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Emotional Processing in Institutionalized Adolescents Using an Affective Attachment-related Database - an fMRI study

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STATEMENT OF INTEGRITY

I hereby declare having conducted this academic work with integrity. I confirm that I have not used plagiarism or any form of undue use of information or falsification of results along the process leading to its elaboration. I further declare that I have fully acknowledged the Code of Ethical Conduct of the University of Minho.

Universidade do Minho, 04/09/2020

Assinatura: Ana Sofia Moreiras Pinto

Processamento emocional em adolescentes institucionalizados, durante a visualização de imagens afetivas relacionadas com vinculação- um estudo de fMRI

Resumo

A institucionalização é uma opção para crianças e adolescentes consideradas em risco, apesar de as privar de experiências expectáveis para o desenvolvimento típico, tais como o desenvolvimento de uma relação de vinculação com o cuidador. Ter uma relação de vinculação é um marco para as crianças, e um fator a ter em consideração quando se estuda o comportamento adolescente. Em relação ao impacto da institucionalização no processamento emocional e correlatos cerebrais, alguns estudos indicam dificuldades em áreas tipicamente associadas ao processamento de recompensas. Este estudo visa compreender o processamento cerebral de estímulos positivos relacionados com vinculação numa população de adolescentes institucionalizados. Para este fim, foram recrutados um grupo de adolescentes em acolhimento residencial, e um grupo de adolescentes que sempre viveu com as suas famílias biológicas. A tarefa experimental apresentada aos participantes foi uma tarefa de visualização passiva de imagens, utilizando a base de dados *Besançon Affective Picture Set-Adolescents* (*the BAPS-Ado*). Para este estudo, apenas foi analisada a categoria de imagens de *Joy-Complicity*, de imagens positivas mostrando cumplicidade entre amigos, pais e filhos e casais. Foram utilizados questionários de autorrelato sobre vinculação, os quais não revelaram diferenças entre os grupos. As diferenças entre os grupos surgiram na atividade cerebral, com o grupo institucionalizado a apresentar uma maior ativação no cerebelo, uma área recentemente associada a processamento emocional e estímulos sociais.

Palavras-chave: adolescência, acolhimento residencial, processamento emocional, vinculação, fMRI

Emotional processing in institutionalized adolescents using an affective attachment-related database- an fMRI study

Abstract

Institutionalization is a worldwide option for at-risk children and adolescents, despite depriving them of the expected experiences to typical development, such as creating a selective relationship with a caregiver. Having an attachment relationship is a milestone in children, and a factor to have into consideration when studying adolescent behaviour. Relative to the impact of institutionalization in the emotional processing and brain correlates some studies indicate alterations associated with reward system areas. This study aimed to understand the brain processing of positive stimulus, more specifically, attachment-related ones in a population of institutionalized adolescents. For this purpose, a group of adolescents currently living In institutional settings, and a group of adolescents in family care were recruited. The experimental task presented to the participants was a passive visualization task, using the Besançon Affective Picture Set-Adolescents (the BAPS-Ado) database. For this study, only the category of joy-complicity images was analysed, positive images showing complicity between friends or parents. The attachment-related self-report questionnaires did not reveal differences between the groups. Although, differences between groups emerged in the brain activity, with the institutional reared group having a higher activation in left cerebellum, an area recently associated with emotional processing and social stimuli.

Keywords: Adolescence, institutional rearing, emotional processing, attachment, fMRI

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Introduction

A vast number of children begin their early life in adverse situations that could result in them being considered at risk and consequently, in some cases, removed from their families. The Portuguese law, defines a child at risk to be children a) abandoned and living on their own, b) suffering from physical, mental or sexual abuse, c) not receiving care and affect appropriate for their age, d) whose parents don't practice the duties associated with their role, e) who have to do unappropriated work for their age, f) whose emotional balance and safety are being negatively affected, and g) those who are being engaged in situations or consumptions that affect their health, safety, education or development (Lei n 147/99. 3, 1999). For the children removed from their families, institutionalization is still a common practice. In Portugal for instance, in the year 2018, around 6118 (87%) of the children in this situation, lived in institutional rearing (Instituto de Segurança Social, 2019).

Along with Portugal, institutionalization is the current measure in some countries, despite being recognized as an adverse environment for children development, since it does not support normative development and often, compromises it. Additionally, it is considered an atypical experience of care and is consistent with the conceptualization of deprivation (Fareri & Tottenham, 2016). However, there are differences in the severity of the deprivation and the nature of the institutionalization between countries. In one hand, it is often seen in the literature descriptions of institutions with children in profound global deprivation, lacking adequate nutrition, sensory input (i.e., deprivation of touch, light stimulation), and linguistic and cognitive stimulation, having a profound effect on the brain development and in the appearance of severe medical, emotional and behavioural problems (Nelson, 2007). On the other hand, some institutional environments have satisfactory physical resources provided but lack the essential child-caregiver interactions, being considered "social-emotional deprived" (The St. Petersburg–USA Orphanage Research Team, 2005). Besides their differences, institutionalization is associated with maladjustment in cognitive, emotional, and behavioural domains, and in the shaping of the developing brain (Bick & Nelson, 2016; Nelson, 2007; Nelson III, Bos, Gunnar, & Sonuga-Barke, 2011).

Still, regarding the deprivation environment of institutional rearing, another aspect to consider is the hierarchy of needs, created by Gunnar (2001). It states the differences in the quality of caretaking taking into consideration health and nutrition, adequate cognitive, sensorimotor, social and linguistic stimulation and lastly, opportunities to have a stable relationship where an attachment is likely to develop. In this way, the

first level consists on global deprivation and it is the privation of all of the needs mentioned, the second concerns institutions that provide adequate health and nutrition but lack the remaining needs, and finally, the third level corresponds to institutions that appear to meet all the needs except for long, stable relationships with recurrent caregivers. Concerning this, the Portuguese institutions' environment was considered to be in the second level, and some are even considered to be in the third level (Baptista et al., 2014), being a socio-emotional deprived environment for the children.

Socio-emotional characteristics of institutional rearing

Typically, institutional rearing is characterized as i) having a high number of children per caregiver, ii) caregivers changing constantly, iii) little social sensitive interaction with the children, and iv) little training or care being handled by adults that come and go from the children's life (Ijzendoorn et al., 2011).

