88 | 0.66–1.16 | |
| 40–44 | 0.87 | 0.58–1.31 | |
| 45–70 | 1.10 | 0.56-2.15 | |
| **Mother's age at the subject's birth** | | | *< .0019* |
| 14–19 | 1.82 | 1.38–2.40 | |
| 20–24 | 1.19 | 0.99–1.43 | |
| 25–29 | 1 | | |
| 30–34 | 1.04 | 0.83–1.30 | |
| 35–39 | 0.96 | 0.70–1.34 | |
| 40–50 | 0.88 | 0.49–1.57 | |

* Odds Ratio confidence interval; † only variables with a significance < .20 were detailed; a, b, c, d: subject's and parent's academic standard, see Table 1.

large number of siblings was found to be associated with a decrease of child quality. Our analysis, on the contrary (Table 2), effaced the significant influence of "number of brother(s) and sister(s)" factor (Table 1) and showed that only "birth order" revealed itself as significant. Since GM $< 11$ did not seem related to the father's or mother's aging at conception, family changes arising with time and successive births, such as the parental availability and/or the children's behavior, could be involved.

### 4.2. Toxic factors: tobacco and alcohol consumption

*Subject's tobacco consumption*. The Odds Ratio for having GM $< 11$ was maximum when the subject himself – an adult – smoked (Table 2). This result could correspond to the depressive effects of high doses of nicotine on the central nervous system [33]. However, to comment precisely on tobacco's mental effects in the adult we lacked the important information, whether subjects were born of smoker or non-smoker mothers during pregnancy – the first situation being long known to be harmful for progeny's IQ [34].

*Parents' tobacco consumption*. Apart from prenatal exposure to tobacco is the case of passive consumption. Such a relationship was previously described [14] even at extremely low levels of exposure [15]. In our study, the relationship tobacco / GM $< 11$ was approximately the same in the case of the father's or the mother's tobacco consumption. Aside from a possible harmfulness of nicotine in children, this effect could be related to an oxygen deprivation [35].

Finally, our results showed that a low socio-economic and cultural level and a junior birth order were more harmful for the subject's mental aptitudes than the subject's or the parents' smoking.

*Subject's and parents' alcohol consumption*. The univariate analysis (Table 1) did not show a significant influence of alcohol in the subject himself, probably because the duration of the toxic impregnation was too short. On the other hand, parental alcoholism had a significant effect, more important with regard to the father than to the mother. Given that the subjects themselves were not directly affected by alcohol, it seemed possible that the degradation of family socio-economic and cultural factors due to alcohol was involved and that paternal references were more deciding, for boys, than maternal ones. Several previous results agree with such parental influence [16,17] and with the importance of the paternal one on boys [36,37].

The multivariate analysis effaced the significant influence of parental alcoholism on GM value, though the father's influence was close to significance (Table 2). Consequently, we had to consider that the possible harmful influence, on progeny, of family degradation related to the parents' alcoholism, may not be constant.

