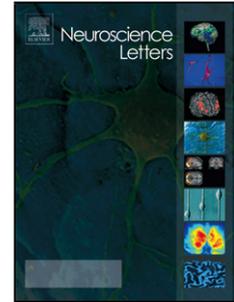# Accepted Manuscript

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Association between self-reported impulsiveness and gray matter volume in healthy adults. An exploratory MRI study

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Highlights

- The variations in fronto-temporal and posterior cerebral areas are crucial for BIS in healthy adults.

- Greater SFD was associated with a decreased GMV in parieto-temporal areas.

- This study suggests that a higher SFD increases self reported impulsiveness.

Abstract

This exploratory study investigated the association between self-reported impulsiveness and cortical gray matter volume (GMV) of the entire cortex in healthy adults. As a secondary objective and based on preliminary findings concerning the positive association between self-reported impulsiveness and the slant of the forehead degrees (SFD), we analyzed associations between SFD, GMV and impulsiveness. We obtained 48 structural magnetic resonances. The participants also completed BIS 11 and profile pictures were obtained. SFD was measured by a photographic support and a protractor. The GMV of the whole cortex was obtained for each participant through Freesurfer. Firstly, we found negative and positive correlations between fronto-temporal and occipital areas respectively and BIS. Second, we found negative correlations between SFD and GMV in right postcentral gyrus, right caudal middle frontal gyrus, right transverse temporal cortex and positive correlation in left entorhinal cortex. Third, we observed a positive correlation between SFD and BIS in all impulsiveness scores. In conclusion, variations in fronto-temporal and posterior cerebral areas are crucial for BIS in healthy adults. Furthermore, SFD was associated with BIS and correlated with GMV areas involved in self-reported impulsiveness.

1. Introduction

Impulsiveness is a personality trait [1] that is generally associated with an "tendency to engage in rash actions without deliberation" [2]. Presently, it is regarded as a multidimensional psychological construct [3] and different neurobiological factors seem to be involved [4]. Therefore, there is a large body of knowledge, where different conceptualizations have arisen with some etiological controversy. [5, 6].

Advances in structural neuroimaging studies suggest high implication of prefrontal cortex on behavioral control [7]. Using Voxel Based Morphometry (VBM) with healthy subjects, it has been found that orbitofrontal bilateral grey matter volume (GMV) correlated inversely with non-planning impulsiveness and motor impulsiveness from BIS, as well as, left anterior cingulate cortex with total score [8]. Other impulsiveness measures have also observed reduced orbitofrontal GMV in healthy adults [9]. Furthermore, BIS scores has been associated with a decrease in cortical thickness (CT) in the fronto-temporal areas [10, 11, 12]. On the other hand, positive associations had been observed in anterior cerebral areas [13, 14, 15].

In clinical population, structural studies have also found negative associations between impulsiveness and GMV in the orbitofrontal cortex, anterior cingulate cortex, parietal and temporal lobes [16, 17]. Recently, by using BIS, its total score was associated with identified damage from multiple areas of bilateral prefrontal cortex, left superior cortex gyrus, middle and inferior temporal gyrus [18]. This reveals that solid evidence seems to suggest that fronto-temporal variations play a crucial role in impulsiveness assessed with BIS, although it is not clear the correlation of these regions with the different factors.

However, there appears to be greater consistency on structural variations of the cortex in clinical subjects than in healthy subjects. Thus, our aim is to explore in healthy adults

the GMV of the entire cerebral cortex to identify relevant structures associated with impulsiveness measured with BIS [19].

On the other hand, few studies have considered a relationship between craniofacial structure and self-reported impulsiveness. In this sense, two recent papers have observed a positive association between self-reported impulsiveness and the slant forehead degrees (SFD) [20, 21]. Therefore, as a secondary objective based on these previous findings and since there are differences in the inclination of the forehead, we consider confirming this relationship in our sample. We also considered exploring the relationship between SFD and the GMV of the entire cortex, a relationship, to our knowledge it hasn't been investigated yet.

