

# Changes of Cognitive Ability and Circulatory Physiological Parameters Among Adolescents Moving From Altitudes of 3600 m to 500 m in China: A 50-Day Follow up Study

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## Abstract

**Background:** Travelling across altitude is increasing these days. The effects of travelling from high to low altitude on cognitive and physiological parameters of native highlander adolescents is not clear. The present study aimed to measure the changes of cognitive ability and circulatory physiological parameters when Tibetan adolescents move from high to low altitude, and to test the association between cognitive function change and changes in circulatory parameters.

**Method:** General fluid intelligence, oxygen saturation, hemoglobin concentration, heart rate and blood pressure of 71 Tibetan adolescents were measured twice, initially at Lhasa city (altitude 3600 m) and again 50 days after arriving at Chengdu (altitude 500 m).

**Results:** The mean intelligence scores remained unchanged when students moved from high to low altitude. However, the mean hemoglobin concentration, diastolic blood pressure and heart rate decreased while mean oxygen saturation and systolic blood pressure increased. No associations between change of intelligence and changes of circulatory physiological parameters were detected.

**Conclusions:** Travelling from high to low altitude altered the mean value of circulatory physiological parameters but not cognition of Tibetan adolescents. Change of cognitive function was not associated with changes in physiological parameters.

**Keywords:** Tibetan, adolescent, altitude, cognitive function, general fluid intelligence, physiological parameter

## 1. Background

The mobility of young populations worldwide occurs for various reasons such as seeking education and work. Populations in high altitudes are younger and potentially more mobile than previous generations due to globalization (West, J. B., Schoene, R. B., Luks, A. M., & Milledge, J. S., 2012). It is important to understand changes to their physiology and cognitive function when they travel to lower altitudes. Cognition is the mental processes involved in gaining knowledge and comprehension. Intelligence as a synonym of cognition affects various parts of life such as school achievement (Colom, R., Escorial, S., Shih, P. C., & Privado, J., 2007), economic success (Strenze, T., 2007) and health (Gottfredson, L. S., & Deary, I. J., 2004).

Several studies exploring the effects of altitude on cognition of children and adolescents of native highlanders have been conducted in South America. Reduction in speed of cognitive ability (Hogan, A. M., Virues-Ortega, J., Botti, A. B., Bucks, R., Holloway, J. W., Rose-Zerilli, M. J., & et al., 2010; Hill, C. M., Dimitriou, D., Baya, A., Webster, R., Gavlak-Dingle, J., Lesperance, V., & et al., 2014), executive function (Virués-Ortega, J., Bucks, R., Kirkham, F. J., Baldeweg, T., Baya-Botti, A., & Hogan, A. M., 2011), and impairment of the neurodevelopment

of infants (Wehby, G. L., 2013) were found in high altitudes. Most of these studies were cross-sectional in nature, limiting the establishment of causal relationships. In follow up studies, visuo-spatial executive function, attention and memory were found to be impaired after acute exposure or prolonged stay in high altitude (Aquino, L.V., Antunes, H. K. M., Santos, R. V. T., Lira, F. S., Tufik, S., & Mello, M. T., 2012; Sharma, V. K., Das, S. K., Dhar, P., Hota, K. B., Mahapatra, B. B., Vashishtha, V., & et al., 2014; Pelamatti, G., Pascotto, M., & Semenza, C., 2003; Hu, S. L., Xiong, W., Dai, Z. Q., Zhao, H. L., & Feng, H., 2016). However, follow up studies on the cognitive function changes of native highlanders, especially children and adolescents, are rare.

To enhance education achievement, free education for Tibetan middle and high school students in mainland China has been implemented since 1985. However, less than 20% of middle and high school students from Tibet Autonomous Region (TAR) of China utilize this. These students travel from Tibet to other areas of China around the end of August and January to start the semester. The cross-altitude traveling of these students has provided an opportunity to investigate their cognitive and physiological changes.

