**MASTER**
DATA ANALYTICS FOR BUSINESS

**MASTER´S FINAL WORK**
INTERNSHIP REPORT

# INVESTIGATING THE ASSOCIATION BETWEEN SOCIOECONOMIC STATUS AND HIPPOCAMPAL AND AMYGDALA GREY MATTER VOLUMES IN YOUNG ADULTS FROM THE I-SHARE COHORT

ALEX JOHN CHARLES SOFRONIOU

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**SUPERVISED BY:**
JOÃO AFONSO BASTOS
MÉLISSA MACALLI

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# Glossary

BPH- Bordeaux Population Health
HEALTHY- Health and Success to Young People
INSERM- National Institute of Health and Medical Research
I-SHARE- Internet-based Students Health Research Enterprise
MRI- Magnetic Resonance Imaging
OLS - Ordinary Least Squares
SES - Socioeconomic Status

# Abstract

This report will outline some of the research that I undertook during my internship at INSERM Bordeaux Population Health U1219. The internship lasted six months between September 2022 and March 2023 as part of my final 30 credits of my Master's in Data Analytics for Business at ISEG – Lisbon School of Economics and Management.

In this internship I was responsible for statistical analysis and reviewing of the relevant literature working amongst a team of epidemiologists whose focus was the mental health of young people. I was given access to a large dataset of French university students to perform my analyses and carried these out primarily using R Studio.

In the field of epidemiology, the goal of research is to provide suggestions for disease prevention methods. Preliminary research by my team found associations childhood SES and mental health, and to build on this, we decided to investigate associations of childhood SES and brain structure. Our research complements the growing literature surrounding importance of childhood SES on the brain in later life.

This report investigates the association between the socioeconomic status in childhood and adolescence of these students and grey matter volumes in the amygdala and hippocampus. This data was collected by means of MRI scans and questionnaires. It is split into the introduction, methods, results, discussion, and conclusion.

The introduction includes information about the company and my role, along with a brief overview of the limbic system, the hippocampus, and the amygdala, as well as the processes behind MRI and the acquisition of images. It also summaries the current literature in the domain.

The methods section describes the cohort in more detail and the gives background information about key variables. It also goes into details about the statistical analysis including population description and model selection. There is also a note about ethical considerations.

The results section presents the results of the analysis explained in the methods section, with demographic tables and summaries of the estimated models and key results stated. The discussion synthesises these results and compares them to the existing literature, with a perspectives section for ideas about further research and reflection on the findings. The conclusion gives a concise summary of the discussion.

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# Acknowledgements

I would like to thank my family, my flatmates, and my friends for their unwavering support. I would also like to thank my supervisors Mélissa and João for their parts in guiding me through my research and development of this report.

# 1. Introduction

## 1.1 The Internship

### 1.1.1 The Centre

The internship, carried out as part of the Masters' final work module in the second year of my Master's in Data Analytics for Business, took place within the "HEALTHY-Health and success of young people" team at the U1219 research centre of the *Institut National de la Santé et de la Recherche Medical* - The national institute of health and medical research, or INSERM, in Bordeaux, France. INSERM was founded in 1964 and is the world's second largest research institute in the health sector and the twenty-second largest worldwide in all sectors combined. It is a public scientific and technological establishment under the supervision of the Ministry of Health and the Ministry of Research (*Inserm at a Glance · Inserm*, n.d.). It is dedicated to biological, medical and human health research, bringing together 15,000 researchers, engineers, technicians and administrative staff, with a common objective: to improve the health of all through development of knowledge about living organisms and diseases, and innovation in treatment and public health research (*L'Inserm en un coup d'œil · Inserm, La science pour la santé*, n.d.). The Inserm-University of Bordeaux research centre U1219 "Bordeaux population health (BPH), directed by Stéphanie Debette, is composed of ten labelled teams and a scientific coordination across teams. The centre brings together more than 400 people including approximately 90 researchers and teacher-researchers. The researchers cover a wide range of pathologies, exposures, methods, and populations through various works and publish between 250 and 300 articles each year in international journals.

### 1.1.2 The team

Led by Cédric Galera and co-directed by Christophe Tzourio, the HEALTHY team is one of the ten BPH teams. The objectives of this multidisciplinary team are:

1. Research epidemiology of mental health problems and their global consequences over the course of life.
2. Test health promotion interventions aimed at preventing mental health problems and their personal, social, and economic consequences.

### 1.1.3 My role

My role in the internship was to be responsible for statistical analysis and the review of the corresponding literature. I was given access to the MRI-share dataset, the details of which are explained in section 2.1.1, with the objective of researching associations between brain structure and both childhood and mental health modalities. A goal that was agreed at the start of the internship, in September 2022, was to commence the writing of an article to be submitted to an international medical journal with the goal of publication of the results with myself as the primary author. In addition, I had the privilege to build on my skills in R Studio while also familiarising myself with SAS (Statistical Analysis System), a popular analysis tool among my colleagues.

With regards to formal structure, I had a weekly meeting with my supervisor Mélissa Macalli to monitor my progress and iron out any doubts I had with regards to my research. I explored linear regression, logistic regression, and mediation, both in R Studio and SAS. Seeing how these tools were used in the health industry gave me a great learning experience in my first ever full-time position.

## 1.2 **Review of brain structures**

### 1.2.1 **Limbic System**

The term 'limbic' was first introduced by Willis in 1664 to assign a cortical border around the brainstem, where limbic comes from the Latin word 'limbus', meaning 'border'(Catani and Schotten, 2012). Its definition, as per the US national cancer institute, is "a network of structures in the brain involved in memory and emotions" (*Definition of limbic system - NCI Dictionary of Cancer Terms - NCI*, 2011). Located underneath the cerebral cortex and above the brainstem, the limbic system is associated with "memory processing, fight-or-flight responses, aggression, sexual responses and emotional responses", acts all attributed to the protection of the individual and the ensuring of the survival of the species (*The limbic system*, 2017) (*Limbic System - an overview | ScienceDirect Topics*, n.d.). In this report, we will focus on two of the main structures of the limbic system; the hippocampus and the amygdala (*The limbic system*, 2017).

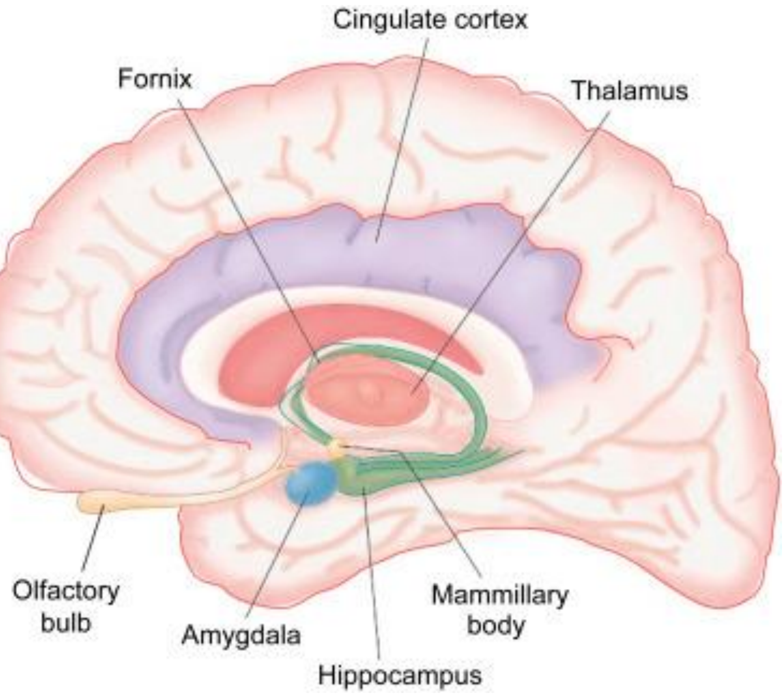


*Figure 1 – The limbic system and surrounding structures, (*Limbic System - an overview | ScienceDirect Topics*, n.d.)*

### 1.2.2 **Hippocampus**

The hippocampus is a plastic structure associated with memory and learning, and it is highly delicate; that is to say, it is susceptible to damage from a variety of stimuli (Anand and Dhikav, 2012). For example, it is the most severely affected region in many neuropsychiatric disorders including epilepsy and Alzheimer's disease. The hippocampus proper and the dentate gyrus make up the two principal sections of the hippocampus, of which the hippocampus proper is further subdivided into CA1, CA2, CA3 and CA4.

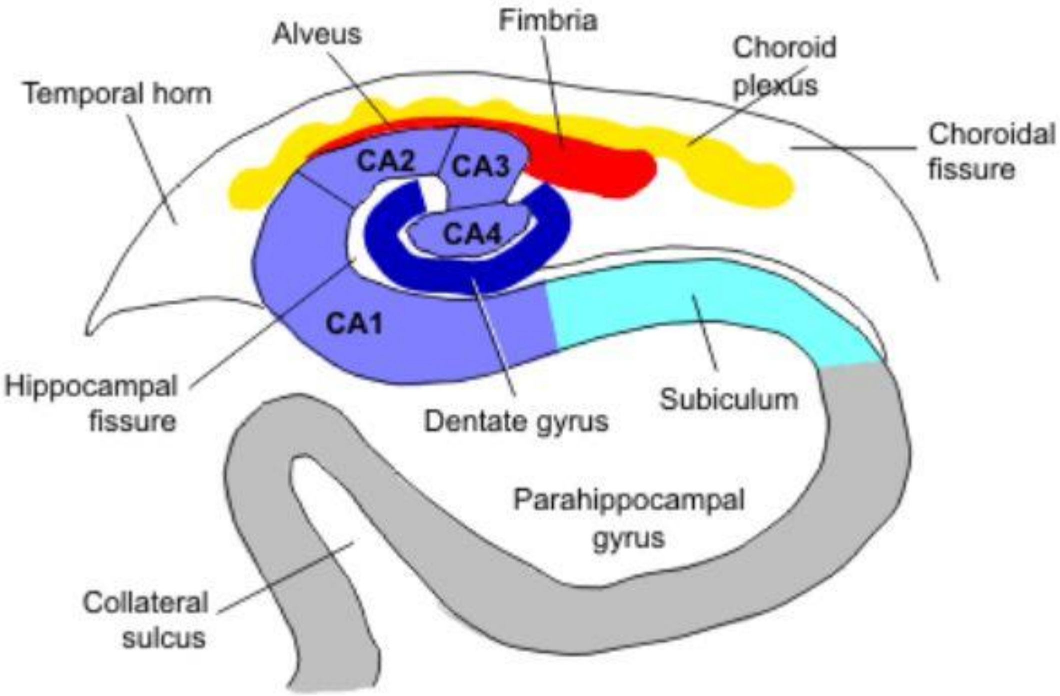


*Figure 2 – Diagram of the hippocampus and the parahippocampal gyrus (*The Temporal lobe and limic system*, n.d.)*

An interesting feature of the hippocampus is that it is one of the only areas of the brain where neurogenesis still occurs in adulthood (Anand and Dhikav, 2012). Neurogenesis has been defined as "the biological process through which new neurons are formed" (Baptista and Andrade, 2018). The exact role of this process in adults in the hippocampus is still difficult to affirm, and its dysregulation is strongly associated with serious mental health issues such as depression and anxiety (Costa, Lugert and Jagasia, 2015) (Jones, Zhou and Jhaveri, 2022).