2. Material and methods

2.1. *Participants*

In order to recruit our sample, two advertisements were placed in training centers and libraries of Barcelona city (Spain). The sample consisted of 48 right-handed volunteers. (66.7% male) with an age mean of 36.2 years-old (SD = 9.9). Their academic level was elementary in 7 subjects (14.6%), intermediate in 16 subjects (33.3%) and high in 25 subjects (52.1%). All volunteers according to Mini-International Neuropsychiatric Interview [22] were healthy. Participants completed BIS and after that they went on to take a profile picture, whose method will be further detailed later. Finally, an appointment was made for magnetic resonance. Each participant signed an informed consent before entering the study and agreed on the use of data for research purposes. The study was approved by the Universitat Autònoma of Barcelona and followed the ethical standards defined in the Declaration of Helsinki.

2.2. *Impulsiveness measurement*

Barratt Impulsiveness Scale (BIS-11) [19]. The Spanish version of the instrument was applied [23]. It has 30 items scored in a Likert-type scale (0: rarely or never, 1: occasionally, 3: often, 4: always or almost always). A higher score indicates greater impulsivity. It has three sub-scales: attentional impulsiveness (8 items), motor impulsiveness (10 items), and non-planning impulsiveness (12 items). Internal consistency in our sample took values of Cronbach's alpha= .836 for the total score, and .476, .705 and .669 for the 3 previous subscales. In a personal communication, Barratt said the scale can be used as follows: 1 rated as 0, 2 as 1, 3 as 3, 4 as 4 (Cited in Oquendo et al. [23]).

2.3. *Measurement of the slant forehead degrees*

Firstly, the profile photographs were taken by a digital reflex Canon camera model EOS 1100 D EF-S 18-55. To avoid any optical distortions, the participants remained seated on a chair previously fixed to a place by the researcher. To that end, they were trained to slant their heads upwards and downwards, until they felt relaxed and adopted a natural head position (NHP) [24]. Therefore, the edge of the photograph was regarded as the true vertical (TV) and as a reference in the measurement of the SFD. The digital photographs were printed in black and white in format DIN-A4 and in vertical position. The degrees of the angle of the forehead inclination were measured by a semicircular protractor brand Staedtler 568 with a 10cm ruler. Two anthropometric points of reference were taken from the methodology created by Farkas [25]: trichion or the point in the middle line of the forehead, which is placed in the hairline, and glabella or the point of the most prominent middle line between both eyelashes. The vertex of the angle was fixed

on the glabella, from which two lines were drawn. Line 1 was vertically drawn, parallel to the edge of the photograph TV and was set as 0º. Line 2 was drawn from the glabella to the trichion. The SFD was measured as the angle, in degrees, formed by the line that goes from the glabella to the trichion (see figure 1). The same measurement procedure can be observed in a previous study [21]. Each participant was independently measured by three experts in craniofacial morphology. The agreement between observers was very high with intraclass correlation coefficient *CCI* = .99. With these results, the average of the SFD was used in posterior analyses.

2.4. *Magnetic Resonance imaging acquisition*

Magnetic resonance imaging (MRI) scans were obtained using 1.5 T (GE BRIVO). High-resolution 3D-FSPGR images, powered in T_1 were taken for each participant. The acquisition parameters were the following: TE= minimum; TI= 300 ms; Flip Angle= 20º; 130 adjacent axial sections; mould 256 x 256, 25 cm FoV; Slice Thickness = 1.2 mm; Receiver Bandwidth 15.63 Khz.

2.5. *Structural MRI data preprocessing*

Data obtained from MRI was processed using Freesurfer 5.3.0 software (http://surfer.nmr.mgh.harvard.edu). Automatic volumetry performed by Freesurfer is a quantitative measurement of specific brain regions, which has been validated in several psychiatric and neurological domains [26]. Freesurfer provides information on the following areas: frontal lobe (superior frontal gyrus, rostral and caudal middle frontal gyrus, parsopercularis, parstriangularis, and parsorbitalis gyrus, lateral and medial orbitofrontal cortex, precentral gyrus, paracentral and frontalpole), parietal lobe (superior

parietal, inferior parietal, supramarginal, postcentral and precuneus), temporal lobe (superior temporal, middle and inferior temporal gyrus , banks of the superior, fusiform gyrus, transverse temporal cortex, entorhinal cortex, temporal pole and parahippocampal gyrus), occipital lobe (lateral occipital cortex, cuneus, lingual gyrus and pericalcarine cortex), cingulate cortex (rostral anterior cingulate cortex, caudal anterior cingulate cortex, posterior cingulate cortex e, isthmus cingulate cortex). In this exploratory study all areas were analyzed and all specifications about Freesurfer parcellations, including reliability, validity and anatomic limits has been described [27]. The images were visually inspected to detect structural artifacts and abnormalities, finding that none of the segmentations needed to be corrected.