In the present study our primary aim was to measure the changes of cognitive ability and circulatory physiological parameters when Tibetan adolescents move from high to low altitudes. Our secondary aim was to test the association between cognitive function change and the changes of the circulatory parameters.

## **2. Methods**

### *2.1 Study Design*

A cohort of students from seven prefectures of TAR was enrolled and followed up (measured twice) at Lhasa city and 50 days after they arrived at Chengdu Tibetan high school, Chengdu city, capital of Sichuan province, China.

#### *Study setting*

Lhasa, with an altitude of 3600 m, is the capital city of TAR of China. There are 12 high schools in mainland China designed by the Chinese government to recruit students from TAR. In Chengdu high school, 2014 approximately 100 TAR students joined. There are approximately 500 students in Chengdu has an altitude of 500 m above sea level, and is the closest city to Lhasa. Forty six students first year students and 33 second year students who had returned home to Tibet for summer vacation travelled from Lhasa to Chengdu by train to attend this high school. The cost of travelling by train was fully supported by the government. The remaining students travelled by plane, the cost of which was partially supported by the Chinese government.

### *2.2 Sampling*

Because students who studied in Chengdu Tibetan High school came from 7 prefectures of Tibet, the train was the only feasible place where we could interview them. Thus, only these 79 students travelling by train were invited to be a part of the study.

### *2.3 Outcome Variables and Measurement*

#### *2.3.1 Cognitive Function*

General fluid intelligence (Gf), as a domain of intelligence, is the ability to solve new problems, apply logic in new situations, and identify patterns. It is independent of previous knowledge and has profound effects on academic achievement ((Colom, R., Escorial, S., Shih, P. C., & Privado, J., 2007; Di Fabio, A., & Palazzeschi, L., 2009; Di Fabio, A., & Busoni, L., 2007; Chamorro-Premuzic, T., & Furnham, A., 2008).

Standard Progressive Matrices (SPM) and the Parallel test are standard tools used to measure general fluid intelligence. These two tests are language free and practical to administer. Both tests use different sets of questions with a similar structure, and a similar number of questions and their results are comparable scores of general fluid intelligence. The Parallel test is used for "re-testing" to avoid using the same questions in the SPM test.

The use of both tests is limited to individuals aged six years and above. Both tests consist of a series of diagrams with one missing part. The correct part to complete the designs must be selected from a set of alternatives. Each test has five parts (A to E), containing 12 questions each, with a maximum score of 60 overall. The items in each part of the test become increasingly difficult and require more cognitive ability to analyze the information.

The SPM was administrated by the participants in a special car on the train and the Parallel test was given 50 days after they arrived at Chengdu Tibetan high school under the guidance of well-trained researchers in a peaceful environment.

At each time, the nature of test and instructions for its completion were explained with solving of the first two items demonstrated. The test was then given to the students in each class consisting of around 40 students, under

the guidance of well-trained teachers. A maximum time period of 60 minutes was allowed. The completed answer sheets were delivered to the study center. The student's scores were subsequently and confidentially divulged to each student.

### 2.3.2 Circulatory Physiological Measurements

The circulatory physiological parameters including hemoglobin concentration (Hb), oxygen saturation (% SpO<sub>2</sub>), blood pressure (BP) and heart rate (HR) were also measured twice, on the train from Lhasa to Chengdu, and 50 days after arriving at Chengdu.

### 2.3.3 Hemoglobin Concentration

The fingertip blood was collected and analyzed with a portable hematology analyzer (brand: HemoCue® (HemoCue® Hb 201+ System).

### 2.3.4 Heart Rate and Oxygen Saturation

A pulse oximeter (brand: NELLCOR® (True Intelligence for Both Monitor & Sensor) was used to assess heart rate and oxygen saturation with the index finger of the left hand for 30 seconds. The highest and lowest readings were recorded and averaged.

### 2.3.5 Blood pressure

Blood pressure was measured twice, three minutes apart, through a digital monitor (brand: Omron® (Omron) with the right upper arm of participants while sitting and at rest for 30 minutes and averaged. The blood pressure was measured between 10:30 a.m. and 1:20 p.m. both on the train and in Chengdu.