### 4.3. Father's and mother's ages at conception and the subject's mental aptitudes

Studies relating to this point are sometimes conflicting. Some show that children born of older parents have lower IQs than those born of younger ones [8]. Relative to the mother's age, a significant correlation between youngest mothers and the poorest scores of male progeny has been found [38]. Our own works have shown, in animals [9,11] and man [10] that both father's youth and aging led to a decrease of success to psychometric tests. According to Drews et al. [18], older mothers are more likely than younger mothers to have a child with both mental retardation and another neurological condition. According to Malaspina et al. [12], young ($<$ 20 years) and old ($>$ 40 y maternal) or ($>$ 50 y paternal) ages were associated with significantly lower intellectual abilities in the offspring, which confirms our previous results [9–11]. The univariate analysis presented here (Table 1) globally found again these results regarding the father's age [10] with a similar association before age 25 (unadjusted Odds Ratio 20–24 = 1.43 [1.26–1.63]) and after 44 (unadj. OR 45–50 = 1.560 [1.003–2.427]). Moreover, it showed an analogous pattern with respect to the mother's age, which led to this association before 25 (unadj. OR 20–24 = 1.45 [1.28–1.65]) and after 39 (unadj. OR 40–50 = 1.48 [1.02–2.14]). However, the multivariate analysis (Table 2) showed that GM $< 11$ was only related to the youngest fathers and mothers (both $< 20$): father adjusted OR 15–19 = 1.62 [1.04–2.52]; mother adj. OR 14–19 = 1.82 [1.38–2.40], which would confirm, for the mother, the Zybert et al. results [38] and, in part, those of Malaspina et al. [12] (concerning the father's age, the lack of effect modification between this factor and the father's academic standard reinforced the result regarding the influence of the father's youth). On the contrary, parents' aging was not related to this GM decrease. On a related topic, there was an apparent discrepancy between (a) the association relating GM to birth order and (b) the absence of such an association between GM and maternal aging. To explain this inconsistency, we could envisage that the majority of the 1863 unworkable questionnaires (see "subjects") corresponded to aging mothers with genetic defects and that their elimination led to a bias in sampling. Questionnaires being unworkable, particularly regarding parental ages, it was impossible to answer this question. Nevertheless, given that, in the population studied, less than 9% (that is to say a minority of the mothers) were 35–50 year old, one could suppose that proportions were the same in the eliminated population. Moreover, it seems difficult to associate systematically consequences of maternal aging with those of birth order: indeed, the latter could play a role independently of the maternal aging through, among other things, modifications of siblings' relationships and/or decrease mother's availability. As for the parental, and particularly the father's youth, given that, from Table 2, its consequences were independent from studied environmental factors, it was possible to hypothesize genetic ones to explain the $GM < 11$ phenomenon. These factors could involve male and/or female gametes: in the post-puberal period, due to the influence of epigenetic factors in the final structural arrangement of DNA in sperm and oocytes, there might be a "run-in" period in some way before maturity is reached [10,11]. Concerning paternal youth, such clinical situations are observed for other complex genetic conditions, including cardiac deficits [39], neural tube defects [40] and type I diabetes mellitus [41]. As for maternal youth, its role in the increase of T 21 is known [42,43]. However, in the case of young mothers, an analogous uterine run-in period might be also considered.

Concerning the parents' aging, the multivariate analysis showed, relatively to the reference age (Table 2, 25–29 years), that it did not increase the risk of mental defect, contrary to what was found by Malaspina et al. [12]. Concerning this discordance it is noticeable: (a) that psychometric tests used were not the same; (b) that Malaspina's results involve male and female adolescents – and differences between male and female successes vary according to nature of tests [44–46] – while ours concern only male adults. However that may be, we have seen above that subtle troubles could be associated to parental and, particularly, father aging. Consequently, how can we explain our own results?

### 4.4. Development of mental aptitudes: independence and complementarity of genetic and environmental factors?

It is known that the synaptic plasticity and learning are conditioned by genetic [47–50] and environmental [51–56] factors. Our own study showed the importance of some of the latter, such as socio-economic and cultural factors, regarding the GM level. Finally, and in spite of the obvious absence of effect – i.e. probably genetic effect – of parental aging at conception on progeny's GM level, we have to wonder whether genetic and environmental factors could not be both independent and complementary.

From all these elements, it is possible to hypothesize a synthesis combining genetic and environmental factors through the notion of "synaptic potential". For example, if an individual is born with the genetic possibility to develop 6 synapses per neuronal surface unity, he will develop them if the environment is favourable but, if it is not, he may only develop 3 or 4. He will in that case perform less well than another individual born with a lower potential of 5 but who will develop them because his environment is favourable. This conception seems be in agreement with Turkheimer and al.'s observations [21]. Thus, if the gametes' genetic changes related to parental aging, those in particular concerning spermatozoa [3,9,10,12], would decrease the progeny's synaptic potential, an important environmental stimulation of the latter could compensate for this decrease. Such a stimulation could be due to an increase of socio-economic and cultural level in older parents (particularly regarding the mother since there was no effect modification between the father's age and his academic status) either through an academic course or, with time, an improvement via self-education. In this way, the absence of risk in progeny that we observed would be explained and that all the more because the homogenization we carried out in our population (see Section 2) perhaps increased the probability to reveal the better socio-cultural situations. Consequently, it would be interesting to verify that such a socio-economic and cultural increase did not concern Malaspina et al.'s aging parental population [12], possibly more heterogeneous than ours. From the general perspective of synaptic potential, let us notice that a greater risk of poor results in children from young couples could – adding itself to the run-in genetic period – result from a lower socio-economic and cultural level in these couples. Finally, genetic factors would operate on the development of synapses not at all in an exact determination of their number, but on the more or less large morphological and physiological capacity to develop them, quantitatively, under the influence of environment. This genetic capacity would vary according to individuals. In this way, it would originate an individual synaptic potential which might change with parental age, sex and cerebral areas.