### 1.2.3 **Amygdala**

The amygdala is located in front of the hippocampus, and is associated with motivation and emotional responses including pleasure, anxiety, fear and anger (*The limbic system*, 2017) (*Limbic System: Amygdala (Section 4, Chapter 6) Neuroscience Online: An Electronic Textbook for the Neurosciences | Department of Neurobiology and Anatomy - The University of Texas Medical School at Houston*, n.d.). When a person is faced by a highly stressful situation, they enter a the fight or flight response, which is kicked off by the amygdala when it sends a distress signal hypothalamus (*Understanding the stress response*, 2011). The hypothalamus then communicates with the rest of the body through the nervous system, and the person could experience rapid-heart rate, tensing of muscles or excessive sweating

(*Understanding the stress response*, 2011). While the hippocampus is the primary structure related to memory, the amygdala is associated with attaching emotion to those memories, which can determine their strength and importance in the long term. (*The limbic system*, 2017).

An example of this can be found in patients with post-traumatic stress disorder (PTSD), defined by the American psychiatry association as "a psychiatric disorder that may occur in people who have experienced or witnessed a traumatic event, series of events or set of circumstances" a condition that has been linked to amygdala hyperactivity (*Psychiatry.org - What is Posttraumatic Stress Disorder (PTSD)?*, n.d.) (Etkin and Wager, 2007). These people could have profound and unsettling thoughts and feelings related to the traumatic experience for a long time after it has occurred, in the form of stressful dreams and flashbacks (*Psychiatry.org - What is Posttraumatic Stress Disorder (PTSD)?*, n.d.).
A phenomenon known as the amygdala hijack can occur when a person is in an extremely stressful situation. An amygdala hijack is when the amygdala makes a near instantaneous decision to initiate the fight-or-flight response before the neocortex, 'the thinking brain', has time to override it (*How to Prevent and Cope From an Amygdala Hijack*, n.d.). The individual may react with highly emotional behaviour such as shouting, crying or verbal abuse, even if this may be seen as extreme for the situation, resulting in feelings of remorse (*Amygdala Hijack and the Fight or Flight Response - Simply Psychology*, n.d.).

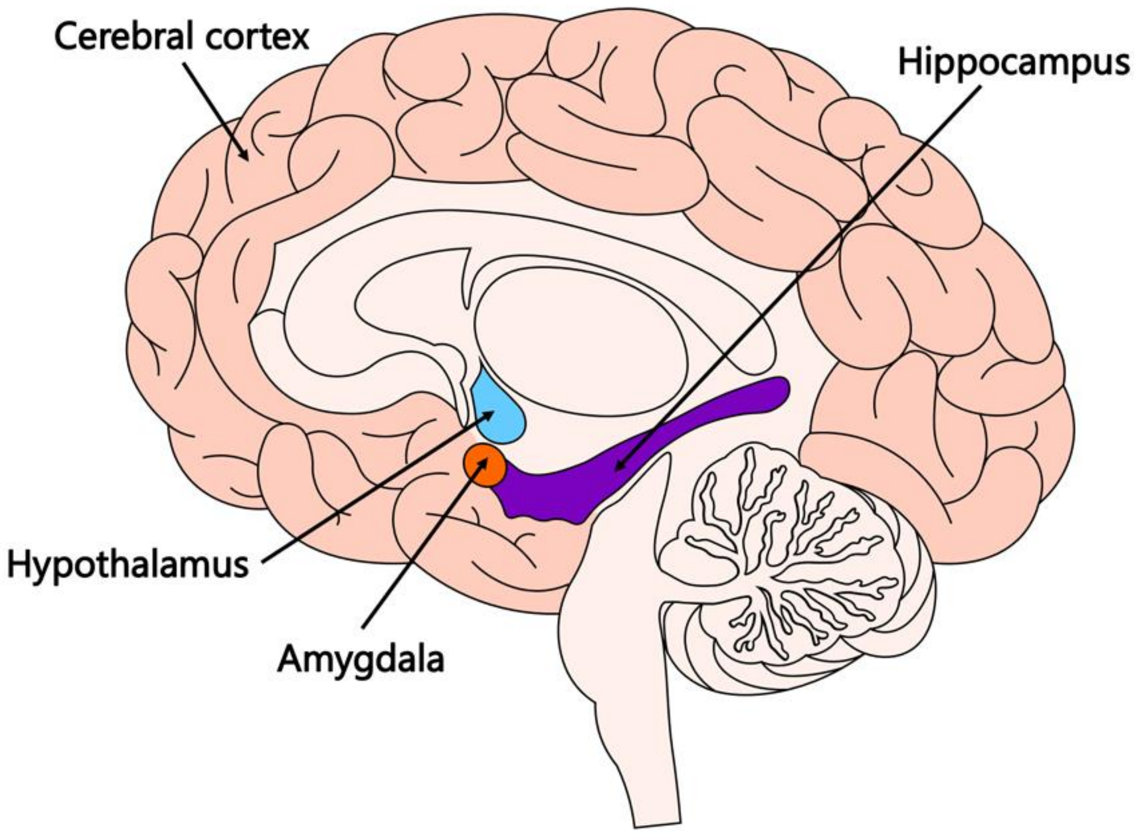


*Figure 3 - Diagram showing positions of the amygdala, hippocampus, and hypothalamus (*Emotion Facts: Emotions in the Brain*, n.d.)*

### 1.2.4 **Grey matter and white matter**

The central nervous system is defined as "the brain and the spinal cord", is made up of grey and white matter (*Definition of CNS - NCI Dictionary of Cancer Terms - NCI*, 2011) (Mercadante and Tadi, 2022). Constituting around 60% of the brain, white matter is the channel of communication, "linking grey matter regions together grey matter regions with the rest of the body" (*The Cerebellum and White and Gray Matter*, n.d.).
Grey matter represents the other 40% and gets its colour from the cells that make it up which contain grey nuclei. Grey matter manages the processing and sending of information through axon signalling, made possible by large numbers of neurons in the grey matter, enabling the release of this information in the white matter (*Grey and White Matter*, n.d.). It permits the individual to control "movement, memory and emotions" (*Grey and White Matter*, n.d.). The amygdala and the hippocampus contain both white and grey matter.

## 1.3 **MRI**

Magnetic Resonance Imaging (MRI) is a "procedure that uses a magnet, radio waves and a computer to make detailed images of areas inside the body", in particular, the brain and spinal cord (*Definition of MRI - NCI Dictionary of Cancer Terms - NCI*, 2011). The process can be broken down into the following 3 steps:

1. Polarization
2. Resonance
3. Relaxation

In step 1, MRIs have "powerful magnets producing a strong magnetic field, forcing the spin of the protons in the body to align with the field" (*Magnetic Resonance Imaging (MRI)*, n.d.). For step 2, the radiofrequency is transmitted through the patient, stimulating the protons, causing them to spin out of equilibrium and hence "strain against the pull of the magnetic field". In step 3, MRI sensors detect the energy released by the protons as they relax and realign with the magnetic field when the radiofrequency field is switched off. Physicians to tell the difference between various types of tissue by measuring magnetic properties the time taken and energy released in relaxation (*Magnetic Resonance Imaging (MRI)*, n.d.). MRI scans can discriminate among grey matter, white matter, and cerebrospinal fluid (*Tool Module: Brain Imaging*, n.d.).

In practice, a patient is placed inside a large magnet and are instructed to keep as motionless as possible to minimise blurring of the resulting MRI image. (*Magnetic Resonance Imaging (MRI)*, n.d.). Depending on which area of the body is being scanned, the time taken to complete the MRI scan varies. For the brain, according to Envision Radiology, the scan will typically take "between 30 and 60 minutes" (Developer, 2019).

*Figure 4 - Patient preparing for an MRI scan (*Prepare for Magnetic Resonance Imaging (MRI)*, 2010)*

Neuroimaging can fall into two different categories:

1. Structural imaging – to visualise anatomical properties of the brain and detect physical abnormalities.
2. Functional imaging – to measure activity in the brain during the carrying out of tasks and identify “underlying processes associated with those tasks” (*Tool Module: Brain Imaging*, n.d.) (Hirsch, Bauer and Merabet, 2015)

With regards to neuroimaging, our research includes volumes of grey matter in the hippocampus and amygdala; therefore, we are using data collected from structural MRI.

## 1.4 Socioeconomic status (SES) and brain structures

According to the American psychological association, SES is defined as the following: “Socioeconomic status is the position of an individual or group on the socioeconomic scale, which is determined by a combination of social and economic factors such as income, amount and kind of education, type and prestige of occupation, place of residence, and—in some societies or parts of society—ethnic origin or religious background” (*Socioeconomic status*, n.d.).
There have been several studies investigating the association between SES and brain structure, with a focus on children and older adults.

### 1.4.1 **State of the art**

Before 2018, the majority of studies investigating associations between SES and hippocampal and amygdala volumes in children and young adults had small sample sizes, inhibiting the validity of the conclusions drawn due to low statistical power (Button et al., 2013). One study from 2015 found positive associations between hippocampal volume in childhood (7-12 year olds) but not in young adulthood (18-25 year olds) (Yu et al., 2018). However, the overall sample size was just 64 participants. In the last five years, there have been many more studies with larger sample sizes aiming to close this gap in research.

An in depth systematic review from 2021 aimed to synthesise findings on neural correlates of SES in youth samples across neuroimaging modalities (Rakesh and Whittle, 2021). The age range for study inclusion required that the mean age be under 18, but maximum age of 24, based on recommendations regarding the adolescence period between 10 and 24. It found positive associations between SES and both hippocampal and amygdala volume, adding that the limited longitudinal research suggested SES was "associated with developmental trajectories of grey matter structure".