## 2.4 Sample Size

The sample size calculation formula for a one sample mean (Kotrlík, J., & Higgins, C., 2001) of the individual changes was used. Both the SPM and Parallel test have a maximum score of 60. With a significance level 0.05, a variance of intelligence score changes of 16, and an estimation of the true difference in mean change of 1, the required sample size was 62. Assuming a loss to follow up rate of 10%, the sample size was increased to 69.

## 2.5 Data Collection

Ethical approval for the present study was granted by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla Province, Thailand (Reference number: 57-187-18-5) before the research was conducted. Prior to the study, written consents from all participants and oral consent from their parents and school authorities were obtained.

### 2.5.1 Data Collection on the Train

Ten trained research assistants were used to collect both cognitive and physiological measurements. The students all boarded the train approximately one hour before the train left Lhasa. The data were collected between half an hour before the train left to four hours after the train left Lhasa as the students had become relaxed and the altitude was still high (4500 m). SPM was administered under the guidance of the research assistants to avoid discussion between students. After completing the SPM, circulatory parameters were measured. For measurement of hemoglobin concentration, blood pressure, heart rate and oxygen saturation, two research assistants took responsibility for each parameter (heart rate and oxygen saturation were measured together); one took the measurement the other recorded the results. At the same time the questionnaire containing the background information was self-administered by the participants.

### 2.5.2 Data Collection at Chengdu

The Parallel test was administered on the weekend in the classroom at Chengdu Tibetan high school under the guidance of four research assistants. The circulatory parameters were measured on another day of the same weekend.

## 2.6 Analysis

The data were double entered in Epidata software 3.1 and analyzed in R software 3.2.2. After assessing normality, paired t tests were used to compare the changes in cognitive and physiological parameters of the same students across different altitudes. Pearson's correlation was used to test the correlations between changes of intelligence score and changes of physiological parameters.

### 3. Results

#### 3.1 Background Characteristics

Out of 79 students who were invited to be a part of the study, 73 agreed to join. In Chengdu, two students refused to be followed up and two students refused to have their blood taken.

Most students were aged 14 or 15 years and grew up in altitudes ranging from 2800 to 4000 m. Females comprised around two thirds of the sample. Most of the students' parents were married and had achieved a primary school level of education only. More than one third of students' households had a monthly income of 3000 CNY (1 CNY = 0.15 USD) and above. However, around one third of the students did not know their family income.

Table 1. Background characteristics of the participants and their family

Variables	Frequency	Percentage
Age (years)		
14-15	30	42.3
16	23	32.4
17-18	18	25.4
Gender		
Male	24	33.8
Female	47	66.2
Birth order		
1	39	54.9
2	20	28.2
3 or higher	12	16.9
Marital status of parents		
Divorced	5	7.0
Married	66	93.0
Education level of mother		
Never been to school	22	31.0
Primary school	24	33.8
Middle school	12	16.9
High school and above	13	18.3
Education level of father		
Never been to school	10	14.1
Primary school	32	45.1
Middle school	14	19.7
High school and above	15	21.1
Monthly household income (CNY)		
<1000	12	16.9
1000-	10	14.1
3000-	23	32.4
Not known	26	36.6
Number of children in household		
1	18	25.4

2	27	38.0
3	18	25.4
4 or above	8	11.3
Altitude where students grew up		
2800m -	4	5.6
3000m -	51	71.8
4000m -4500m	16	22.5

### 3.2 The Changes of Cognitive Score

The mean (standard deviation) SPM score before arriving at Chengdu was 46.3 (7.2). Figure 1 shows the changes of total SPM score by individual before and after participants moved from high to low altitude. In general, total SPM scores increased among those whose scores were lower than the overall mean, while SPM scores decreased among those whose scores were higher than the overall mean. There was no difference in mean SPM scores before and after moving from Lhasa to Chengdu ( $p=0.68$ ).