In this way, the environment does not provide the opportunity for the children to develop a stable and long-term relationship with a caregiver (Van Der Voort, Juffer, & Bakermans-Kranenburg, 2014). According to the attachment theory, only the repeated interaction and proximity with the caregiver can fulfil the children physiological needs, keeping the children safe and allowing them to develop resources of self-regulation and intern schemes of cognitive and emotional availability of the caregiver (i.e., the attachment figure), allowing them to feel worthy of love and secure (Bowlby, 1982).

Moreover, forming a selective relationship with a caregiver is a key aspect of normative development. Through emotional, cognitive, and social input, the caregiver provides support for behavioural and neural development (Bick & Nelson, 2016). Accordingly, institutionalized children revealed more insecure and disorganized attachments when compared to their peers, in the first year of life (Lionetti, Pastore, & Barone, 2015). Insecure or disorganized attachment puts the children at risk of adaptation on emotional and behavioural domains (Van Der Voort et al., 2014), and the lack of caregiver interactions compromises both physical and behavioural development (Ijzendoorn et al., 2011; McCall et al., 2019).

Hence, creating an attachment relationship with the caregiver is a significant milestone and an expected input from the environment. The absence, threats the brain of not reaching its potential, since the timing of the environmental input, heavily shapes the brain potential for normative development (Bick & Nelson, 2016).

Timing of the adversity

Recent studies suggest that by two years of life the human brain has the basic structural and functional framework and that the brain development occurring after is much slower. There is also evidence that the brain functional hierarchy also emerges during infancy. Primary functional networks are formed before birth and the new social, cognitive and emotional experiences parallel the emergence, growth and fine-tuning of the higher-order functional circuits (see Gilmore, Knickmeyer, & Gao, 2018). Consequently, the first years of the children life are considered a sensitive period, meaning a "time window(s) during which the effect of experience on brain development is unusually profound and can strongly modulate the neural circuits." (Ismail, Fatemi, & Johnston, 2017).

Accordingly, institutionalized children are deprived of opportunities needed to optimize development in critical times of development (Nelson III et al., 2011), regardless of the degree of deprivation, leading to underspecification or miswiring of brain circuits (Nelson, 2007).

Similarly, Mackes and colleagues (2020) observed that the exposure of severe deprivation limited to the first year of life corresponded to a linear reduction of the total brain volume in a deprived group of children compared to the nondeprived group of United Kingdom adoptees (Mackes et al., 2020).

That said, institutionalization is a multifaced phenomenon, where the environment of the institution and age of institutionalization interact having emotional and cognitive implications in the way children and later, adolescents, process the environmental inputs. However, adolescence in itself is a period of great changes and can be considered a sensitive period for environmental inputs.

Adolescence as a sensitive period

Adolescence is a sensitive period of development between 10 and 19 years of age (WHO, 2020) and marks the transition from childhood to adulthood. During this period there are great physical, social and emotional changes (Johnson & Wolke, 2013), combined with increased social autonomy and sensation-seeking behaviours that allow accumulation of novel, psychological, social and cognitive demanding experiences, and more sophisticated social interactions. Having these experiences, in the critical time of development of adolescence will lead to higher cognitive processes and more complex behaviours (e.g., socioemotional processing, planning, reasoning), and the development of the brain areas, such as prefrontal cortex (PFC), that support this more complex behaviours (Larsen & Luna, 2018).

Besides the development of PFC, this is also a period of brain remodulation, with network connections becoming more efficient, with more processing resources, including increasing connectivity between frontal and subcortical areas (Griffin, 2017). Nevertheless, it is a period of imbalance between the subcortical regions, such as the amygdala and ventral striatum, relative mature in adolescence, and the prefrontal control system immature during this period of development, accounting for a biased emotional behaviour, typically observed in adolescence (Somerville, Jones, & Casey, 2010).

In this sense, adolescence is a critical risk period for the development of socio-emotional disorders (e.g., major depressive disorder, anxiety disorder and eating disorders) (Rapee et al., 2019), highly influenced by the environment and experience (Dow-Edwards et al., 2019) and characterized by increase negative affectivity, mood dysregulation, and focus on the self (Rapee et al., 2019). As such, it can be a period of opportunities for positive changes in developmental trajectories or, conversely, it can be a period of vulnerability for the development of psychopathology (Larsen & Luna, 2018).

Having this in consideration, institutionalization in adolescence can be an adverse environment, leading to the development of psychopathology. This is illustrated, in a sample of the Bucharest Early Intervention Project (BEIP), which is to the date, "the first randomized controlled trial", comparing children assigned between the ages of 6 and 11 months, to three different groups: 1) A group that went to a foster care program, 2) a group that stayed in the institution (i.e., the care as usual group) and 3) a never institutionalized group. In a sample of adolescents that participated this project, differences between the adolescents in atypical care emerged in the adolescence period, with the adolescents that stayed in care as usual, having significantly higher levels of psychopathology when compared with ones in a foster care program (Wade, Fox, Zeanah, & Nelson, 2018).

Besides institutionalization, other factors influence adolescent's behaviour. For example, secure attachment relationships in adolescence negatively predict internalizing problems (Pace, Zappulla & Maggio, 2016). Thus, attachment is still an important factor to have into consideration when measuring emotional processing in adolescents.

Attachment relationships in adolescence

Adolescents are expected to have more romantic interests, become more responsible and independent academic wise, and have more social expectations in becoming a functioning member of society (Waylen & Wolke, 2004). This is coupled with a shift in attachment relationships, during early and middle adolescence resulting in a greater reliance on peers than on the caregivers for support (Furman & Buhrmester, 1992).

Additionally, in adolescence, there is this strong shared feeling of complicity with the peers, meaning shared intimacy, and support for the share of emotions and experiences (Werebe, 1987).

Nevertheless, despite turning to their peers for support and to fulfil attachment needs, caregivers are still important in adolescence, providing support for adolescents to explore other relationships (Nickerson & Nagle, 2005). As a matter, the quality of the relationship with peers was found to be influenced by the quality of the caregiver relationship, since secure attachment relationships with the caregivers were related to secure attachment relationship with friends (Gorrese & Ruggieri, 2012). Also, the security of the relationship representations with parents was associated with the quality of the friendship interaction (Shomaker & Furman, 2009). This goes in line with attachment theory, considering that the working models created in childhood continue to be influential in adolescence and adulthood since the interaction with the caregiver can create positive or negative views of themselves and others (Gillath, Karantzas, & Fraley, 2016)

Moreover, both adolescents' secure attachment with parents and peers was associated with more emotional and social competence (Laible, 2007). Additionally, feelings of isolation with peers were associated with more emotional problems, like anxiety, sadness, and worry (Schoeps, Mónaco, Cotolı, & Montoya-Castilla, 2020). Another longitudinal study suggested that insecure attachment with parents was predictive of later emotion problems in the adolescent, specifically depressive problems (Sund & Wichstrøm, 2002).