## 5. Conclusions

On the whole, our results confirmed the relative importance of socio-economic, cultural family and birth order factors, as well as active and passive tobacco consumption, for success in psychometric tests given to young adult males before entering French military service. This confirmation validated the method we used. As for parents' age at conception, youth in the mother and the father (both $< 20$) was related with increased probability of low performances. On the contrary, parents' aging did not seem to have any repercussion on the mental quality of their progeny. But it would remain, here, to study possible effect modifications between the variables concerned and, through these modifications, to investigate again the influence of cultural and socio-économic stimulations. However that may be, it is possible, from a genetic point of view and relatively to previous epidemiological and experimental results, to discuss this lack of effect of parental aging by evoking the complementarity between genetic and environmental factors. Thus, there might exist a compensation for some genetic detrimental effect due to aging through an increase of family socio-economic and cultural levels, coming with age in parents, and favouring the expression in the progeny of a genetically determined individual synaptic potential. This hypothesis, involving the development of cerebral synaptic systems, could account for quantitative aspects of the complementarity between innate and acquired characters and of their inter-individual variations.

## Acknowledgements

The authors' grateful thanks are extended to Médecin-Général Fromentin, Médecin-Colonel Battier and Médecin-Colonel Hédon (Service de Santé des Armées) for their help with the realization of this investigation, Miss Christelle Descot for her help with statistical calculations, Mr Damien Schoevaert for his precious aid with computer transcription and Mr Peter Freeman for his invaluable advice in the multiple re-readings of the manuscript.

## References

[1] M. Auroux, Male age and progeny, The Aging Male 1 (1998) 172–179.

[2] J.J. Tarin, J. Brines, A. Cano, Long-term effects of delayed parenthood, Hum. Reprod. 13 (1998) 2371–2376.

[3] A.J. Wyrobek, B. Eskenazi, S. Young, N. Arnheim, I. Tiemann-Boege, E.W. Jabs, R.L. Glaser, F.S. Pearson, D. Evenson, Advancing age has differential effects on DNA damage, chromatine integrity, gene mutations, and aneuploidies in sperm, Proc. Natl. Acad. Sci. (USA) 103 (2006) 9601–9606.

[4] L.A. Gavrilov, N.S. Gavrilova, V.N. Kroutko, G.N. Evdokushkina, V.G. Semyonova, A.L. Gavrilova, E.V. Lapshin, N.N. Evdokushkina, Y.E. Kushnareva, Mutation load and human longevity, Mutat. Res. 377 (1997) 61–62.

[5] E.H. Hare, P.A. Moran, Raised parental age in psychiatric patients: Evidence for the constitutional hypothesis, Br. J. Psychiatry 134 (1979) 169–177.

[6] D. Malaspina, S. Harlap, S. Fenning, D. Heiman, D. Nahon, D. Feldman, E.S. Susser, Advancing paternal age and the risk of schizophrenia, Arch. Gen. Psychiatry 58 (2001) 361–367.

[7] A. Sipos, F. Rasmussen, G. Harrison, P. Tynelius, G. Lewis, D.A. Leon, D. Gunnel, Paternal age and schizophrenia: a population based cohort study, B.M.J. 329 (2004) 1070–1073.

[8] J. Roberts, A. Engel, Family background, early development and intelligence of children 6–11 years, USA, Vital Health Statistics 11 (142) (1974) 42.

[9] M. Auroux, Decrease of learning capacity in offspring with increasing paternal age in the rat, Teratology 27 (1983) 141–148.

[10] M.R. Auroux, M.J. Mayaux, M.L. Guihard-Moscato, M. Fromantin, J. Barthe, J. Schwartz, Paternal age and mental functions of progeny in man, Hum. Reprod. 4 (1989) 794–797.

[11] M. Auroux, N.N.Y. Nawar, N. Naguib, M. Baud, N. Lapaquellerie, Post-pubescent to mature fathers: increase in progeny quality? Hum. Reprod. 13 (1998) 55–59.

[12] D. Malaspina, A. Reichenberg, M. Weiser, S. Fenning, M. Davidson, S. Harlap, R. Wolitzky, J. Rabinowitz, E. Susser, H.Y. Knobler, Paternal age and intelligence: implications for age-related genomic changes in male germ cells, Psychiatr. Genet. 15 (2005) 117–125.