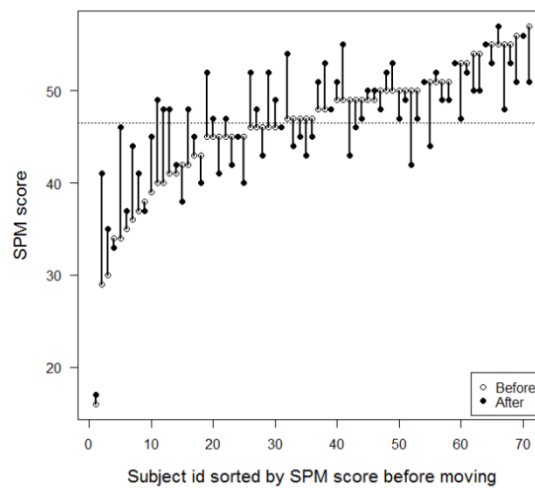


Figure 1. Distribution of total SPM scores by individual before and after moving from high to low altitude. The dotted horizontal line represents the overall mean SPM score.

### 3.3 Changes of Physiological Parameters

Figure 2 describes the changes of physiological parameters by subjects before and after participants moved from high to low altitude. Oxygen saturation and systolic blood pressure increased in most students after arriving at Chengdu, while hemoglobin concentration and heart rate decreased in most students.

The physiological parameters of students before and after moving to Chengdu are presented in Table 2. The means of oxygen saturation, systolic blood pressure significantly increased, while the means of diastolic blood pressure, heart rate and oxygen saturation significantly decreased.