2.6. Statistical analysis

Data was analyzed with Stata 14. To analyze the association between BIS and GMV and SFD adjusted Pearson correlation coefficient was calculated, previous verification of linearity of the relationships. Academic level and age were introduced in correlation analysis as adjustment terms. The *ICC* was calculated for interobserver agreement in the SFD measurement. Type I error was set at the usual 0.05 level. With the aim of not hiding possible relevant associations and because exploratory nature of our research, without a priori hypothesis, no correction of the Type I error was applied to results presented in the tables [28].

3. Results

Table 1 shows a description of the BIS scores and the SFD. There are no cut-off values well established for BIS scores. Impulsiveness in our sample has similar mean values to those obtained in the Spanish validation of the questionnaire [23].

3.1. Association between BIS and GMV

Table 2 shows adjusted correlations between BIS and GMV for the areas with at least one statistically significant result. Overall there were five significant negative correlations (three in right and two in left hemisphere) and seven positives (five in right and two in left hemisphere). Practically all of them had absolute correlation values above .3. Right lingual area showed the highest association because having three out four correlations statistically significant. About impulsiveness, non-planning has correlated significantly with six brain regions (five negative and one positive).

3.2. Association between BIS and SFD

Last row of Table 2 presents correlation between impulsiveness and SFD. All the results are positive and highly significant, with two correlation values above .4.

3.3. Association between SFD and GMV

Figure 2 presents statistically significant adjusted correlations between SFD and GMV. Four significant results were found, the three negatives with areas located in right hemisphere and the only positive was located in the left one. As in previous analysis absolute correlation values were all above .3.

4. Discussion

In the present exploratory study, we have found significant correlations, both positive and negative, between BIS and GMV in all cerebral areas. On our second objective, a greater SFD was associated with a decreased GMV in parieto-temporal areas and we found that greater SFD was associated with higher impulsiveness.

Firstly, we note that BIS scores have correlated with the four brain lobes. This observation supports that a great number of brain areas seem to be involved on impulsiveness [4] and that the BIS factors correspond to different neurological substrates [1, 29]. Specifically, our data shows that attentional impulsiveness has positively correlated with GMV in front-temporal areas. Fusiform gyrus is included in temporal lobe [27] whose variations in GMV [14, 30, 31] and CT [11] are involved on impulsiveness traits in healthy adults. Our finding in fusiform gyrus supports the previous studies, although the observation in frontal area appears to provide more evidence. This region is implicated in impulsive decision and impulsive control [14, 32, 33] and a crucial role of the cingulate cortex has been suggested in response inhibition [34] and attention impulsiveness [31]. Also, precentral gyrus has been implicated in inhibitory control [35] and control of response inhibition [36].

In addition, by using surface-based analysis, attention impulsiveness was positively correlated with the precentral gyrus [31]. This is consistent with our finding in precentral gyrus and supports the evidence of increased GMV in front-temporal areas on attentional impulsiveness in healthy adults. However, other studies by using VBM did not find significant variations in GMV in this factor [8].

With respect to motor impulsiveness, our finding in right lingual gyrus reveals the existence of increased GMV for this factor. This finding is consistent with previous studies. Lingual gyrus is included in occipital lobe [27] and recently, Barratt