#### 1.4.1.1 **SES measures: Household income**

Similarly, in cross-sectional design controlling for age, sex and total brain volume, income was positively associated with hippocampal grey matter volume for both the left and right hippocampus (Hanson et al., 2011) (Lotze et al., 2020). Hanson focused on children and adolescents, with an age range of 4-18 for eligibility while Lötze had a far larger range; 21-90 years old. A study from 2017 of 1196 3–21-year-olds from the pediatric imaging, neurocognition and genetics study examining potential associations between socioeconomic disadvantage and amygdala volume (Merz, Tottenham and Noble, 2018). It found a significant positive association for ages 13-21 but not for ages 3-12, implying that the effects are more pronounced in adolescents than younger children. It controlled for brain scanner, age, $age^2$, sex, family history of anxiety/depression and total intracranial volume.
In contrast, in a study of 1099 typically developing individuals between 3-20 years old, there were no associations between income and either right or left hippocampal volumes (Noble et al., 2015). This study controlled for age, sex, and total brain volume, but also for $age^2$ and MRI scanner.

#### 1.4.1.2 **SES measures: Neighbourhood poverty**

The ongoing longitudinal Adolescent Brain Cognitive Development (ABCD) study is the "largest long-term study of brain development and child health in the United States of America", and it has provided valuable data for research in this domain (ABCD Study, n.d.). Notably, a study with a subsample of 11875 9-10 year olds from the ABCD study, (47.8% girls), if there existed an association between neighbourhood poverty and hippocampal brain structure which was separate from household socioeconomic status (Taylor et al., 2020). Household SES was measured using both household income and parent-reported financial adversity; the former being more objective but the latter giving more indication of the financial situation relative to the area cost-of-living. Greater Neighbourhood poverty (NP) was associated with smaller right hippocampal volume even when adjusting for household income, and greater household income was associated with larger hippocampal volume for both the left and right sides. The control variables were age, sex, and intracranial volume.

A study of 166 participants who had structural MRI scans on 3 occasions between 11 and 20 years old aimed to investigate the effect of neighbourhood socioeconomic disadvantage on brain structure along with possible moderating effects of positive parenting behaviours (Whittle et al., 2017). No associations were found with hippocampal volume, but greater neighbourhood disadvantage was associated with greater increases in right and left amygdala volume longitudinally. The amygdala results contrast the findings from Merz in cross-sectional design, however, it has a longitudinal design as opposed to a cross-sectional, a much smaller sample size, and a different measure of SES. This confirms the fact that further research is needed with regards to the amygdala. It also found that positive maternal parenting did not improve negative effects of low neighbourhood SES on the amygdala. Another study took a sub-sample of 9390 9–10-year-olds from the ABCD study and aimed to investigate racial differences in the effect of SES on hippocampal volume, adjusting for age, sex, and marital status (Assari, 2020). It also found a relationship between higher SES and larger hippocampal volume, but the effect was smaller for black families than white, indicating race was indeed an effect modifier in the association between SES and hippocampal volume.

#### 1.4.1.3 SES measures: Combined measure

In longitudinal studies, researchers conduct several observations of the same participants over a period of time, giving them the ability to spot changes in the characteristics of the participants at the group and the individual level (*Cross-sectional vs. longitudinal studies*, n.d.). One such study of 551 adolescents recruited by the IMAGEN consortium defined SES as a combination of income, parental education, and neighbourhood. MRI scans at age 14 and 19 years old, and a positive association between SES and hippocampal volume was found at age 14 but not at age 19 (Judd et al., 2020). There was no significant difference in amygdala volume. In a post-hoc analysis, the SES components were split into independent measures, with parental education remaining significant. The study controlled for age and sex of participants. A separate longitudinal study used the Amherst modification of the Hollingshead two-factor index to quantify childhood SES (Watt, 1976) (Hollingshead, 1957) (McDermott et al., 2019). 1243 MRI scans of 623 individuals between 5-25 years old found a significant positive association between SES and both hippocampal and amygdala volume. It also found that the effect on hippocampal volume of SES grows with age, suggesting that age is an effect modifier. The control variables were IQ, age, and sex.

### 1.4.2 Gaps in research

Most studies have reported a positive association between SES and hippocampal volumes. Amygdala volumes are not well represented, indicating further research is needed. The measure of SES is also varied across studies but focuses more on the current SES of the participant in the months leading up to/at the time of the MRI scan. Furthermore, there is a lack of longitudinal studies in the literature, and hence a lack of understanding of the temporal nature of the associations between brain development and SES (McDermott et al., 2019). As of 2023, there have not been any studies with samples from university students, and most age ranges for studies with young participants are around 3-20 years old. Lastly, most studies have focused on raw volumes as opposed to grey matter volumes.

## 1.5 **Objectives**

The objective of the research is to investigate associations between variables in the form of questions about the life of the participant during their childhood and adolescence and grey matter volumes in the Hippocampus and Amygdala, with a focus on SES in childhood and adolescence, in young adults from the MRI-share cohort. We were interested in estimating inference and aim to fill the gaps in the literature with regards to age range, students, grey matter, and the amygdala. Based on the literature, we would expect to see some positive association with the hippocampal grey matter volumes. However, for the amygdala, there have been mixed results, indicating that further research is needed.

# 2. **Methods**

## 2.1 **i-share cohort**

In this report, the dataset used originates from the i-Share cohort. I-Share (Internet-based Students HeaAlth Research Entreprise) is a prospective cohort study designed and conducted at INSERM-University of Bordeaux U1219 "Bordeaux Population Health". Its objective is to study the health and well-being of students and to investigate the determinants of certain diseases that may potentially occur at follow-up. Data was collected between 2013-2019, and with a total of over 20,000 French University students, it is the largest study ever carried out on students' health (*Accueil*, n.d.). The health and well-being of students was broken down into the following 12 avenues of investigation:

- Stress
- Sleep
- Diet
- Exercise
- Migraines
- Substance use (alcohol, drugs, and tobacco)
- Depression
- Cerebral development through MRI scans
- STI's
- Accidents
- Concentration
- Healthcare usage

The recruitment, which began in 2013 at the universities of Bordeaux and Versailles Saint-Quentin-en-Yvelines, was carried out throughout the French student population in France. To enrol, students had to meet the following criteria:

- Being enrolled in a French higher education institution
- Over the age of 18 at the time of enrolment
- Declaring that they understand French.

Once participants have registered on the i-Share website (http://www.i-share.fr/), they were given an initial online self-questionnaire covering socio-demographic characteristics as well as the living conditions, diet, alcohol etc. They were then asked every year to complete online self-questionnaires, known as follow-up questionnaires, with a follow-up objective of 10 years.

### 2.1.1 **MRI-share**

In this report, we will be focusing on a subset of participants who volunteered to undergo structural and functional MRI scans, and answer questionnaires regarding mental health.

Directed by Professor Bernard Mazoyer, the MRi-Share project had three main objectives:

- To study the structural and functional changes of the brain in subjects aged 18 to 35 and to identify their determinants.
- To detect early markers of age-related diseases in MRI scans.

- To become an MRI data platform for international biomedical research. (IRM cérébrales - Mri-Share c'est quoi ?, n.d.)

This project, set up within the i-Share cohort, was carried out in conjunction with the Bio-Share project, whose principal investigator is Professor Stéphanie Debette. All the students previously included in the cohort were approached between November 2015 and July 2017 using social networks, email and/or word of mouth to participate in the biobank. As a result, participation in the MRI scan was made up of a subpopulation of the i-Share cohort in the cross-sectional MRi-Share neuroimaging ancillary study. MRI scans were performed between November 2015 and July 2017, regardless of the time of follow-up in the study.
The inclusion criteria were:

- Being included in the i-Share cohort and to have completed the inclusion questionnaire.
- Being a student enrolled at the University of Bordeaux (since Bordeaux was the location of the examination).
- Being between 18 and 35 years old.
- Completed the MRi-Share study consent form.

The exclusion criteria, corresponding to contraindications to MRI, were:

- Being a pacemaker holder
- Wearing clips (especially surgical or thoracic)
- Wearing metal prostheses or prostheses with electronic timers
- Wearing ferromagnetic metal equipment
- Having declared themselves claustrophobic before or during the examination
- Being pregnant

## 2.2 Measures

### 2.2.1 Exposure variable

Our SES measure was represented by the self-reported financial situation in childhood and adolescence of the participant. In the questionnaire, this was the answer to the following question: 'How was your financial situation in childhood and adolescence?'. The possible answers were 'Very Difficult', 'Difficult', 'Adequate', 'Comfortable' and 'Very Comfortable'. The 'Very Difficult' were re-coded to become part of the 'Difficult group', as the number of participants in the 'Very Difficult' group were very low. Those who answered 'Very Comfortable' were also re-coded to be put into the 'comfortable' group, as these answers were seen to provide very similar information, leaving a total of three groups: 'Difficult', 'Adequate' and 'Comfortable'. The variable aimed to capture retrospective SES of the participant.

### 2.2.2 Outcome variables – hippocampal and amygdala grey matter volumes

The variables were brain measures from MRI images acquired by a state-of-the-art Siemens Prisma 3 Tesla imager. The examination at rest lasted approximately 45 minutes. The determination of brain volumes was carried out from the 3D T1-weighted sequences (fat appears hyperintense (light colour) and water appears hypointense) and FLAIR (Fluid

Attenuated Inversion Recovery: a technique allowing a better definition of the boundary between cerebrospinal fluid and grey matter) (MRi-Share – Groupe d'imagerie neurofonctionnelle (GIN-IMN), n.d.).

During the MRI examination, a visual quality control of the images was carried out by the team during which abnormalities could be identified. If any finding was likely to be significant for the participant's health, the participant was informed and referred to a specialist. In a second step, the acquired data was transferred to the GIN-IMN computer system and analysed in detail using ABACI software (The Automated Brain Anatomy for Cohort Imaging). The purpose of this data management software is to link the scanner, the database and the data analysis software (ABACI – Groupe d'imagerie neurofonctionnelle (GIN-IMN), n.d.). In the MRi-Share project, the Freesurfer analysis software was used to model the cortical surface. It allowed us to determine the boundary between white and grey matter as well as the boundary between cerebrospinal fluid and grey matter. MRIs with abnormalities were identified and excluded from the analyses. All volumes are given in $mm^3$.