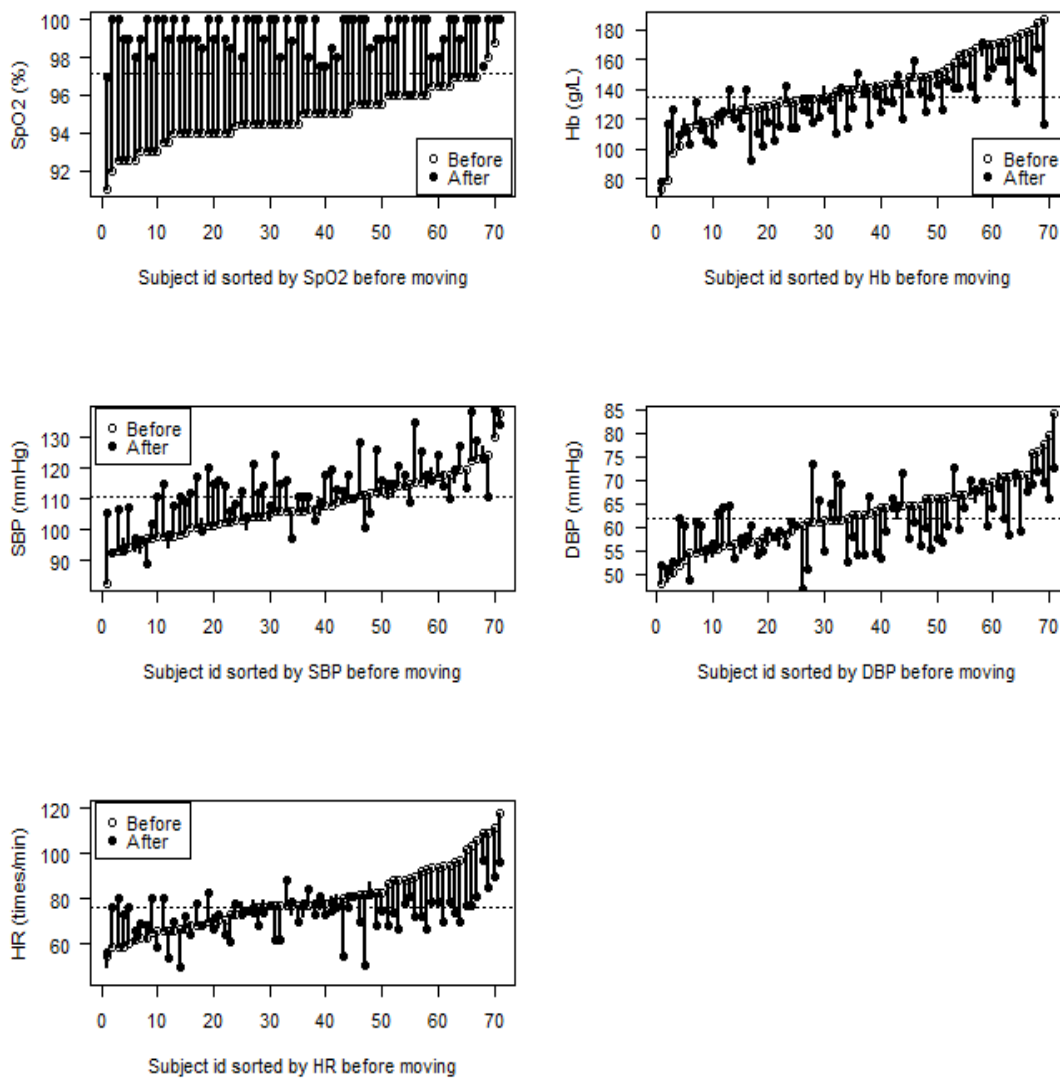


Figure 2. Distribution of physiological parameters before and after moving from high to low altitude

Table 2. Comparison of mean cognitive and physiological parameters before and after moving from high to low altitude

Variables	High altitude	Low altitude	Changes	P value
	Mean (S.D)	Mean (S.D.)		
General fluid intelligence	46.3 (7.2)	46.8 (6.2)	0.5 (0.6)	0.68
Hemoglobin oxygen saturation	95.0 (1.6)	99.3(0.9)	4.3 (0.2)	<0.01
Hemoglobin concentration	141.2 (23.3)	130.1 (18.7)	-11.1 (2.0)	<0.01
Systolic blood pressure	107.7 (9.7)	113.2(10.3)	5.5 (1.0)	<0.01
Diastolic blood pressure	62.8(7.0)	60.9(6.5)	-1.9 (0.8)	0.02
Heart rate	79.7(14.0)	73.2(9.2)	6.5 (1.9)	<0.01

#### Association between change in intelligence and change in physiological parameters

The association between change in intelligence and changes in physiological parameters are described in Table 3. Change in intelligence was not associated with changes in any physiological parameter.

Table 3. Correlations between change in intelligence and changes in physiological parameters

	Change of general fluid intelligence	P value
Change of oxygen saturation	0.04	0.73
Change of hemoglobin concentration	0.11	0.38
Change of systolic blood pressure	0.07	0.58
Change of diastolic blood pressure	-0.06	0.64
Change of heart rate	-0.23	0.06

#### 4. Discussion

Most of the participants in the present study were female, had parents with a low education level and a moderate or high household income. Mean SPM scores were unchanged after students moved from high to low altitude. The mean hemoglobin concentration, diastolic blood pressure and heart rate decreased after moving to a lower altitude, while the mean oxygen saturation and systolic blood pressure increased. Change in intelligence was not associated with and changes of any physiological parameters.

A previous study conducted in Andean residents found no significant difference in general fluid intelligence among those from altitudes of 500m and 3700 m (Hill, C. M., Dimitriou, D., Baya, A., Webster, R., Gavlak-Dingle, J., Lesperance, V., & et al., 2014). Similarly, in the current study, the mean change in fluid intelligence score was not significant after students moved from the altitude of 3600 m to 500 m. Virués - Ortega, et al. (2010) proposed cognitive ability impairment threshold of highland natives at an altitude of about 4000 m (Virués-Ortega, J., Bucks, R., Kirkham, F. J., Baldeweg, T., Baya-Botti, A., & Hogan, A. M., 2011). Since most of the participants in the present study resided at an altitude lower than 4000 m, this altitude may not be high enough to observe any change in fluid intelligence after travelling to a lower altitude.