Altogether, emotional problems in adolescence are strongly associated with attachment relationships, both with peers, and caregivers. These difficulties make it relevant to explore the processing of emotional stimulus in this age, particularly when attachment related.

Impact of institutionalization on adolescent's emotional processing and brain correlates

Behavioural studies suggest difficulties in social and emotional processing in children and adolescents with a history of early adversity. For instance, young children showed to be less capable of engaging positively with positive and novel stimuli having more fearful responses when compared to maltreated children (Perry, DePasquale, Fisher, & Gunnar, 2019).

The socio-affective difficulties are supported by differences observed in brain development in older children and teenagers, and point towards long term impacts, such as in a study with Romanian adoptees (between 7.1 to 11.3 years old), indicating bilateral dysfunction of medial temporal structures including the amygdala, hippocampus and inferior temporal cortex (Chugani et al., 2001).

In this way, a variety of studies indicate an atypical greater activation of amygdala when exposed to negative stimuli when compared to same-age peers. An activation not observed in positive stimuli. Additionally, the time spent in institutional reared is positively correlated with the developmental impacts (Gee, Gabard-Durnam, et al., 2013; Maheu et al., 2010; Tottenham et al., 2011).

The Fronto-amygdala circuitry seems to be particularly sensitive to aberrant care such as institutionalization (Herzberg & Gunnar, 2020). This has been previously suggested to be an adaptation of institutionalization adversity, since children show an adult-like maturation, enhancing detection of negative stimuli and reducing the need for external regulation from a caregiver (Gee, Gabard-Durnam, et al., 2013; Gee, Humphreys, et al., 2013). However, while this could be helpful responding to a threat, it can also create a developmental cost to other neural systems leading to an impairing in positive emotion processing and reward (Herzberg & Gunnar, 2020).

Although less information is available concerning the processing of positive stimuli in this population, in a BEIP sample, institutionalized children required more information, i.e. more intensity of the displayed emotion, for identifying happy faces when compared to other children, in favourable environments. This was not the case for negative stimuli (Bick, Luyster, Fox, Zeanah, & Nelson, 2017).

In line with this, some studies suggest more blunted neural responses, such as a significantly lower activation of the nucleus accumbens (NAcc) while viewing happy and sad faces, in adolescents who have experienced early life stress, when compared with a comparison group. Differences only evident in adolescents participants (Goff et al., 2013).

Additionally, attachment quality also seems to play a role in emotional processing. In fact, in older children (mean age of 9,5-year-old), there was an activation of caudate and putamen, for a securely attached group, when compared to children insecurely attached, when viewing attachment-related scenes. These areas are strongly linked to reward and initiating behaviours motivationally relevant, thus authors suggest a strong motivation to be with their attachment figure while viewing attachment-related scenes (Choi, Taylor, Hong, Kim, & Yi, 2018).

Other studies have indicated that watching positive pictures activates areas of the reward circuitry, nucleus accumbens (NAc) and medial prefrontal cortex (mPFC), in adults. This activation is due to the emotional intensity of the images, instead of the arousal, since both erotic and romantic pictures had the same pattern of BOLD signal (Sabatinelli, Bradley, Lang, Costa, & Versace, 2007).

Altogether, while negative stimulus activates strongly fronto-amygdalar areas in institutionalized children, processing of positive stimulus seems to activate reward-related circuits when compared with peers. Additionally, activation in this area for securely attached children suggests the importance of these areas for the institutionalized population, which, as seen previously, it is evidenced to be at risk of abnormal attachment relationships.

Aim of the study

Bearing in mind the emotional processing problems found in the literature in children and adolescent who have experienced aberrant care, as well as the long term impact of that experience, this study aims to understand the impact of institutionalization on the brain function through an emotion processing task. Specifically, we will compare a group of institutionalized adolescents with never institutionalized ones to understand if there are differences in brain activity in these teenagers when visualizing positive stimuli– a less researched topic. Additionally, we will assess the impact of time of institutionalization and the role of adolescent's attachment perception with caregivers in brain activity. For this purpose, we will use validated attachment-related pictures, namely pictures that display a feeling of shared joy and complicity. Differences in emotion processing of the stimuli between groups are expected as well as differences in the attachment scores. Additionally, we intend to see whether attachment scores with caregivers, might influence the processing of the stimuli.

Specifically, the hypotheses are 1) Family-Reared group adolescents will have increase activation in the pre-frontal areas compared to institutional reared adolescents; 2) Institutionalized adolescents will exhibit lower activation in reward processing areas of the brain when compared to family-reared group adolescents; 3) Time spent in institutional rearing is negatively correlated with activation in reward processing areas of the brain; 4) Institutionalized adolescents will have lower attachment scores when compared to the family-reared adolescents.

Methodology

Participants

The sample was recruited from a bigger project and consisted of 13 participants (nine male) from two groups: an institutionalized group (IG) (n=5) that consisted of institutionally reared adolescents by the time of the assessment and the second, a family-reared comparison group (CG) (n=8), which consisted of adolescents raised in typical care with their biological families. The participants' ages ranged between 14 and

18 years old (M=15,8 years, SD= 1,21) and all the participants had Portuguese as the native language. Exclusion criteria included disabling genetic syndromes, autism spectrum disorder, having intellectual disabilities, serious clinical conditions, and anything that impossibilities collection of data (e.g., having a pacemaker, metallic implants, braces and tattoos in the head and neck).

Relative to the institutional-reared participants, this is the first protection measure for two of the participants but is the first time in institutional rearing for most of them (n=4). The length of institutionalization at assessment time ranged between 2 months and 180 months (*M*= 41,2, *SD*= 77,75) and the age of entry in the institution was between 3 and 18 years old (*M*=12,6, *SD* = 5,77). Institutionalization occurred due to a range of reasons, including neglect (n=4), being in a risk family (n=2), lack of habitational conditions (n=1), lack of parental competence (n=2), and dysfunctional relationship (n=2), and risk of physical maltreatment (n=1) risk of sexual abuse (n=1), risk of psychological maltreatment (n=3), and risk of being neglected (n=3). Lastly, all the participants had contact with the biologic families and four of them go home for the weekend weekly (n=2), or monthly (n=2).