## 2.3 **Covariates**

The following variables were used as covariates in the models:

- Age
- Sex
- eTIV – Total intracranial volume, in $mm^3$
- Maternal history of depression or anxiety
- Maternal history of alcoholism
- Paternal history of depression or anxiety
- Paternal history of alcoholism
- Level of education of the principal adult
- Perceived parental support in childhood and adolescence

Omitted variable bias occurs when a relevant variable is left out of a statistical model; it is the "bias in the OLS estimator when the regressor X is correlated with an omitted variable, and the omitted variable is a determinant of the dependent variable Y" (Schmelzer, n.d.). The covariates were included to mitigate this bias on the estimate of the coefficient of the exposure.

The covariates age and sex were included in the model as was strongly advised by my team of experts in epidemiological studies. Total intracranial volume was included to isolate the unique effect of childhood and adolescent SES on the grey matter volume in question. The remaining variables were included to isolate direct effect of our self-reported SES variable on grey matter volumes.

The variables for maternal and paternal history of depression or anxiety and alcoholism originally had four possible answers: 'Yes', 'No', 'Don't know' and 'Did not wish to respond'. The answers 'Don't know' and 'Did not wish to respond' were regrouped into a single 'Did not answer' variable, due to very low numbers of participants in each group. The variable for perceived parental support had answers 'none', 'a little', 'moderate', 'a lot' and 'an enormous amount'. The groups 'a lot' and 'an enormous amount' were recoded into a single category ‘a lot’, as they were seen to provide very similar information. The variable ‘level of education of the principal adult’ had six levels: ‘don’t know’, ‘primary school’, ‘secondary school up to 15 years old’, high school up to 18 years old’, ‘higher education post high-school’ and ‘professional diploma’, and it was recoded into ‘university’ and ‘no university’ levels, for simplification. Here, the ‘principal adult’ referred to the adult who brought up the child with the highest level of education, or simply the adult that brought them up if they were the only adult.

## 2.4 Statistical analysis

All data processing and analysis was carried out using R Studio 4.1.3. The data in SAS tables was loaded into R Studio where further cleaning, re-coding and analysis took place.

### 2.4.1 Sample description

Firstly, a flow chart was produced to describe the selection of participants for the study, including specific information of the exclusion criteria along with the number of participants excluded at each step. Next, the characteristics of the included participants were described in a table, with frequency and percentage used for the groups of the qualitative variables, and means, medians, ranges, and standard deviations for the qualitative. Two tables were presented, one including a split by sex and the other a split by SES. Student’s t-tests were performed to evaluate the difference in means of the quantitative variables by sex, Kruskal-Wallis tests to evaluate difference in means of the quantitative variables by SES, and chi-squared tests of independence between both sex, SES, and the categorical variables. The p-values were reported in the last columns of the tables. All tests were evaluated at the 5% level.

### 2.4.2 Regression Analysis: association between SES and hippocampal and amygdala grey matter volumes

The beta coefficients and their 95% confidence intervals were estimated by OLS. The associated p-values were calculated using the student’s t-test, with the computation executed by R and printed in the model summary.

The models were of the following design:

$$VOL_i = \beta_0 + \beta_1 SIT1_i + \beta_2 SIT2_i + \beta_3 SEX_i + \beta_4 AGE_i + \beta_5 eTIV_i + \beta_6 MDEP1_i + \beta_7 MDEP2_i + \beta_8 FDEP1_i + \beta_9 FDEP2_i + \beta_{10} MALC1_i + \beta_{11} MALC2_i + \beta_{12} FALC1_i + \beta_{13} FALC2_i + \beta_{14} EDU_i + \beta_{15} SOUT1_i + \beta_{16} SOUT2_i + \beta_{17} SOUT3_i + \beta_{18} SOUT4_i + \varepsilon_i$$

Where

$$\varepsilon_i \sim_{i.i.d} N(0, \sigma^2) \quad (1)$$

And

- SIT1-financial situation in childhood and adolescence, 1 if difficult, 0 otherwise
- SIT2-financial situation in childhood and adolescence, 1 if adequate, 0 otherwise
- SEX- Sex of participant, 1 if male, 0 otherwise
- AGE-Age of participants (years)
- eTIV-Total intracranial volume ($mm^3$)
- MDEP1 – Maternal history of depression or anxiety, 1 if yes, 0 otherwise
- MDEP2 – Maternal history of depression or anxiety, 1 if did not answer, 0 otherwise
- FDEP1 – Paternal history of depression or anxiety, 1 if yes, 0 otherwise
- FDEP2 – Paternal history of depression or anxiety, 1 if did not answer, 0 otherwise
- MALC1 – Maternal history of alcoholism, 1 if yes, 0 otherwise
- MALC2 – Maternal history of alcoholism, 1 if did not answer, 0 otherwise
- FALC1 – Paternal history of alcoholism, 1 if yes, 0 otherwise
- FALC2 – Paternal history of alcoholism, 1 if did not answer, 0 otherwise
- EDU- Education level of the principal adult, 1 if no university, 0 otherwise
- SOUT1- Perceived parental support in childhood and adolescence, 1 if none, 0 otherwise
- SOUT2- Perceived parental support in childhood and adolescence, 1 if a little, 0 otherwise
- SOUT3- Perceived parental support in childhood and adolescence, 1 if moderate, 0 otherwise
- SOUT4- Perceived parental support in childhood and adolescence, 1 if did not wish to respond, 0 otherwise
- VOL- grey matter volume of either left or right hippocampus or amygdala

The coefficients were estimated by Ordinary Least Squares. We also stratified for Sex and estimated the models again, with the same covariates. Throughout the analysis, the significance level was set to 5%.

## 2.5 Missing data

There was very little missing data in the variables that were investigated, and so the participants with the missing data were simply excluded from the analysis.

## 2.6 Ethical considerations

Once enrolled in the biobank project, participants committed to attending three appointments: a visit with a doctor to check suitability for the scan, a blood sample and a brain MRI followed by neuropsychological testing. Participants in the biobank project received an information note explaining the procedures for the blood and the MRI. In a second step they also signed a consent form to participate in the Bio-Share biobank project. Both projects were approved by the Comité de Protection des Personnes (CPP) Sud-Ouest and Overseas III. The biobank of blood samples has been authorised by the French National Agency for the Sécurité du Médicament et des Produits de Santé (ANSM). Each MRi-Share participant received 40 euros.

# 3. Results

## 3.1 Description of study sample

Of the participants included in the i-share cohort, 1997 were voluntary participants in the MRi-share study. Before the analysis took place, some participants were removed from this initial sample. 166 participants had anomalies related to MRI measurements and were therefore excluded. A further participant who had missing data with relation to the date of the MRI scan was removed, along with two more participants with missing data relating to parental education and parental alcohol. As represented in the flux diagram, we were left with 1828 participants for analysis.

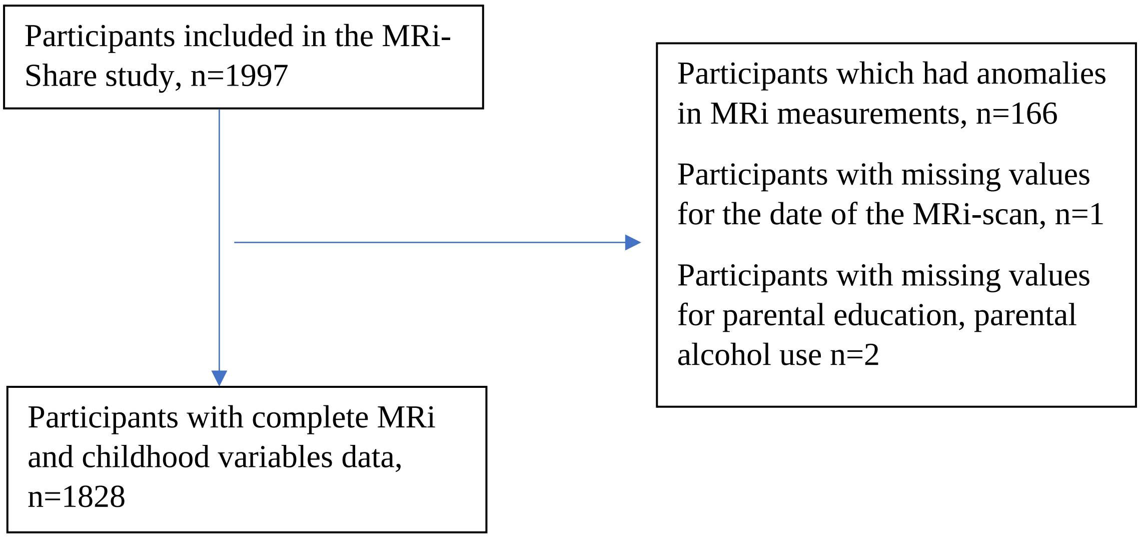


*Figure 5- Flux diagram demonstrating inclusion criteria.*

## 3.2 Demographic tables

Demographics of participants included in the analysis were summarised in the following tables. A split to compare sexes was included in the first table and split by SES was included in the second table. The mean age of participants was 20.8 (s.d. 2.32) years old. 1319 (72.1%) of participants were female and 509 (28.9%) were male (**p<0.001,** z-test for difference in proportions**)**, while 1065 participants (58.3%) reported having had a *comfortable* financial situation in childhood and adolescence, compared to 611 participants (33.4%) *adequate* (**p<0.001)**, and 152 participants (8.3%) *difficult* **(p<0.001)**.

### 3.2.1 Sex differences

The mean age was 21.1 (s.d. 2.26) years for female participants 20.7 (s.d. 2.43) years for male participants (**p<0.001,** t-test test for difference in means**)**. Maternal history depression or anxiety was reported by 31.3% of females against 23.6% of males (**p=0.003,** chi-squared test of independence between categorical variables) and paternal history of depression or anxiety was reported by 17.4% of females against 12.6% of males (**p=0.019**). Females had a significantly larger mean number of months between the MRI scan and the completion of the questionnaire (11.8 months) against (9.3 months), 2.5 mean months difference, (**p=0.003**) than males, and a significantly lower current year of study (**p<0.001**) than males. For the brain measures, females were significantly smaller in mean volume than males with p-values **<0.001** in all cases.