Consistent with previous studies, the mean hemoglobin concentration decreased with the descending altitude (Wu, T., Wang, X., Wei, C., Cheng, H., Wang, X., Li, Y., & et al., 2005; McKenzie, D., Goodman, L., Nath, C., Davidson, B., Matheson, G., Parkhouse, W, & et al., 1991), whereas the mean oxygen saturation increased (Beall, C. M., Strohl, K. P., Blangero, J., Williams-Blangero, S., Decker, M. J., Brittenham, G. M., & et al., 1997). As in high altitude de-adaptation, which occurs in lowlanders who stay at high altitude for a period and return to low altitude, the mean heart rate decreased in Tibetan adolescents after they arrived at low altitude (McKenzie, D., Goodman, L., Nath, C., Davidson, B., Matheson, G., Parkhouse, W, & et al., 1991; Banchero, N., Sime, F., Peñaloza, D., Cruz, J., Gamboa, R., & Marticorena, E., 1966).

We found that the mean systolic blood pressure increased after moving to a low altitude while the mean diastolic blood pressure decreased. This phenomena was observed in lowlanders presenting with high altitude de-adaptation; both the prevalence of hypertension and low blood pressure were higher than those who had never been to a high altitude (Zhou, Q., Yuan, Z., Zhang, X., Zhang, Y., Peng, Q., Luo, H., & et al., 2014). The blood pressure trends to be unstable in these people (Zhou, Q., Yang, S., Yuan, Z., Wang, Y., Zhang, X., Gao, W., & et al., 2014), especially in our study since the first measurement was done during traveling. This might explain the result of our study.

Heart rate (Petrie Thomas, J. H., Whitfield, M. F., Oberlander, T. F., Synnes, A. R., & Grunau, R. E., 2012), hemoglobin concentration (Ai, Y., Zhao, S. R., Zhou, G., Ma, X., & Liu, J., 2012) and blood pressure (Lande, M. B., Kaczorowski, J. M., Auinger, P., Schwartz, G. J., & Weitzman, M., 2003) were found to be predictors of cognitive function in previous cross-sectional studies at low altitudes. However, change of general fluid intelligence in Tibetan adolescents who move from high to low altitude was not associated with the changes of any physiological parameters. This result seems reasonable because the mean of SPM score was unaltered by cross altitude travelling while mean of all physiological parameter were alter significantly.

The fluid intelligence score and diastolic blood pressure of those with extreme values of high altitude tended to

be closer to the average values at low altitude. This is the so-called “regression to the mean” effect (Bland, J. M., & Altman, D. G., 1994). It occurs in two measurements on the same group of subjects with imperfect correlation. The second group mean will be closer to the mean for all subjects than is the first, and the weaker the correlation between the two variables the bigger the effect.

This study observed the cognitive and physiological parameters of participants before and after they arrived at low altitude. In another study, the hemoglobin concentration of plateau migrants who returned to low altitude took more than one year to recover (Zhou, Q., Yang, S., Yuan, Z., Wang, Y., Zhang, X., Gao, W., & et al., 2014). The reduction in gray matter density at bilateral prefrontal cortex, where fluid intelligence, as measured by Raven’s Progressive Matrices (RPM), has been partially mapped to, among lowland migrants persisted for more than one year after they returned to sea level (Yan, X., Zhang, J., Shi, J., Gong, Q., & Weng, X., 2010). Brain structural modulation was observed in Tibetan adolescents who moved to sea level for at least four years (Zhang, J., Zhang, H., Chen, J., Fan, M., & Gong, Q., 2013). Therefore, cognitive and physiological parameters may continue to change long after 50 days as measured in our study. A longer duration for investigation is needed.

### 5. Limitation

Students who travelled to Chengdu from Lhasa via air were excluded from this study. These students were probably from a higher SES than the study students, thus creating selection bias. However, since cognitive and physiological parameters were compared in the same individual, this selection bias would not have distorted any causal relationship.

### 6. Conclusion

Travelling from a high to low altitude altered the mean values of circulatory physiological parameters but not cognition of Tibetan adolescents. Change in cognitive function was not associated with changes in any physiological parameters.

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