Procedure

This study is part of a larger MRI research study "How does early adversity shapes brain function through DNA methylation? Unveiling the mechanisms of the problems of emotional and behavioural regulation in institutionalized teenagers." on Portuguese institutionalized teenagers approved by the Portuguese Social Services, the National Commission for Data Protection and from the Ethical Committee for Research in Life and Health Sciences from the University of Minho.

For the IG, the project was presented to the staff of the institution and the adolescents were asked if they had an interest in taking part in the experiment. Depending on the institution politics either the written informed consent was signed by the team responsible, or the biological parents of the participants. For the CG a convenience sample was used and written informed consent was asked from participants or biological parents.

The acquisition was in a Clinical Center (SMIC-Boavista) in Oporto. The total acquisition, of the multi-modal study, was 45 minutes for the image acquisition and 60 minutes for the different questionnaires, some described below.

Instruments/Measures

Sociodemographic information. The questionnaire was constructed by the investigators' team and was filled by the staff of the institution or by the adolescent caregiver. This was a comprehensive questionnaire with information about the school, health, filiation, and socioeconomic elements.

Attachment Profile. To have a dimensional analysis of the core structures that underlie attachment styles in older age (Collins & Read, 1990), we used the Adult Attachment scale Revised (AAS-R) (Adult Attachment scale; Collins & Read, 1990; Portuguese version: Canavarro, Dias, & Lima, 2006). This is a self-report questionnaire, composed of three factors. The first factor, "Anxiety", pertains anxiety in relations, such fear of abandonment, the second factor, "Close", reflect if the subject is comfortable with intimacy, and lastly, the third-factor "Dependent" regarding if individuals trust others. Each factor is composed of 6 items in a Likert- scale format, with "1" meaning "not characteristic in me" and "5" meaning, "extremely characteristic in me". The reliability of the scale for the Portuguese population is an alpha of Cronbach of .81 for the total scale (Canavarro et al., 2006).

For the evaluation of the adolescent perception of the quality of their relationships with parents or caregivers and peers, the Inventory of The Parent and Peer attachment Revised (IPPA-R) (Armsden & Greenberg, 1987; Portuguese Version: Neves, Soares, & Silva, 1999) was applied. It is a self-report questionnaire composed by three subscales: Trust, regarding trust, mutual respect and comprehension; Communication regarding the quality of verbal communication; Alienation regarding the feelings of isolation (Machado & Oliveira, 2007). The format of the questions is a 5-point Likert- scale with "1" meaning "Almost Never or Never True" and "5" meaning "Almost Always or Always True" and it's divided into 25 questions regarding the adolescents' feelings about the mother or father or adult that has that part in their lives (Part I), and about the friends (part II). To obtain the subscales total scores, the questions of each dimension were added. For the total attachment score the sum of the dimensions Communication and Trust were added and the sum of the score of alienation was subtracted, this was calculated for both parts separately (Greenberg & Armsden, n.d.). Additionally, is a reliable instrument in the population of Portuguese adolescents, with an alpha value of .87 (Machado & Oliveira, 2007).

The BAPS-Ado experimental task

The total experiment is composed of three parts: a passive visualisation task, a classification task, and an emotional assessment task.

For the passive visualization task, pictures from Besançon Affective Picture Set-Adolescents (the BAPS-Ado) were selected for each stimuli condition. The database is divided into three different emotional categories of stimuli, considered to be attachment-related, namely Distress, Comfort, Joy-Complicity and a Neutral. The first category depicted scenes of Distress, composed with images of faces expressing sadness and suffering or scenarios of loss and separation. The second category showed comfort-related situations such as a parent comforting an infant or an adolescent after an episode of distress. The third category presented joyful moments of shared complicity, with parent and child, peers, or partners interactions. Lastly, the fourth category was neutral scenarios of people walking in the street, subway, with no expression of emotions (Szymanska et al., 2015). For our study we used 10 pictures of each category, therefore, a total of 40 pictures were used in the fMRI experimental design.

Specifically, this task was composed of 8 blocks, two for each condition with 10 trials per block. The presenting time of each picture was 3800 milliseconds with an interstimulus interval of 200 milliseconds. In total, each block had a duration of 40000 milliseconds, i.e. 40 seconds with a rest interval of 18000 milliseconds between each block, making the total duration of the experiment 8 minutes. The stimuli were randomized within each block, but the order of presentation was the same for all the participants. The order being, Blocks = [4, 0, 1, 0, 2, 0, 3, 0, 1, 0, 3, 0, 4, 0, 2] with 0=Rest; 1=Neutral; 2=Comfort; 3=Complicity; 4=Distress- see figure 1.

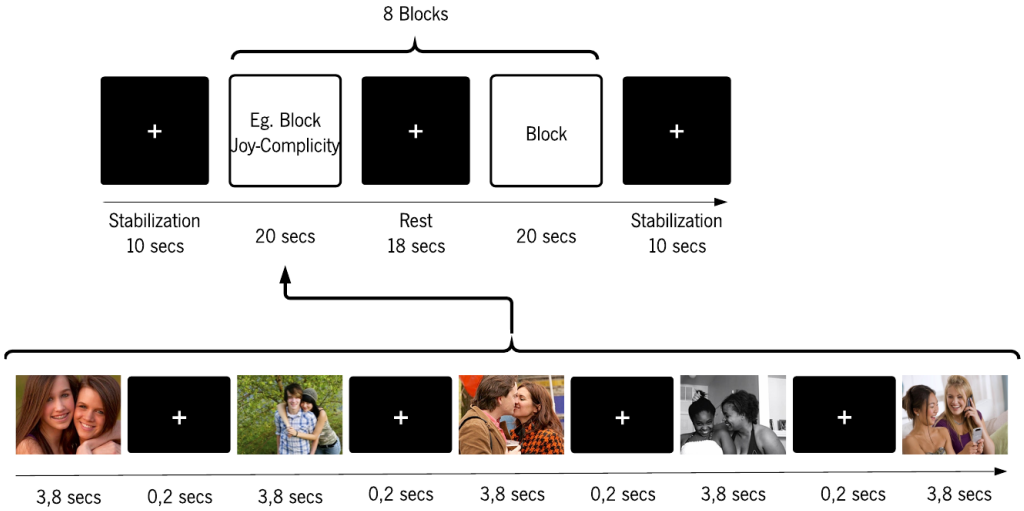

Figure 1. Scheme of the passive visualization task.