*Table I- Demographics table with Sex stratification*

| | Overall (N=1828) | Female (N=1319, 72.1%) | Male (N=509, 28.9%) | p-values <0.001 |
|---|---|---|---|---|
| **Age** | | | | |
| Mean (SD) | 20.8 (2.32) | 20.7 (2.26) | 21.1 (2.43) | **<0.001** |
| Median [Min, Max] | 20.0 [16.0, 33.0] | 20.0 [16.0, 33.0] | 21.0 [17.0, 31.0] | |
| **Months between baseline and MRI scan** | | | | |
| Mean (SD) | 10.6 (11.6) | 11.1 (11.8) | 9.30 (10.9) | **0.003** |
| Median [Min, Max] | 5.00 [0, 55.0] | 6.00 [0, 55.0] | 4.00 [0, 47.0] | |
| **Financial situation in childhood and adolescence** | | | | |
| Difficult | 152 (8.3%) | 114 (8.6%) | 38 (7.5%) | 0.709 |
| Adequate | 611 (33.4%) | 438 (33.2%) | 173 (34.0%) | |
| Comfortable | 1065 (58.3%) | 767 (58.2%) | 298 (58.5%) | |
| **Perceived parental support in childhood and adolescence** | | | | |
| None | 25 (1.4%) | 22 (1.7%) | 3 (0.6%) | 0.369 |
| A little | 94 (5.1%) | 64 (4.9%) | 30 (5.9%) | |
| Moderate | 329 (18.0%) | 237 (18.0%) | 92 (18.1%) | |
| A lot | 1356 (74.2%) | 980 (74.3%) | 376 (73.9%) | |
| Did not wish to respond | 24 (1.3%) | 16 (1.2%) | 8 (1.6%) | |
| **Current year of study** | | | | |
| Mean (SD) | 3.27 (2.58) | 3.13 (2.46) | 3.66 (2.84) | **<0.001** |
| Median [Min, Max] | 2.00 [1.00, 9.00] | 2.00 [1.00, 9.00] | 2.00 [1.00, 9.00] | |
| **Maternal history of depression or anxiety** | | | | |
| No | 1135 (62.1%) | 798 (60.5%) | 337 (66.2%) | **0.003** |
| Yes | 533 (29.2%) | 413 (31.3%) | 120 (23.6%) | |
| Did not answer | 160 (8.8%) | 108 (8.2%) | 52 (10.2%) | |
| **Paternal history of depression or anxiety** | | | | |
| No | 1313 (71.8%) | 924 (70.1%) | 389 (76.4%) | **0.019** |
| Yes | 294 (16.1%) | 229 (17.4%) | 65 (12.8%) | |
| Did not answer | 221 (12.1%) | 166 (12.6%) | 55 (10.8%) | |
| **Maternal history of alcoholism** | | | | |
| No | 1732 (94.7%) | 1246 (94.5%) | 486 (95.5%) | 0.488 |
| Yes | 45 (2.5%) | 36 (2.7%) | 9 (1.8%) | |
| Did not answer | 51 (2.8%) | 37 (2.8%) | 14 (2.8%) | |
| **Paternal history of alcoholism** | | | | |
| No | 1549 (84.7%) | 1103 (83.6%) | 446 (87.6%) | 0.093 |
| Yes | 153 (8.4%) | 117 (8.9%) | 36 (7.1%) | |
| Did not answer | 126 (6.9%) | 99 (7.5%) | 27 (5.3%) | |
| **Principal adult's education level** | | | | |
| No university | 462 (25.3%) | 327 (24.8%) | 135 (26.5%) | 0.477 |
| University | 1366 (74.7%) | 992 (75.2%) | 374 (73.5%) | |
| **Total intracranial volume[2] ($mm^3$)** | | | | |
| Mean (SD) | 157 (13.7) | 152 (10.5) | 170 (11.7) | **<0.001** |
| Median [Min, Max] | 155 [114, 206] | 151 [114, 192] | 170 [137, 206] | |
| **Hippocampus L ($mm^3$)** | | | | |
| Mean (SD) | 3650 (328) | 3540 (270) | 3930 (300) | **<0.001** |
| Median [Min, Max] | 3630 [2700, 5290] | 3530 [2700, 4540] | 3940 [2890, 5290] | |
| **Hippocampus R ($mm^3$)** | | | | |
| Mean (SD) | 3650 (329) | 3550 (273) | 3920 (314) | **<0.001** |
| Median [Min, Max] | 3630 [2680, 5230] | 3540 [2680, 4480] | 3930 [3050, 5230] | |
| **Amygdala L ($mm^3$)** | | | | |
| Mean (SD) | 1610 (145) | 1550 (110) | 1750 (125) | **<0.001** |
| Median [Min, Max] | 1600 [1200, 2260] | 1550 [1200, 1910] | 1760 [1410, 2260] | |
| **Amygdala R ($mm^3$)** | | | | |
| Mean (SD) | 1800 (164) | 1740 (124) | 1960 (147) | **<0.001** |
| Median [Min, Max] | 1780 [1330, 2560] | 1730 [1330, 2240] | 1950 [1560, 2560] | |

1- P-value for differences between sexes

### 3.2.2 **SES differences**

In the tests of independence, the null hypothesis of no relationship between the variables was rejected for all the categorical variables and the SES variable except for Sex.

Participants in the *'comfortable'* group had a significantly proportions and means than both those in the *'difficult'* and '*adequate'* groups in most cases. They had a significantly smaller proportion of paternal history of depression or anxiety (13.2%), *'adequate'* (19.1%, **p=0.001**) and *'difficult'* (23.7%, **p<0.001**) and paternal alcoholism (4.7%), *'adequate'* (11.8%, **p<0.001**) and 'difficult' (20.4%, **p<0.001**). They had a significantly greater proportion of participants who reported a lot of parental support, (81.5%), *'adequate'* (67.1%, **p<0.001**) and *'difficult'* (51.3%, **p<0.001**). They had a significantly smaller proportion of maternal alcoholism (1.7%), *'difficult'* (7.9%, **p<0.001**).

With regards to volumes, they had a significantly larger mean intracranial volume (158cm$^3$) than both '*adequate*' (156cm$^3$, **p=0.014**) and '*difficult*' (155cm$^3$, **p=0.014**). They were significantly larger volume than those in the *'difficult'* group for both sides of the hippocampus and amygdala: Hippocampus L (3660mm$^3$), *'difficult'* (3570mm$^3$, **p<0.001**), Hippocampus R (3670mm$^3$), *'difficult'* (3590mm$^3$, **p=0.008**), Amygdala L (1620mm$^3$), *'difficult'* (1580mm$^3$, **p=0.011**) and Amygdala R (1800mm$^3$), *'difficult'* (1770mm$^3$, **p=0.030**).

*Table II- Demographic table with SES stratification*

| | Overall (N=1828) | Adequate (N=611, 33.4%) | Comfortable (N=1065, 58.3%) | Difficult (N=152, 8.3%) | p[1] <0.001 | p[2] <0.001 | p[3] <0.001 |
|---|---|---|---|---|---|---|---|
| **Sex** | | | | | | | |
| Male | 509 (27.8%) | 173 (28.3%) | 298 (28.0%) | 38 (25.0%) | 0.709 | 0.895 | 0.439 |
| Female | 1319 (72.2%) | 438 (71.7%) | 767 (72.0%) | 114 (75.0%) | | 0.895 | 0.439 |
| **Age** | | | | | | | |
| Mean (SD) | 20.8 (2.32) | 20.8 (2.33) | 20.7 (2.25) | 21.3 (2.68) | 0.076 | 0.664 | **0.006** |
| Median [Min, Max] | 20.0 [16.0, 33.0] | 20.0 [17.0, 30.0] | 20.0 [16.0, 33.0] | 21.0 [17.0, 30.0] | | | |
| **Months between baseline and MRI scan** | | | | | | | |
| Mean (SD) | 10.6 (11.6) | 10.9 (11.2) | 10.5 (11.9) | 10.1 (11.4) | 0.123 | 0.447 | 0.744 |
| Median [Min, Max] | 5.00 [0, 55.0] | 6.00 [0, 47.0] | 5.00 [0, 55.0] | 5.00 [0, 47.0] | | | |
| **Perceived parental support in childhood and adolescence** | | | | | | | |
| None | 25 (1.4%) | 15 (2.5%) | 4 (0.4%) | 6 (3.9%) | **<0.001** | **<0.001** | **<0.001** |
| A little | 94 (5.1%) | 33 (5.4%) | 39 (3.7%) | 22 (14.5%) | | 0.099 | **<0.001** |
| Moderate | 329 (18.0%) | 141 (23.1%) | 146 (13.7%) | 42 (27.6%) | | **<0.001** | **<0.001** |
| A lot | 1356 (74.2%) | 410 (67.1%) | 868 (81.5%) | 78 (51.3%) | | **<0.001** | **<0.001** |
| Did not wish to respond | 24 (1.3%) | 12 (2.0%) | 8 (0.8%) | 4 (2.6%) | | **0.032** | **0.039** |
| **Current year of study** | | | | | | | |
| Mean (SD) | 3.27 (2.58) | 3.00 (2.39) | 3.43 (2.69) | 3.27 (2.44) | **0.005** | **<0.001** | 0.479 |
| Median [Min, Max] | 2.00 [1.00, 9.00] | 2.00 [1.00, 9.00] | 2.00 [1.00, 9.00] | 3.00 [1.00, 9.00] | | | |
| **Maternal history of depression or anxiety** | | | | | | | |
| No | 1135 (62.1%) | 359 (58.8%) | 710 (66.7%) | 66 (43.4%) | **<0.001** | **0.001** | **<0.001** |
| Yes | 533 (29.2%) | 197 (32.2%) | 262 (24.6%) | 74 (48.7%) | | **<0.001** | **<0.001** |
| Did not answer | 160 (8.8%) | 55 (9.0%) | 93 (8.7%) | 12 (7.9%) | | 0.835 | 0.742 |
| **Paternal history of depression or anxiety** | | | | | | | |
| No | 1313 (71.8%) | 416 (68.1%) | 816 (76.6%) | 81 (53.3%) | **<0.001** | **<0.001** | **<0.001** |
| Yes | 294 (16.1%) | 117 (19.1%) | 141 (13.2%) | 36 (23.7%) | | **0.001** | **<0.001** |
| Did not answer | 221 (12.1%) | 78 (12.8%) | 108 (10.1%) | 35 (23.0%) | | 0.090 | **<0.001** |
| **Maternal history of alcoholism** | | | | | | | |
| No | 1732 (94.7%) | 575 (94.1%) | 1025 (96.2%) | 132 (86.8%) | **<0.001** | **0.047** | **<0.001** |
| Yes | 45 (2.5%) | 15 (2.5%) | 18 (1.7%) | 12 (7.9%) | | 0.259 | **<0.001** |
| Did not answer | 51 (2.8%) | 21 (3.4%) | 22 (2.1%) | 8 (5.3%) | | 0.106 | **0.018** |
| **Paternal history of alcoholism** | | | | | | | |
| No | 1549 (84.7%) | 488 (79.9%) | 966 (90.7%) | 95 (62.5%) | **<0.001** | **<0.001** | **<0.001** |
| Yes | 153 (8.4%) | 72 (11.8%) | 50 (4.7%) | 31 (20.4%) | | **<0.001** | **<0.001** |
| Did not answer | 126 (6.9%) | 51 (8.3%) | 49 (4.6%) | 26 (17.1%) | | **0.002** | **<0.001** |
| **Principal adult's education level** | | | | | | | |
| No university | 462 (25.3%) | 220 (36.0%) | 168 (15.8%) | 74 (48.7%) | **<0.001** | **<0.001** | **<0.001** |
| University | 1366 (74.7%) | 391 (64.0%) | 897 (84.2%) | 78 (51.3%) | | **<0.001** | **<0.001** |
| **Total intracranial volume ($mm^3$)** | | | | | | | |
| Mean (SD) | 157 (13.7) | 156 (13.7) | 158 (13.8) | 155 (13.2) | **0.009** | **0.014** | **0.014** |
| Median [Min, Max] | 155 [114, 206] | 155 [114, 206] | 155 [123, 204] | 154 [125, 195] | | | |
| **Hippocampus L ($mm^3$)** | | | | | | | |
| Mean (SD) | 3650 (328) | 3640 (331) | 3660 (326) | 3570 (313) | **0.002** | 0.223 | **<0.001** |
| Median [Min, Max] | 3630 [2700, 5290] | 3620 [2810, 5290] | 3650 [2700, 4920] | 3540 [2710, 4480] | | | |
| **Hippocampus R ($mm^3$)** | | | | | | | |
| Mean (SD) | 3650 (329) | 3640 (332) | 3670 (328) | 3590 (310) | **0.018** | 0.146 | **0.008** |
| Median [Min, Max] | 3630 [2680, 5230] | 3620 [2680, 5230] | 3640 [2700, 4850] | 3570 [2710, 4480] | | | |
| **Amygdala L ($mm^3$)** | | | | | | | |
| Mean (SD) | 1610 (145) | 1600 (144) | 1620 (146) | 1580 (144) | **0.012** | 0.113 | **0.011** |
| Median [Min, Max] | 1600 [1200, 2260] | 1600 [1200, 2260] | 1600 [1210, 2040] | 1570 [1230, 2040] | | | |
| **Amygdala R ($mm^3$)** | | | | | | | |
| Mean (SD) | 1800 (164) | 1790 (165) | 1800 (163) | 1770 (165) | **0.024** | 0.094 | **0.030** |
| Median [Min, Max] | 1780 [1330, 2560] | 1780 [1390, 2560] | 1790 [1330, 2330] | 1750 [1360, 2320] | | | |