[13] R. Plomin, J.C. DeFries, G.E. McClearn, M. Rutter, Behavioral Genetics, W.H. Freeman and Co., New York, 1997.

[14] D.L. Johnson, P.R. Swank, C.D. Baldwin, D. McCormick, Adult smoking in the home environment and children's IQ, Psychol. Rep. 84 (1999) 149–154.

[15] K. Yolton, K. Dietrich, P. Auinger, B.P. Lanphear, R. Hornung, Exposure to environmental tobacco smoke and cognitive abilities among US children and adolescents, Environ. Health Perspect. 113 (2005) 98–103.

[16] L. Nordberg, P.A. Rydelius, R. Zetterstrom, Children of alcoholic parents: health, growth, mental development and psychopathology until school age. Results from a prospective longitudinal study of children from the general population, Acta Paediatr. 387 (Suppl.) (1993) 1–24.

[17] M. Mena, M.L. Alcazar, H. Iturrialde, R. Frits, E. Ripoll, P. Bedregal, Alcohol consumption and family: a descriptive study in adolescents, Rev. Med. Chil. 124 (1996) 749–755.

[18] C.D. Drews, M. Yeargin-Allsopp, P. Decoufle, C.C. Murphy, Variation in the influence of selected sociodemographic risk factors for mental retardation, Am. J. Public Health 85 (1995) 329–334.

[19] D.A. Lawlor, G.D. Batty, S.M. Morton, I.J. Deary, S. Macintyre, G. Ronalds, D.A. Leon, Early life predictors of childhood intelligence: evidence from the Aberdeen children of the 1950s study, J. Epidemiol. Community Health 59 (2005) 656–663.

[20] G. Guo, K.M. Harris, The mechanisms mediating the effects of poverty on children's intellectual development, Demography 37 (2000) 431–447.

[21] E. Turkheimer, A. Haley, M. Waldron, B. D'Onofrio, I.I. Gottesman, Socioeconomic status modifies heritability of IQ in young children, Psychol. Sci. 14 (2003) 623–628.

[22] L. Belmont, J. Wittes, Z. Stein, Relations of birth order, family size and social class to psychological functions, Percept. Mot. Skills 45 (1977) 1107–1116.

[23] Bulletin Officiel Chronologique des Armées (France) 50 (1981) 5001–5031.

[24] R. Sichieri, J.A. Taddei, J.E. Everhart, Influence of parental height and sociodemographic factors on adolescent height in Brazil, J. Adolesc. Health 26 (2000) 414–419.

[25] C. Padez, Stature and stature distribution in Portuguese male adults 1904–1998: the role of environmental factors, Am. J. Hum. Biol. 14 (2002) 39–49.

[26] M.S. Pearce, I.J. Deary, A.H. Young, L. Parker, Growth in early life and childhood IQ at age 11 years: the Newcastle Thousand Families Study, Int. J. Epidemiol. 34 (2005) 673–677.

[27] T. Tuvemo, B. Jonsson, I. Persson, Intellectual and physical performance and morbidity in relation to height in a cohort of 18-year-old Swedish conscripts, Horm. Res. 52 (1999) 186–191.

[28] M. Colombo, A. de la Parra, I. Lopez, Intellectual and physical outcome of children undernourished in early life is influenced by later environmental conditions, Dev. Med. Child Neurol. 34 (1992) 611–622.

[29] M. Winick, A. Noble, Cellular response in rats during malnutrition at various ages, J. Nutri. 89 (1966) 300–306.

[30] L. Dowdney, D. Skuse, K. Morris, A. Pickles, Short normal children and environmental disadvantage: a longitudinal study of growth and cognitive development from 4 to 11 years, J. Child Psychol. Psychiatry 39 (1998) 1017–1029.

[31] W. Velandia, G.M. Grandon, E.B. Page, Family size, birth order, and intelligence in a large South American sample, Am. Educ. Res. J. 15 (1978) 399–416.

[32] J. Blake, Family size and the quality of children, Demography 18 (1981) 421–442.

[33] D.V. Poltavski, T. Petros, Effects of transdermal nicotine on prose memory and attention in smokers and nonsmokers, Physiol. Behav. 83 (2005) 833–843.

[34] K. Fogelman, Smoking in pregnancy and subsequent development of the child, Child Care Health Dev. 6 (1980) 233–249.

[35] K.E. Bauman, R.L. Flewelling, J. LaPrelle, Parental cigarette smoking and cognitive performance of children, Health Psychol. 10 (1991) 282–288.