The participants were instructed to lay still since the task is visualization only but to stay attentive since in the end there was a small test about the pictures being visualised.

When the passive visualization was over and still within the scanner, there was the classification task. In this, the participants were told through the microphone that they were going to watch a set of pictures and they had to reply if they had previously seen the picture or if it is a new one. 16 pictures were presented, 8 of them have been presented previously and 8 are completely new, for each picture they have to answer "Was this pictured presented previously? Yes or No?" The participant has feedback for the response, appearing "Correct" or "Incorrect" according to the response.

Lastly, and to ensure the perception of the images was as in Szymanska et al., (2015), a computerized version of SAM (Self-Assessment Manikin) scale was presented to the participants. The objective of this task was to validate the arousal, valence, and dominance of each stimulus. Valence was rated from positive to negative with "1" meaning "happy" and "9" meaning "unhappy", the arousal being evaluated from hight to low, with "1" meaning "aroused" and "9" meaning "calm". For the dominance, it was rated from low to hight with "1" meaning "dominated" and "9" meaning "dominating".

For the fMRI analysis, we decided to include Joy-Complicity images. For this category, participants classified the joy-complicity images as positive (N=10; M=0,93, SD=0,21), and one participant classifying some of the images as neutral. Afterwards, the mean and standard deviation of the valence, arousal and dominance measures, assessed by the SAM scale, were calculated. The results are summarized in Table 1 and are similar to the Szymanska et al., (2015) paper.

Table 1

Summary statistic mean and standard deviation (S.D.) of valence, arousal, and dominance

	Joy-Complicity (n=10) Mean (SD)
Valence	3,07 (1,53)
Arousal	6,03 (2,28)
Dominance	6,03 (1,94)

Note. 1=Happy, 9=unhappy, 1=aroused, 9=calm, 1=dominated, and 9=dominating.

fMRI Data acquisition

Images were acquired on a clinical approved MRI Scanner, Siemen Magnetom TrioTim (Siemens Medical Solutions, Eralngen, Germany), with a configuration of 32 channels. The structural acquisition was

obtained with a MPRAGE (magnetization prepared rapid acquisition gradient echo) sequence. The established protocol was as follows – Repetition time (TR) = 2,700 ms, Echo time (TE) = 2,33 ms, Inversion Time (TI) = 1,000 ms, flip angle (FA)= 7°, field of view (FoV)= 256 mm, 192 slices and 0,8 mm voxel size. For functional acquisition a blood oxygenation level-dependent (BOLD) sensitive sequence was used with the parameters: TR= 2000 ms, TE= 29 ms, FA= 90°, FOV 256 mm^2, voxel size= 3 x 3 x 3.75 mm and 318 interleaved slices.

fMRI Data analysis

The fMRI data were analysed using the neuroimaging analysis toolbox SPM12 (Statistical Parametric Mapping, Welcome Trust Center for Neuroimaging, London, UK). For the image pre-processing, the functional imaging data had the following steps applied: slice-timing correction, motion correction, anatomical images co-registered to the functional images, followed by unified segmentation and estimation of normalization parameters used for registering to the MNI space with parameters from the T1 images. Images were than smoother (FWHM Gaussian kernel 8x8x8mm). For the first-level analysis, the contrast complicity > Neutral was established for each participant. The resulting contrast images were entered in a separated second-level analysis for group differences.

Relative to the second-level analysis, first, we performed the main effect analysis. Afterwards, we performed a two-sample t-test, whole-brain analysis, to compare between groups, using the following comparisons: Institutionalized group > Control group (IG>CG); Control Group > Institutionalized group (CG>IG).

Additionally, considering the previously discussed attachment with caregivers' patterns in institutionalized samples, we measured the impact of attachment in the group differences, during the passive visualization task. For this, we entered the Total Attachment Score, from Part I of the IPPA-R questionnaire in the model i.e. about the caregiver, as a covariate. Also, we measure how the attachment score with caregivers affects brain activation during the passive visualization task regardless of the group. For this, we used multiple regression analysis and assessed if there was a negative correlation between the brain activation maps and the Total Attachment Score (Attachment score -) and If there was a positive correlation (Attachment score +).

We also assessed the impact of the time of institutionalization in the brain activation maps. Therefore, we used only the IG for this analysis and using the same contrasts established In the first-level analysis (Complicity>neutron) we performed a multiple regression analysis using the time spent in institutionalization as a covariate. In this way, we used two contrasts, one for testing a positive correlation (Time+) and the other

to test a negative correlation (Time-), of the time spend in institutionalization and the brain activation during the Visualization Task.

All the clusters were determined using a based threshold of p< .001 (uncorrected) and a 50-voxel spatial extend.

Behavioural Data Analysis

The statistical analyses were conducted using the SPSS 25 software (Statistical Package for Social Science, IBM Corp.), and included assessment of the AAS-R, IPPA and the Classification task. For AAS-R we performed an independent sample t-test for the factors that met the assumptions underlying the use of parametric tests (Anxiety and Dependent) and the Mann-Whitney test for the remaining factor (Close). Similarly, in IPPA-R, exploratory data analysis revealed that the assumptions underlying the use of parametric tests were met for most factors, except for the factor Trust in the caregiver dimension. In this analysis, we performed an independent sample t-test for the parametric factors and Mann-Whiney test for the non-parametric factor. Lastly, for the Classification test, the information was collected with only 8 of the 13 participants, for this reason, we performed a descriptive analysis.

Results

Behavioural Data

Concerning AAS-R results, no differences between groups emerged in the factors Anxiety (t = .149, p = .302), Dependent (t = -.026, p = .604) and Close (Z = -1.388, p = .165).

Likewise in IPPA- R, no differences between groups emerged in the factors of Trust (Z = -.151, p = .880), Communication (t = -1.420, p = .355), Alienation (t = 1.525, p = .503) and attachment score (t = -1.091, p = .526). The adults used as reference by the CG were the mother (n=4), the father (n=3) and grandparent (N=1). For the IG, the adults used as reference were the mother (n=2), the grandparent (n=1), a social worker (n=1) and the psychologist (n=1).