1- P-value for tests of independence
2- P-value for z-test of difference in proportions between *'adequate'* and *'comfortable'* groups
3- P-value for z-test of difference in proportions between *'difficult'* and *'comfortable'* groups

## 3.3 **Regression Analysis**

The association between SES and hippocampal and amygdala grey matter volumes was investigated by means of multiple linear regression. There were twelve models in total: one set for each sub-cortical region of interest (Hippocampus L, Hippocampus R, Amygdala L and Amygdala R) and each model was re-run with stratification by sex. The models each contained 10 predictor variables (9 for the stratified models), of which two were numerical and were 8 categorical (7 for the stratified models). The reference levels for the factor variables were chosen so that the level with the largest number of participants was put as a reference level. In the case of the exposure variable, this was those who reported having a *comfortable* financial situation in childhood and adolescence.

### 3.3.1 **Models without stratification**

For the financial situation variable, participants in the *'difficult'* category had significantly smaller left hippocampal grey matter volume than those in the '*comfortable'* reference category (-42.84mm$^3$, 95% C.I.: -74.70, -10.98, **p=0.008**). Grey matter volumes were not significantly different between levels of SES of participants for any of the other regions. Adjustment was made for Sex, Age, Maternal history of depression or anxiety, Paternal history of depression or anxiety, Maternal history of alcoholism, Paternal history of alcoholism, Education level of the principal adult, Total intracranial volume and perceived parental support.

The participants who answered *'none'* for the perceived parental support question had a significantly smaller left hippocampal grey matter volume (-76.55 mm$^3$, 95% C.I.: -146.98, -6.12, **p=0.033**), left amygdala grey matter volume (-34.96 mm$^3$, 95% C.I.: -64.46, -5.45, **p=0.020**), and right amygdala grey matter volume (-49.45 mm$^3$, 95% C.I.: -82.13, -16.76, **p=0.003**) than those in the reference '*a lot'* category. Participants with a principal adult having '*no university*' level had a significantly larger right hippocampal grey matter volume (21.46, 95% C.I.: 1.14, 41.78, **p=0.038**).

*Table III- Results for regression models with **hippocampal grey matter volume** as the response variable*

| | Hip Left | | | Hip Right | | |
|---|---|---|---|---|---|---|
| Characteristic | Beta | 95% CI[1] | p-value[2] | Beta | 95% CI[1] | p-value[2] |
| **Family's Financial situation in childhood and adolescence** | | | | | | |
| *Comfortable* | — | — | | — | — | |
| *Difficult* | **-42.84** | **-74.70, -10.98** | **0.008** | -28.35 | -61.91, 5.21 | 0.098 |
| *Adequate* | 12.25 | -6.03, 30.52 | 0.189 | 4.92 | -14.33, 24.17 | 0.616 |
| **Sex** | | | | | | |
| *Female* | — | — | | — | — | |
| *Male* | 3.53 | -19.53, 26.60 | 0.764 | -17.08 | -41.38, 7.22 | 0.168 |
| **Age** | **4.90** | **1.39, 8.42** | **0.006** | **5.38** | **1.68, 9.08** | **0.004** |
| **Total intracranial volume** | **<0.01** | **>0.00, <0.01** | **<0.001** | **<0.01** | **>0.00, <0.01** | **<0.001** |
| **Mother history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -1.26 | -20.27, 17.74 | 0.896 | -3.84 | -23.87, 16.18 | 0.707 |
| *Did not answer* | 7.23 | -28.00, 42.45 | 0.687 | 9.29 | -27.82, 46.40 | 0.624 |
| **Father history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 4.82 | -18.39, 28.03 | 0.684 | 3.08 | -21.38, 27.54 | 0.805 |
| *Did not answer* | 6.29 | -26.58, 39.17 | 0.707 | -1.33 | -35.96, 33.31 | 0.940 |
| **Mother alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 1.23 | -52.13, 54.59 | 0.964 | -20.08 | -76.29, 36.14 | 0.484 |
| *Did not answer* | -25.70 | -81.41, 30.01 | 0.366 | -12.42 | -71.11, 46.28 | 0.678 |
| **Father alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -2.26 | -32.78, 28.26 | 0.885 | 6.09 | -26.06, 38.25 | 0.710 |
| *Did not answer* | 5.09 | -34.27, 44.45 | 0.800 | 23.06 | -18.40, 64.53 | 0.276 |
| **Principal adult education level** | | | | | | |
| *University* | — | — | | — | — | |
| *No university* | 13.21 | -6.08, 32.50 | 0.179 | **21.46** | **1.14, 41.78** | **0.038** |
| **Perceived parental support** | | | | | | |
| *A lot* | — | — | | — | — | |
| *None* | **-76.55** | **-146.98, -6.12** | **0.033** | -56.57 | -130.77, 17.64 | 0.135 |
| *A little* | -6.00 | -43.84, 31.84 | 0.756 | 4.52 | -35.35, 44.39 | 0.824 |
| *Moderate* | 2.62 | -19.09, 24.32 | 0.813 | 6.68 | -16.18, 29.54 | 0.567 |
| *Did not wish to respond* | 15.34 | -56.29, 86.97 | 0.675 | 16.17 | -59.29, 91.63 | 0.674 |

1- 95% confidence interval
2- **Bold** p-values if they were significant at the 5% level.

*Table IV- Results for regression models with **amygdala grey matter volume** as the response variable*

| | Amy L | | | Amy R | | |
|---|---|---|---|---|---|---|
| Characteristic | Beta | 95% CI | p-value | Beta | 95% CI | p-value |
| **Family's Financial situation in childhood and adolescence** | | | | | | |
| *Comfortable* | — | — | | — | — | |
| *Difficult* | -7.29 | -20.64, 6.05 | 0.284 | -2.05 | -16.83, 12.74 | 0.786 |
| *Adequate* | 2.81 | -4.84, 10.47 | 0.471 | 2.14 | -6.34, 10.62 | 0.620 |
| **Sex** | | | | | | |
| *Female* | — | — | | — | — | |
| *Male* | **44.73** | **35.07, 54.39** | **<0.001** | **39.43** | **28.73, 50.13** | **<0.001** |
| **Age** | 0.80 | -0.67, 2.28 | 0.284 | 0.46 | -1.17, 2.09 | 0.582 |
| **Total intracranial volume** | **<0.01** | **>0.00, <0.01** | **<0.001** | **<0.01** | **>0.00, <0.01** | **<0.001** |
| **Mother history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -7.85 | -15.81, 0.12 | 0.053 | -4.64 | -13.46, 4.18 | 0.302 |
| *Did not answer* | **-17.83** | **-32.59, -3.08** | **0.018** | 1.86 | -14.48, 18.21 | 0.823 |
| **Father history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 8.00 | -1.72, 17.73 | 0.107 | 4.07 | -6.70, 14.84 | 0.459 |
| *Did not answer* | 11.30 | -2.47, 25.07 | 0.108 | -0.91 | -16.17, 14.34 | 0.907 |
| **Mother alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 3.40 | -18.95, 25.76 | 0.765 | -0.94 | -25.70, 23.82 | 0.940 |
| *Did not answer* | 1.27 | -22.06, 24.61 | 0.915 | 8.90 | -16.95, 34.75 | 0.499 |
| **Father alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -0.74 | -13.52, 12.05 | 0.910 | 6.85 | -7.32, 21.01 | 0.343 |
| *Did not answer* | -3.76 | -20.25, 12.72 | 0.654 | 0.09 | -18.18, 18.35 | 0.993 |
| **Principal adult education level** | | | | | | |
| *University* | — | — | | — | — | |
| *No university* | -2.33 | -10.41, 5.75 | 0.571 | -2.62 | -11.57, 6.33 | 0.566 |
| **Perceived parental support** | | | | | | |
| *A lot* | — | — | | — | — | |
| *None* | **-34.96** | **-64.46, -5.45** | **0.020** | **-49.45** | **-82.13, -16.76** | **0.003** |
| *A little* | 8.57 | -7.28, 24.42 | 0.289 | 5.54 | -12.02, 23.10 | 0.536 |
| *Moderate* | 0.67 | -8.42, 9.76 | 0.885 | 7.34 | -2.73, 17.41 | 0.153 |
| *Did not wish to respond* | 21.85 | -8.15, 51.86 | 0.153 | 30.77 | -2.47, 64.00 | 0.070 |