[36] P.W. Harden, R.O. Pihl, Cognitive function, cardiovascular reactivity, and behavior in boys at high risk for alcoholism, J. Abnorm. Psychol. 104 (1995) 94–103.

[37] T. Ozkaragoz, P. Satz, E.P. Noble, Neuropsychological functioning in sons of active alcoholic, recovering alcoholic, and social drinking fathers, Alcohol 14 (1997) 31–37.

[38] P. Zybert, Z. Stein, L. Belmont, Maternal age and children's ability, Percept. Mot. Skills 47 (1978) 815–818.

[39] A.F. Olshan, P.G. Schnitzer, P.A. Baird, Paternal age and the risk of congenital heart defects, Teratology 50 (1994) 80–84.

[40] G.C. McIntosh, A.F. Olshan, P.A. Baird, Paternal age and the risk of birth defects in offspring, Epidemiology 6 (1995) 282–288.

[41] T.Y. Tai, C.Y. Wang, L.L. Lin, L.T. Lee, S.T. Tsai, C.J. Chen, A case-control study on risk factors for Type I diabetes in Taipei City, Diabetes Res. Clin. Pract. 42 (1998) 197–203.

[42] J.D. Erickson, Down syndrome, paternal age, maternal age and birth order, Ann. Hum. Genet. Lond. 41 (1978) 289–298.

[43] L. Iselius, J. Lindsten, Changes in the incidence of Down syndrome in Sweden during 1968–1982, Hum. Genet. 72 (1986) 133–139.

[44] J. McGlone, Sex differences in human brain asymmetry: a critical survey, Behav. Brain Sci. 3 (1980) 215–263.

[45] H. Nyborg, Performance and intelligence in hormonally different groups, in: G.J. De Vries, J.P.C. De Bruin, H.B.M. Uylings, M.A. Corner (Eds.), Sex Differences in the Brain, in: Progress in Brain Research, vol. 61, Elsevier, Amsterdam, 1984, pp. 491–508.

[46] C. Persson Bendow, R.M. Bendow, Biological correlates of high mathematical reasoning ability, in: G.J. De Vries, J.P.C. De Bruin, H.B.M. Uylings, M.A. Corner (Eds.), Sex Differences in the Brain, in: Progress in Brain Research, vol. 61, Elsevier, Amsterdam, 1984, pp. 469–490.

[47] D. Bovet, F. Bovet-Nitti, A. Oliverio, Genetic aspects of learning and memory in mice, Science 163 (1969) 139–149.

[48] S. Davis, B. Bozon, S. Laroche, How necessary is the activation of the early gene zif268 in synaptic plasticity and learning? Behav. Brain Res. 142 (2003) 17–30.

[49] M. Brackmann, C. Zhao, D. Kuhl, D. Manahan-Vaughan, K.H. Braunewell, MgluRs regulate the expression of neuronal calcium sensor proteins NCS-1 and VILIP-1 and the immediate early gene arg3.1/arc in the hippocampus in vivo, Biochem. Biophys. Res. Commun. 322 (2004) 1073–1079.

[50] A.L. Oliveira, S. Thams, O. Lidman, F. Piehl, T. Hokfelt, K. Karre, H. Linda, S. Cullheim, A role for MHC class I molecules in synaptic plasticity and regeneration of neurons after Axotomy, Proc. Natl. Acad. Sci. USA 101 (2004) 17843–17848.

[51] F. Valverde, Apical dendritic spines of the visual cortex and light deprivation in the mouse, Exp. Brain Res. 3 (1967) 337–352.

[52] M.R. Rosenzweig, E.L. Bennet, M.C. Diamond, Brain changes in response to experience, Scientific American 226 (1972) 22–29.

[53] T.N. Wiesel, Postnatal development of the visual cortex and the influence of environment, Nature 299 (1982) 583–591.

[54] D. Purves, G.J. Augustine, D. Fitzpatrick, L.C. Katz, A.S. LaMantia, J.O. McNamara, Neuroscience, Sinauer Associates Inc., New York, 1997.

[55] F. Engert, T. Bonhoeffer, Dendritic spine changes associated with hippocampal long-term synaptic plasticity, Nature 399 (1999) 66–70.

[56] N. Toni, P.A. Buchs, I. Nikonenko, C.R. Bron, D. Muller, LTP promotes formation of multiple spine synapses between a single axon terminal and a dendrite, Nature 402 (1999) 421–425.