Similarly, no group differences emerged regarding the teenagers perception of the relationship with the peers in the factors of Trust (t = 1.017, p = .062), Communication (t = .152, p = .877), Alienation (t = -.422, p = .065) and attachment score (t = .616, p = .236).

Concerning the classification of the experimental paradigm Images, all the participants responded correctly in the comfort pictures (100%). For the distress, neutral and the new pictures, they responded

correctly above 90% (93%). This was not verified in the Joy-complicity images, in which they responded correctly to only 57% of the images.

Neuroimaging Results

Main effect of Task

We first investigated the effects of Complicity-Joy images (Main effect), in the IG and CG. There was no observable suprathreshold voxels in either of the groups.

Group differences In the Joy-Complicity Condition

As mentioned above, the main interest of the study was to observe group differences, during the passive visualization of joy-complicity images.

We observed a higher activation of the left cerebellum in the IG ([-28, -52, -24]; k= 62; Z= 3,67), when compared to CG. No suprathreshold voxels were observed for the comparison between CG>IG -see table 2; figure 2.

Table 2

Between groups comparison during the visualization of Joy-Complicity images

Contrast	Coordinates (x y z)	Z value	Cluster-size	Regions
IG>CG	-28 -52 -24	3.67	62	Left Cerebellum
	-22 -46 -20	3.29		
	-30 -46 -30	3.26		

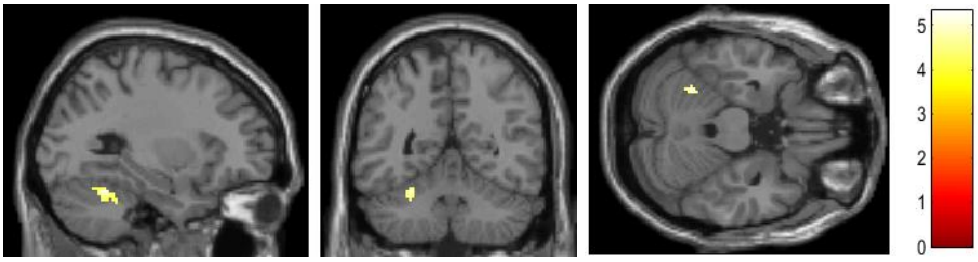

Figure 2. Sagittal, coronal e Axial view of Cerebellum activity of IG > CG during the visualization of Joy-Complicity images.

Interaction of Group and Attachment Score

To analyse if the group brain activation maps varied with attachment scores with caregivers, we entered Total attachment score with caregivers in the analysis, as a covariate. No suprathreshold voxels were found either for IG> CG and CG>IG when this score entered as a covariate.

Following the previous analysis, we analysed the impact of the Total Attachment Score with caregivers in the brain activation during the passive visualization task, regardless of the group. The analysis revealed a positive correlation between the Total Attachment Score with caregivers and brain activation in a variety of clusters during the visualization of the Joy-Complicity images, namely in Left Middle Occipital gyrus ([-22, -68, 28]; k= 463; Z= 3,96), and Right prefrontal Cortex ([22, 34, 44]; k= 282; Z= 3,69) -see table 3; figure 3. The opposite contrast, a negative correlation between Total Attachment Score with caregivers and brain activation did not reveal suprathreshold voxels.

Table 3

Correlation between Total Attachment Score with caregivers and activation during Visualization task

Contrast	Coordinates (x y z)	Z value	Cluster-size	Regions
Attachment Score +	-22 -68 28	3.96	463	Left Superior Occipital gyrus
	-20 -58 38	3.87		Left Superior Parietal gyrus
	-28 -52 42	3.75		
	-34 -62 26	3.50	57	Left Middle Occipital gyrus
	22 34 44	3.69	282	Right Superior frontal gyrus
	20 42 34	3.56		Right prefrontal Cortex
	12 42 46	3.36		
	38 54 0	3.46	59	Right Dorsal Prefrontal Cortex
	-34 50 0	3.69	67	Left Dorsal Prefrontal Cortex

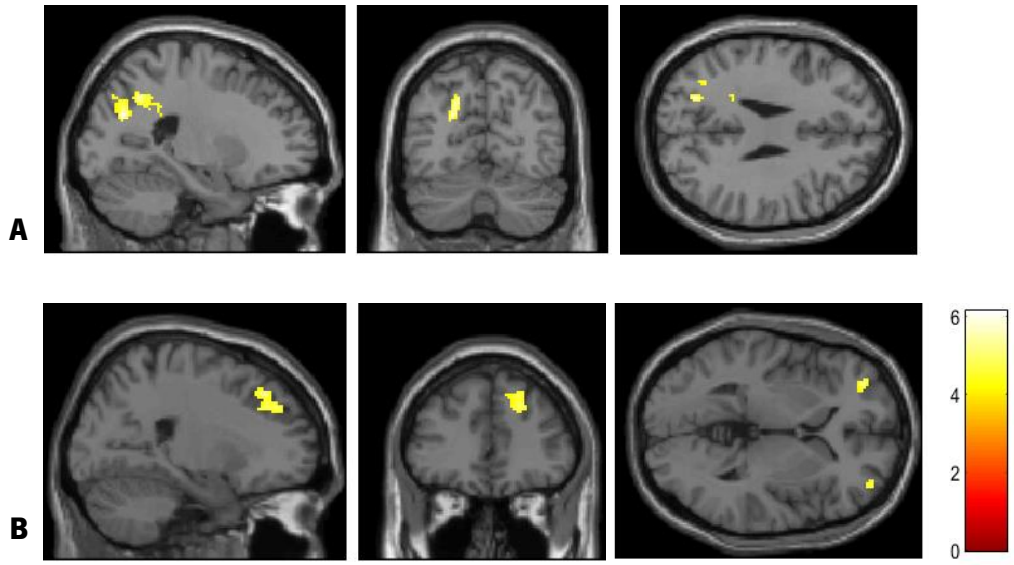

Figure 3. Sagittal, Coronal e Axial view of (A) Left Superior Occipital gyrus, and (B) Right Prefrontal Cortex activation for Total Attachment Score + during the Visualization of Joy Complicity Images.

Main effect of Time of institutionalization

As previously described, one of the variables of interest was the time spent in institutionalization. Therefore, we analysed the relation between time spend In Institutional rearing and brain activation during the visualization of the Joy-complicity Images in the IG. Results showed that less time in the institution (negative correlation) was associated with an increase activation in the right inferior occipital gyrus, ([48, -74, 0]; k= 72; Z= 4,28)- see table 3; figure 3. No suprathreshold voxels emerged for the positive correlation.