### 3.3.2 **Models with stratification**

After stratification, male participants in the *'difficult'* category had significantly smaller left and right hippocampal grey matter volumes (-85.91mm$^3$ 95% C.I. -156.6, -15.25, **p=0.017**) and (-78.19mm$^3$, 95% C.I.: -153.13, -3.25, **p=0.041**). Female participants did not have significantly smaller grey matter volumes for any of the regions. Given that right hippocampal grey matter volume for participants in the *'difficult'* category was not significantly smaller in the non-stratified model, this implied an interaction with sex. To verify this, another model was estimated including the interaction term SES x Sex, and indeed the model yielded a significant coefficient (**p=0.045**) for the interaction term for males in the '*difficult´* category, indicating that sex was an effect modifier in the relationship between SES and right hippocampal grey matter volume.

Females who reported '*none'* for perceived parental support retained significantly smaller amygdala volumes on both sides than those reporting 'a lot' of parental support.

*Table V- Results for regression models with **hippocampal grey matter volume** as the response variable, **Males***

| | Hip Left | | | Hip Right | | |
|---|---|---|---|---|---|---|
| Characteristic | Beta | 95% CI | p-value | Beta | 95% CI | p-value |
| **Family's Financial situation in childhood and adolescence** | | | | | | |
| *Comfortable* | — | — | | — | — | |
| *Difficult* | **-85.91** | **-156.57, -15.25** | **0.017** | **-78.19** | **-153.13, -3.25** | **0.041** |
| *Adequate* | 20.15 | -18.25, 58.55 | 0.303 | -0.33 | -41.06, 40.40 | 0.987 |
| **Age** | 4.33 | -2.69, 11.35 | 0.226 | 10.00 | 2.55, 17.44 | **0.009** |
| **Total intracranial volume** | **<0.01** | **>0.00, <0.01** | **<0.001** | **<0.01** | **>0.00, <0.01** | **<0.001** |
| **Mother history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -27.10 | -68.73, 14.54 | 0.202 | -29.74 | -73.90, 14.41 | 0.186 |
| *Did not answer* | -43.71 | -117.50, 30.08 | 0.245 | -43.25 | -121.52, 35.01 | 0.278 |
| **Father history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 12.06 | -40.31, 64.43 | 0.651 | 4.05 | -51.49, 59.60 | 0.886 |
| *Did not answer* | 26.13 | -49.81, 102.07 | 0.499 | 18.20 | -62.34, 98.74 | 0.657 |
| **Mother alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 38.59 | -98.15, 175.33 | 0.580 | -9.01 | -154.04, 136.02 | 0.903 |
| *Did not answer* | -66.21 | -192.97, 60.55 | 0.305 | -12.70 | -147.14, 121.75 | 0.853 |
| **Father alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 49.51 | -19.56, 118.58 | 0.160 | 41.73 | -31.53, 114.98 | 0.264 |
| *Did not answer* | 76.67 | -18.37, 171.72 | 0.114 | 59.17 | -41.64, 159.97 | 0.249 |
| **Principal adult education level** | | | | | | |
| *University* | — | — | | — | — | |
| *No university* | 5.27 | -34.75, 45.30 | 0.796 | 5.60 | -36.85, 48.04 | 0.796 |
| **Perceived parental support** | | | | | | |
| *A lot* | — | — | | — | — | |
| *None* | -125.16 | -347.17, 96.85 | 0.269 | -77.57 | -313.04, 157.89 | 0.518 |
| *A little* | -57.40 | -132.46, 17.66 | 0.134 | -54.93 | -134.54, 24.68 | 0.176 |
| *Moderate* | 3.60 | -41.05, 48.26 | 0.874 | 11.37 | -35.99, 58.73 | 0.637 |
| *Did not wish to respond* | -30.18 | -167.25, 106.88 | 0.665 | -18.19 | -163.56, 127.18 | 0.806 |

*Table VI- Results for regression models with **hippocampal grey matter volume** as the response variable, **Females***

| | Hip L | | | Hip R | | |
|---|---|---|---|---|---|---|
| Characteristic | Beta | 95% CI | p-value | Beta | 95% CI | p-value |
| **Family's Financial situation in childhood and adolescence** | | | | | | |
| *Comfortable* | — | — | | — | — | |
| *Difficult* | -29.88 | -65.74, 5.98 | 0.102 | -11.64 | -49.30, 26.02 | 0.544 |
| *Adequate* | 10.97 | -9.79, 31.72 | 0.300 | 8.35 | -13.45, 30.14 | 0.453 |
| **Age** | **5.36** | **1.30, 9.41** | **0.010** | 3.74 | -0.52, 8.00 | 0.085 |
| **Total intracranial volume** | **<0.01** | **>0.00, <0.01** | **<0.001** | **<0.01** | **>0.00, <0.01** | **<0.001** |
| **Mother history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 8.00 | -13.24, 29.25 | 0.460 | 4.88 | -17.43, 27.18 | 0.668 |
| *Did not answer* | 27.60 | -12.71, 67.90 | 0.179 | 29.91 | -12.42, 72.24 | 0.166 |
| **Father history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 1.93 | -23.71, 27.56 | 0.883 | 2.33 | -24.60, 29.25 | 0.865 |
| *Did not answer* | 2.87 | -33.46, 39.20 | 0.877 | -5.07 | -43.23, 33.08 | 0.794 |
| **Mother alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -3.53 | -61.01, 53.94 | 0.904 | -18.83 | -79.19, 41.53 | 0.541 |
| *Did not answer* | -25.20 | -87.19, 36.79 | 0.425 | -19.31 | -84.41, 45.79 | 0.561 |
| **Father alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -20.42 | -54.20, 13.36 | 0.236 | -6.87 | -42.34, 28.60 | 0.704 |
| *Did not answer* | -14.08 | -57.01, 28.84 | 0.520 | 9.68 | -35.40, 54.76 | 0.674 |
| **Principal adult education level** | | | | | | |
| *University* | — | — | | — | — | |
| *No university* | 17.74 | -4.25, 39.73 | 0.114 | **29.92** | **6.83, 53.02** | **0.011** |
| **Perceived parental support** | | | | | | |
| *A lot* | — | — | | — | — | |
| *None* | -63.73 | -136.42, 8.96 | 0.086 | -51.85 | -128.19, 24.49 | 0.183 |
| *A little* | 16.94 | -27.07, 60.96 | 0.450 | 29.97 | -16.26, 76.19 | 0.204 |
| *Moderate* | 1.79 | -23.17, 26.75 | 0.888 | 2.72 | -23.49, 28.94 | 0.839 |
| *Did not wish to respond* | 31.08 | -53.40, 115.56 | 0.471 | 27.67 | -61.04, 116.39 | 0.541 |

*Table VII-* ***Results for regression models with amygdala grey matter volume as the response variable, Males***

| | Amy Left | | | Amy Right | | |
|---|---|---|---|---|---|---|
| Characteristic | Beta | 95% CI | p-value | Beta | 95% CI | p-value |
| **Family's Financial situation in childhood and adolescence** | | | | | | |
| *Comfortable* | — | — | | — | — | |
| *Difficult* | -18.40 | -47.79, 10.99 | 0.219 | -22.22 | -55.73, 11.29 | 0.193 |
| *Adequate* | -2.60 | -18.58, 13.37 | 0.749 | -7.73 | -25.94, 10.48 | 0.405 |
| **Age** | 1.39 | -1.53, 4.31 | 0.351 | 0.80 | -2.53, 4.13 | 0.637 |
| **Total intracranial volume** | **<0.01** | **>0.00, <0.01** | **<0.001** | **<0.01** | **>0.00, <0.01** | **<0.001** |
| **Mother history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -17.22 | -34.54, 0.09 | 0.051 | -16.56 | -36.31, 3.18 | 0.100 |
| *Did not answer* | **-46.06** | **-76.75, -15.36** | **0.003** | -22.55 | -57.55, 12.45 | 0.206 |
| **Father history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 12.77 | -9.02, 34.55 | 0.250 | 13.99 | -10.85, 38.83 | 0.269 |
| *Did not answer* | **34.14** | **2.56, 65.73** | **0.034** | 27.09 | -8.92, 63.10 | 0.140 |
| **Mother alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -0.31 | -57.19, 56.56 | 0.991 | 5.79 | -59.06, 70.64 | 0.861 |
| *Did not answer* | -18.37 | -71.10, 34.35 | 0.494 | 9.46 | -50.66, 69.57 | 0.757 |
| **Father alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 12.90 | -15.82, 41.63 | 0.378 | **34.54** | **1.78, 67.30** | **0.039** |
| *Did not answer* | 25.10 | -14.43, 64.63 | 0.213 | 18.63 | -26.45, 63.70 | 0.417 |
| **Principal adult education level** | | | | | | |
| *University* | — | — | | — | — | |
| *No university* | -6.16 | -22.80, 10.49 | 0.468 | -2.93 | -21.91, 16.05 | 0.762 |
| **Perceived parental support** | | | | | | |
| *A lot* | — | — | | — | — | |
| *None* | -36.99 | -129.33, 55.35 | 0.432 | -82.31 | -187.60, 22.98 | 0.125 |
| *A little* | 6.14 | -25.08, 37.35 | 0.700 | 3.36 | -32.24, 38.96 | 0.853 |
| *Moderate* | 16.94 | -1.63, 35.51 | 0.074 | 16.25 | -4.93, 37.43 | 0.132 |
| *Did not wish to respond* | -0.75 | -57.75, 56.26 | 0.979 | 11.44 | -53.56, 76.45 | 0.730 |