Table 4

Correlation between Time spent in institution and activation during the Visualization Task

Contrast	Coordinates (x y z)	Z value	Cluster-size	Regions
Time-	48 -74 0	4.28	72	Right inferior occipital gyrus
	52 -60 -10	3.82		
	42 -72 -8	3.79		

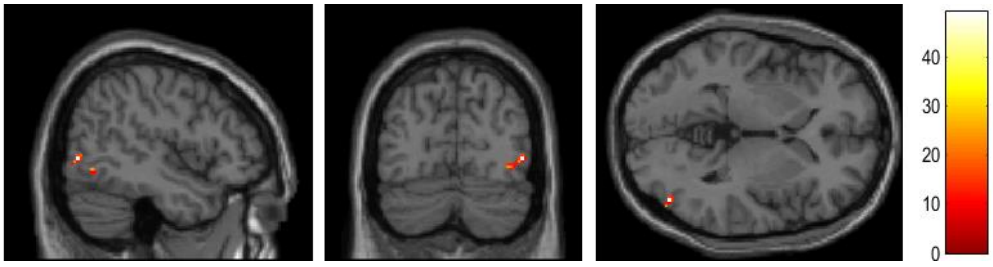

Figure 4. Sagittal, Coronal e Axial view of Right Inferior Occipital gyrus activation for Time- during the Visualization of Joy- Complicity images.

Discussion

The main goal of our study was to do evaluate the difference in brain activation between adolescents in typical care, and institutionalized ones. In our study, we used a paradigm with pictures from a validated database of attachment-related pictures, combined with attachment self-report measures, In order to control for attachment-related results. Specifically, for the present study, the category chose to be presented to the participants was joy-complicity. A variety of positive valence images, which is understudied in the institutionalized population (Herzberg & Gunnar, 2020), displaying close relationships among parent and child, peers, or partners.

First, differences emerged between groups during the processing of the images, as hypothesized, with the IG presenting greater activation, namely of the left cerebellum.

There is evidence of the cerebellum involvement in the implicit processing of happy facial expressions, supporting the cerebellum as a part of the affective processing (Critchley et al., 2000; Schutter, Enter, & Hoppenbrouwers, 2009). In a more recent study, targeting specifically the left cerebellum the data showed that there is an implication of this area in the emotional processing of faces even when the emotional processing is irrelevant for the task. Additionally, this region plays a specific role of extracting the emotional content of the faces instead of being part of the face perception network (Ferrari, Oldrati, Gallucci, Vecchi, & Cattaneo, 2018).

Significant activation of the cerebellum was also seen in adolescents during visualization of images of peers being accepted *versus* being rejected in an interactive experience of social exclusion paradigm (Masten, Eisenberger, Pfeifer, & Dapretto, 2013).

These previous studies show that cerebellum is an important brain area for the emotional processing of faces and particularly in peers' social interaction. The greater cerebellar response may be suggestive of implicit attention for positive social stimuli. Also, can reflect the left cerebellum sensitivity for institutionalization.

Accordingly, structural studies also showed that previously institutionalized children showed smaller cerebellar volumes suggesting an impact of social deprivation in this area (Bauer, Hanson, Pierson, Davidson, & Pollak, 2009). Evidence from animal studies presents this structure as a sensitive area for deprivation, measure as lack of maternal care that produces and altered connectivity of the cerebro-cerebellar circuits involved in the control of emotionality and cognition resulting in behavioural changes (Roque, Lajud, Valdez, & Torner, 2019).

However, for our sample, there is no information about early deprivation during the maturation of this area, known to maturate in the first year of life (Roque et al., 2019). Most of our participants started institutionalization in the period of adolescence. Although is important to notice that there is no detailed information about the quality of care in their biologic families, meaning that adverse experiences could have happened.

Admittedly, institutionalization can be a very stressful experience in this period of development, a period known to be o highly sensitivity to stress exposure, including increase sensitivity to psychopathology. Furthermore, stress exposure has been associated with cerebellar changes both in human and animal

studies, proving to be a sensitive area (Moreno-Rius, 2019). Also, the cerebellar-subserved functions continue to improve during childhood and adolescence, suggesting a longer developmental course for this area (Tiemeier et al., 2010).

All in all, Cerebellum seems to have a sensitive period of development in adolescence as well, that coupled with the stress of undergoing through institutionalization could have had an impact in this structure.

Along with the differences between groups regarding institutionalization, the differences observed could be related to attachment differences expected in the participants since the joy-complicity images are attachment-related and expected to be relevant for the adolescence period. To control for this, a self-report measure of attachment was used.

Differences between groups were not found when accounting for Total Attachment score with caregivers, what could mean that this is a relevant variable to have into account to explain the higher activation of the cerebellum during the visualization of the stimuli used.

Furthermore, when accounting for the activation in the participant's brain activation maps when accounting for the attachment scores with caregivers, regardless of the group, a positive correlation emerged. This activation indicates that greater scores of Attachment with the caregivers result in higher activations in Occipital and Frontal areas.

First, regarding Prefrontal activations, in typical development, there is a developmental decrease of the activation in the limbic subcortical area while activation in frontal regions increases, prefrontal cortex, during emotion regulation (Hare et al., 2008; Vink, Derks, Hoogendam, Hillegers, & Kahn, 2014). This suggests an increase in frontal control over cortical regions in adolescence, on emotional processing (Marusak, Martin, Etkin, & Thomason, 2015). The activation found can suggest that the images presented to the participants were more emotionally relevant, for the participants with greater attachment scores.

Additionally, in our study, we observed bilateral activation in Dorsal Prefrontal Cortex. This activation can be related to an affective evaluation of the scene presented to the participants since a bilateral activation of dorsolateral prefrontal areas has been observed during the processing of emotional attachment-related scenes. An activation not observed in insure children. The authors suggested that secure attachment is functionally correlated with frontal areas that support the skill of understanding the state of mind of others (Choi et al., 2018). In this way, the stimuli may not be more relevant for the adolescents with greater attachment scores, but that they may be better in understanding the state of mind of people in the images presented to them.

These conclusions should be interpreted with caution but highlight the involvement of such structures in the cognitive processing of these positive stimuli, In adolescents with greater attachment score.

Having in consideration all the above, differences in participants don't seem to be explained by the hypothesis presented previously, since the IG did not present blunted activation in the typical reward processing areas when compared to CG.

However, the research in cerebellum points towards a strong role in this area in affective processing, and not only the traditional motor role. Interestingly, recent studies with mouse, show a strong projection from the cerebellum to the ventral tegmental area (VTA), despite not being clear, how does it contribute to social behaviour and reward processing. The authors also conclude that the cerebellum contacts with the VTA neurons that contact to the NAc (Carta, Chen, Schott, Dorizan, & Khodakhah, 2019).

Following this, even though there was no activation in the reward processing areas, it would be expected that the differences found on the activation of left cerebellum would be correlated to more time spend in institutionalization. This was not observed in the analysis. Still, we found a negative correlation between time spent in institutionalization, and Right Inferior Occipital gyrus, meaning that more time in institutional rearing is related to less activation of this area, during visualization of the complicity images. This effect could be associated with visual perception since the causal role of this area for the perception of the individuality of the face was found previously (Jonas et al., 2014).

Finally, for the behavioural results, no differences were found in the groups in the attachment measures, as it was expected. Suggesting that in this sample, the institutionalized teenagers have normative relationships with their peers and caregiver figures and the same perception of the core features of attachment styles as their peers. Relative to the caregiver, this can be, for instance, an indication of less adverse backgrounds in these adolescents. In another point of view, two participants chose as reference caregiver the psychologist and the social worker. This can be indicative of professionals' competence, reflecting the emergence of an attachment relationship. Regarding the relationship with peers, a study with Portuguese institutionalized teenagers suggests that despite the negative schemes that the adolescent may have, the peer's relationships create a new opportunity for the secure attachment of adolescents, crucial for communication skills and feelings of trust (Pinheiro Mota & Matos, 2013).

Concerning the Classification test, this information was only collected with 8 of the 13 participants. However, is surprising that the in the joy-complicity images used in the study, the participants only responded correctly to 53%, this was specific to this category since all the other stimuli had higher than 90% rates of

right responses As stated earlier in this work, institutionalized children need more information identifying happy faces when compared to typical care children (Bick et al., 2017), but only two participants from the IG responded to this part. We could argue that the emotional relevance of the stimuli was not enough for the participants to remember but neutral pictures had high rates of correct responses.

In summary, differences between groups emerged, that can be accounted for by the effect of the institutionalization. The main result found, was the difference in the activation between groups in the Left Cerebellum, an area with complex connections and very heterogenic in the functional connectivity within the cerebral cortex. Additionally, the limbic cerebellum Is incorporated into the neural circuits necessary for emotion processing (Schmahmann, 2019). Furthermore, is an area sensitive to stress and previously found to be associated with deprivation.

In this way, even though we were not able to verify our hypothesis, this can be a starting point for the understanding of the positive stimuli processing in this population.

Limitations

Although interesting results emerged in this study, some limitations need to be considered.

The main limitation of this study is in the sample. First, regarding the number of participants. There were only 13 participants in total, and only 5 belonged to the IG. As a result, caution is need when accounting for conclusions since the smaller sample size translates in less power of the activations. Second, concerning the characteristics of the sample used, most of the participants in IG, wherein institutional rearing for just some months, and there is no information about the life of the adolescents before institutional rearing. Some difficulties with the caregivers before institutionalization can be accounting for the differences, but this is all speculation. Also, concerning attachment relationships, differences were not observed between groups, this can mean that the groups compared were not different in this regard.

Some problems must be taken into consideration in the methodology. About the experimental visualization task, it would be optimal if there were more pictures in the paradigm since participants saw only 20 pictures of each category in total. Additionally, the results may be due to the positive valence of the pictures, and not because of the social and attachment-related component of them.

Another important consideration is the Classification test, that showed only 53% right responses in the category of images used, this result can be a big limitation of our study, since show that the other images in this study were more relevant for the participants that the ones used.

Future Directions

Certainly, a variety of answers remain unanswered. The differences between adolescents in typical care and institutionalized ones regarding the processing of attachment-related images are important and could be further explored. For this, it would be interesting to use the complete database Baps-Ado. Additionally, the way the processing of emotional related scenes is related to attachment with peers and romantic partners should be considered.

Regarding the activations found in our study, the number of participants did not allow to account for sex differences which would be important since developmental trajectories of the cerebellum are sexually dimorphic (Tiemeier et al., 2010). Moreover, differences in the processing of positive emotional stimuli are not well studied and it is important to expand the field of study beyond frontolimbic circuitries. Additionally, in this study, it was not clear the reason why the IG had higher activation, besides the speculation that could be due to implicit attention to the positive stimulus. For this, it would be interesting to use positive face pictures without the attachment component in institutional rearing participants compared to typical ones.

Another important point that should be taken into consideration is psychopathology. Self-report measures could be used to account for the differences in the processing of positive stimuli.

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Annex

Ethics Committee document

Universidade do Minho

SECVS

Subcomissão de Ética para as Ciências da Vida e da Saúde

Identificação do documento: SECVS 022/2016

Título do projeto: *Avaliação do funcionamento cerebral em repouso e dependente de tarefa em adolescentes com distintas trajetórias de desenvolvimento: contribuição de mecanismos epigenéticos*

Investigador(a) responsável: Doutora Isabel Soares, Doutora Adriana Sampaio e Doutora Ana Mesquita, Escola de Psicologia, Universidade do Minho,

Subunidade orgânica: Centro de Investigação em Psicologia – CIPsi, Escola de Psicologia, Universidade do Minho

Outras Unidades: Instituto de Segurança Social, I.P.

PARECER

A Subcomissão de Ética para as Ciências da Vida e da Saúde (SECVS) analisou o processo relativo ao projeto intitulado *"Avaliação do funcionamento cerebral em repouso e dependente de tarefa em adolescentes com distintas trajetórias de desenvolvimento: contribuição de mecanismos epigenéticos"*.

Os documentos apresentados revelam que o projeto obedece aos requisitos exigidos para as boas práticas na experimentação com humanos, em conformidade com o Guião para submissão de processos a apreciar pela Subcomissão de Ética para as Ciências da Vida e da Saúde.

Face ao exposto, a SECVS nada tem a opor à realização do projeto.

Braga, 29 de setembro de 2016.

A Presidente

MARIA CECÍLIA DE LEMOS PINTO ESTRELA LEÃO

Digitally signed by MARIA CECÍLIA DE LEMOS PINTO ESTRELA LEÃO
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