*Table VIII- Results for regression models with **amygdala grey matter volume** as the response variable, **Females***

| | Amy Left | | | Amy Right | | |
|---|---|---|---|---|---|---|
| Characteristic | Beta | 95% CI | p-value | Beta | 95% CI | p-value |
| **Family's Financial situation in childhood and adolescence** | | | | | | |
| *Comfortable* | — | — | | — | — | |
| *Difficult* | -2.05 | -17.12, 13.02 | 0.790 | 6.11 | -10.32, 22.55 | 0.466 |
| *Adequate* | 5.66 | -3.06, 14.38 | 0.203 | 6.32 | -3.19, 15.84 | 0.192 |
| **Age** | 0.59 | -1.12, 2.29 | 0.499 | 0.36 | -1.50, 2.22 | 0.706 |
| **Total intracranial volume** | **<0.01** | **>0.00, <0.01** | **<0.001** | **<0.01** | **>0.00, <0.01** | **<0.001** |
| **Mother history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -3.88 | -12.80, 5.04 | 0.394 | 0.34 | -9.39, 10.08 | 0.945 |
| *Did not answer* | -8.69 | -25.63, 8.24 | 0.314 | 9.56 | -8.91, 28.03 | 0.310 |
| **Father history of depression** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 6.99 | -3.78, 17.76 | 0.203 | 1.31 | -10.44, 13.06 | 0.827 |
| *Did not answer* | 6.22 | -9.04, 21.49 | 0.424 | -8.80 | -25.45, 7.85 | 0.300 |
| **Mother alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | 3.18 | -20.97, 27.33 | 0.796 | -4.72 | -31.06, 21.62 | 0.725 |
| *Did not answer* | 1.69 | -24.35, 27.74 | 0.899 | 4.49 | -23.92, 32.90 | 0.757 |
| **Father alcoholic history** | | | | | | |
| *No* | — | — | | — | — | |
| *Yes* | -5.27 | -19.46, 8.92 | 0.467 | -2.23 | -17.71, 13.25 | 0.778 |
| *Did not answer* | -10.26 | -28.29, 7.78 | 0.265 | -5.01 | -24.68, 14.66 | 0.618 |
| **Principal adult education level** | | | | | | |
| *University* | — | — | | — | — | |
| *No university* | -0.20 | -9.44, 9.04 | 0.966 | -1.57 | -11.65, 8.50 | 0.759 |
| **Perceived parental support** | | | | | | |
| *A lot* | — | — | | — | — | |
| *None* | **-33.51** | **-64.06, -2.97** | **0.032** | **-43.43** | **-76.74, -10.12** | **0.011** |
| *A little* | 9.13 | -9.36, 27.63 | 0.333 | 4.63 | -15.54, 24.80 | 0.653 |
| *Moderate* | -5.74 | -16.23, 4.75 | 0.283 | 3.20 | -8.24, 14.64 | 0.583 |
| *Did not wish to respond* | 32.06 | -3.43, 67.56 | 0.077 | 37.17 | -1.54, 75.89 | 0.060 |

# 4. Discussion

## 4.1 Synthesis of results and comparison with literature

### 4.1.1 Synthesis of results

The primary objective was to investigate the association between childhood and adolescent SES and grey matter volume in the hippocampus and amygdala. We found that participants having reported a ‘*difficult’* SES had significantly smaller left hippocampal grey matter volume than their counterparts having reported a ‘*comfortable’* SES. The right hippocampal and left and right amygdala grey matter volumes did not have any significant SES coefficients. Meanwhile, those who answered *‘none’* for perceived parental support in childhood and adolescence had significantly smaller left hippocampal, right amygdala and left amygdala grey matter volumes than those who answered, ‘*a lot’*. There was also a significantly larger right hippocampal grey matter volume for those with a principal adult having ‘*no university’*.

After stratifying for sex, we found that male participants having reported ‘*difficult’* SES still had significantly smaller left hippocampal grey matter volumes than those who reported having had a ‘*comfortable’* SES. This relationship was not retained in females. We also found that male participants having reported a *difficult* SES had significantly smaller right hippocampal grey matter volume than their counterparts having reported a *comfortable* SES. On the other hand, female participants did not have significantly differences in right hippocampal grey matter volume between levels of SES. This indicated that sex was an effect modifier in the relationship between right hippocampal grey matter volume and SES. We confirmed this by means of an interaction test, where the interaction term between SES x Sex was significant.

The population description allowed us to investigate SES based distributional differences across the variables. For SES, the differences in distribution of characteristics were almost entirely significant between participants who answered *‘comfortable’*, and their counterparts who answered *‘adequate’* and ‘*difficult*’. The lower the level of SES reported, the larger the proportion of parents divorced, history of depression and alcoholism in both parents, and the smaller the percentages in the principal adult at university level and high levels of parental support. These findings gave us an initial view on the importance of the variable in our data, and highlight the increased levels of adversity faced by those in less fortunate socioeconomic situations in childhood and adolescence. The variable captures several measures of adversity in childhood, and this could explain its association with grey matter volumes.

### 4.1.2 Interpretation with respect to the literature

As of 2023, there have been no studies to my knowledge investigating the relationship between SES and brain measures on university students and young adults in general in our age range, so this study was a first step towards closing that gap.

Before 2018, most of the studies on this topic had small sample sizes, with mixed results. Studies presented a range of measures for SES including income, neighbourhood poverty, and combined measures such as the Amherst modification of the Hollingshead two-factor index (Watt, 1976) (Hollingshead, 1957) (McDermott et al., 2019). For those studies using income as a measure, positive associations between both left and right hippocampal grey matter volume and income were present, meanwhile our results only found a positive association between self-reported SES and left hippocampal grey matter volume (Hanson et al., 2011) (Lotze et al., 2020).

There has been a growing interest in the use of neighbourhood poverty as a measure for SES in a bid to differentiate its effects from those of family income. One study found that hippocampal volume was positively associated with neighbourhood poverty, but not with family income (Taylor et al., 2020). Another found greater neighbourhood poverty to be associated with smaller hippocampal volume, in line with our results which used a self-reported economic situation measure (Assari, 2020).

Our research found that sex was an effect modifier in the association between right hippocampal volume and SES, such that this association was positive and significant in males, but not females. Even though previous studies have also stratified by sex, an interaction has not been found before for the hippocampus, implying further research is needed to investigate moderating effects of sex on this association (McDermott et al., 2019).

The literature has also found associations between amygdala volume and SES in both positive and negative directions (Rakesh and Whittle, 2021) (Assari, 2020). On the contrary, our research did not find any significant association between SES and amygdala grey matter volume.

## 4.2 **Strengths and limitations**

### 4.2.1 **Strengths**

Firstly, we can consider that the sample size analysed was large at 1828 participants. In fact, as found in the literature, it is rare to have large sample sizes in the field of neuroimaging due to the high cost of MRI examination (purchase of equipment, image acquisition and data processing).

In addition, our study regarding the method of acquisition of brain volumes uses validated image reading methods widely used in the literature. The measurements were all acquired by the same device and by a standardised procedure, to prevent potential measurement bias.

With the aid of the literature and the demographic tables, regression models were estimated and adjusted for other variables related to childhood and adolescence to mitigate for omitted variable bias on the coefficients.

### 4.2.2 **Limitations**

First, the recruitment inherent in the i-Share cohort and the MRi-Share study may have incorporated selection bias. Indeed, the inclusion of participants in this study was based on voluntary participation at two levels (for inclusion in the cohort, and then for participation in MRi-Share). The selection bias should be minimal as participants were not informed that a study on the association between SES and brain structure was going to be conducted. This may prevent a potential selection bias that could have affected these associations. Nevertheless, the generalisability of our results may be limited.

Secondly, could be measurement bias present in this research, given that the measurement of SES that is used is a self-reported measure of financial situation in childhood and adolescence. In addition, there could be omitted variable bias in the estimates of the direct effect of our SES variable given that we were unable to adjust for other measures of SES such as family income, neighbourhood poverty, and composite SES indices.

In addition, this cohort only included university students from Bordeaux. The fact that higher SES is linked with higher levels of education may decrease generalisability to the non-student population (*Education and Socioeconomic Status Factsheet*, n.d.). Also, as this was not a nationwide student study, city-based differences in student life could impact generalisability to other student populations in the country.

Another limitation is that only one MRI scan was performed, therefore it is a cross-sectional study. A longitudinal study with at least two MRI scans performed several years apart could allow the effect of developmental changes in grey matter structure still to come to be considered.

## 4.3 **Perspectives**

As a result of this work, further research and analysis should be carried out to improve the understanding of the association between SES and hippocampal and amygdala grey matter volumes. For example, lower SES has been linked to higher levels of stress and mental health problems, which are linked to reduced hippocampal and amygdala volumes (Baum, Garofalo and Yali, 1999; Weissman et al., 2020).

There have been many studies which use income as a principal indicator for SES, therefore one avenue of further research would be to increase prevalence of research of the effects of other measures of SES such as neighbourhood poverty along with combined measures. This would allow for comparison of the importance of different measures of SES on brain development, in a bid to investigate more possible interventions.

Furthermore, our study only considers grey matter volumes in the brain. It could also be interesting to investigate other measurements such as cortical thickness and surface area, which were found to be significantly smaller for those with low SES in the literature (Rakesh and Whittle, 2021).

In addition, it might be interesting to look at associations between SES and functional MRI data, which has little previous research. One study found a relationship between socioeconomic background and reading behaviour (Noble et al., 2006). It also indicated that at lower SES levels there are large differences in brain activation for individual skill differences.

# 5. **Conclusion**

The MRI-share study, which consisted of a large database with high-quality MRI images allowed for the exploration of the association between SES in childhood and adolescence and sub-cortical grey matter volumes among young adults from the i-share cohort, with stratification by sex. The results complement the existing literature surrounding the positive association between SES and left hippocampal grey matter volume, and indicate further research needed to investigate the role of sex as an effect modifier of the association between SES and right hippocampal grey matter volume. It also brought to light the possible association between low perceived parental support left hippocampal, right amygdala and left amygdala grey matter volume, which is another interesting prospect for further research.

As this is still a very new area of research there are not yet immediate implications on public health, however it does underline the possible biological impact of childhood and adolescent environment and therefore the importance of limiting consequences of adversity early in life.

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