impulsiveness was associated with higher GMV in areas of the occipital sulcus bilaterally [37] and motor impulsiveness was positively correlated with lingual gyrus [31]. However, in rostral anterior cingulate cortex it seems that variations are not so clear, at least, in healthy adults. In fact, we found a decrease whit motor impulsiveness which contrasts with the reported increase in anterior cingulate cortex for non-planning impulsiveness [13]. In the current study, non-planning impulsiveness, has correlated with the largest number of brain regions. We have observed an increase in right caudal anterior cingulate cortex and decreased in the left hemisphere. This suggests a volumetric asymmetry of this region in its correlation with non-planning impulsiveness. In this direction, it is not surprising to find variations in this region, since it has been associated with impulse control, novelty seeking, persistence and impulse behavior [29, 14] and a crucial role in action monitoring has been suggested [34]. In this factor, we have also found decreased in right parsopercularis gyrus, whose area is involved in careful thinking and planning [38] and has also been observed positive correlation in local gyrification index of this region [31]. Although, it is also not clear the variations in parsopercularis gyrus, along with our fact, these findings might point towards interaction between inferior frontal cortex that is associated with non-planning impulsiveness [39].

Other areas that have also negatively correlated with non-planning impulsiveness in our study were right postcentral gyrus and right transverse temporal cortex. Postcentral gyrus is included in parietal lobe [27]. In contrast, Barratt impulsiveness is associated with higher GMV in areas of the parietal sulcus bilaterally [37] and this area has been implicated in inhibitory control [35]. Conversely, emotion-based rash impulsivity was associated with smaller GMV in right temporal pole [40]. This finding is consistent with our observation in right transverse temporal cortex, though contrary to what was found

by other authors in CT [11]. This region could be involved in the general impulsivity [41] and the regulation of social care [42] so it seems logical to find changes in this region.

However more studies are needed to assess GMV's changes in this area in healthy adults. In addition, it appears that variations in all cortical regions in healthy adults with higher impulsiveness are not clear, nevertheless, there seems to be growing evidence of increased occipital regions. Our results appear to support this hypothesis. Thus, non-planning impulsiveness and total score have also positively correlated with lingual gyrus, whose region is part of occipital lobe [27]. Recently, in local gyrification index by using a surface-based analysis was also found a positive association between attention impulsiveness, motor impulsiveness and right lingual gyrus. This result may suggest that increased GMV in right lingual gyrus may be an influence structural correlate on BIS in healthy adults.

Respect to our secondary objective, at higher SFD, GMV decreases in right caudal middle frontal gyrus, right post central gyrus and right transverse temporal cortex were observed, as well as an increase in left entorhinal cortex.

Our exploration should be considered with caution, since as far as our review goes no studies have been found to compare our results. In fact, it is not clear whether SFD influences the underlying frontal tissue or other structures. However, it should be noted that SFD has not significantly correlated with posterior areas of the brain, whose observation seems to be expected given that frontal lobes influence the shape of the forehead [43]. Besides that, we observed a generalized positive correlation between SFD and impulsiveness, which is consistent with two previous studies [20, 21]. These results seem to suggest that greater SFD may be associated with increased in self-reported impulsiveness.

Some limitations of this study should be noted. Firstly, the sample size was modest, which may limit the generalization of the results. However, the sample size is in the range of comparable previous studies [9, 11]. Second, our work has focused exclusively on subjective measures of impulsiveness. In this context, differences between self-report and behavioural measures have been observed [44] so we must be careful and limit our findings to BIS. Furthermore, internal consistency for attentional impulsiveness was low (.476) suggesting that conclusions related to this dimension of impulsivity may be biased. However, it was found that only 2 of the 8 items on the subscale had low correlations with the rest (items 4 and 24), and that excluding them the alpha value went up to 0.65. For this reason we decided to maintain the original definition of the subscale and to interpret results based on it. Finally, in studies investigating structural correlates of impulsiveness, studies using VBM are now more frequent [38, 14, 8]. However, GMV derived from VBM is a composite measure depending on the variability of cortical thickness, area and gyrification and each of these parameters could have a different impact on GMV [45]. On the other hand, it has been described that FreeSurfer provides equivalent accuracy to other brain volumetric methods used [46].

5. Conclusions

The current study provide evidence about the involvement of numerous areas in self-reported impulsiveness on healthy adults. On the other hand, changes were observed in all brain lobules except the occipital area, so more studies will be needed to clarify whether SFD influences anterior and posterior brain tissue. Finally, this study suggests that a higher SFD increases self reported impulsiveness.

Acknowledgements

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Figure 1. Measurement of the angle of
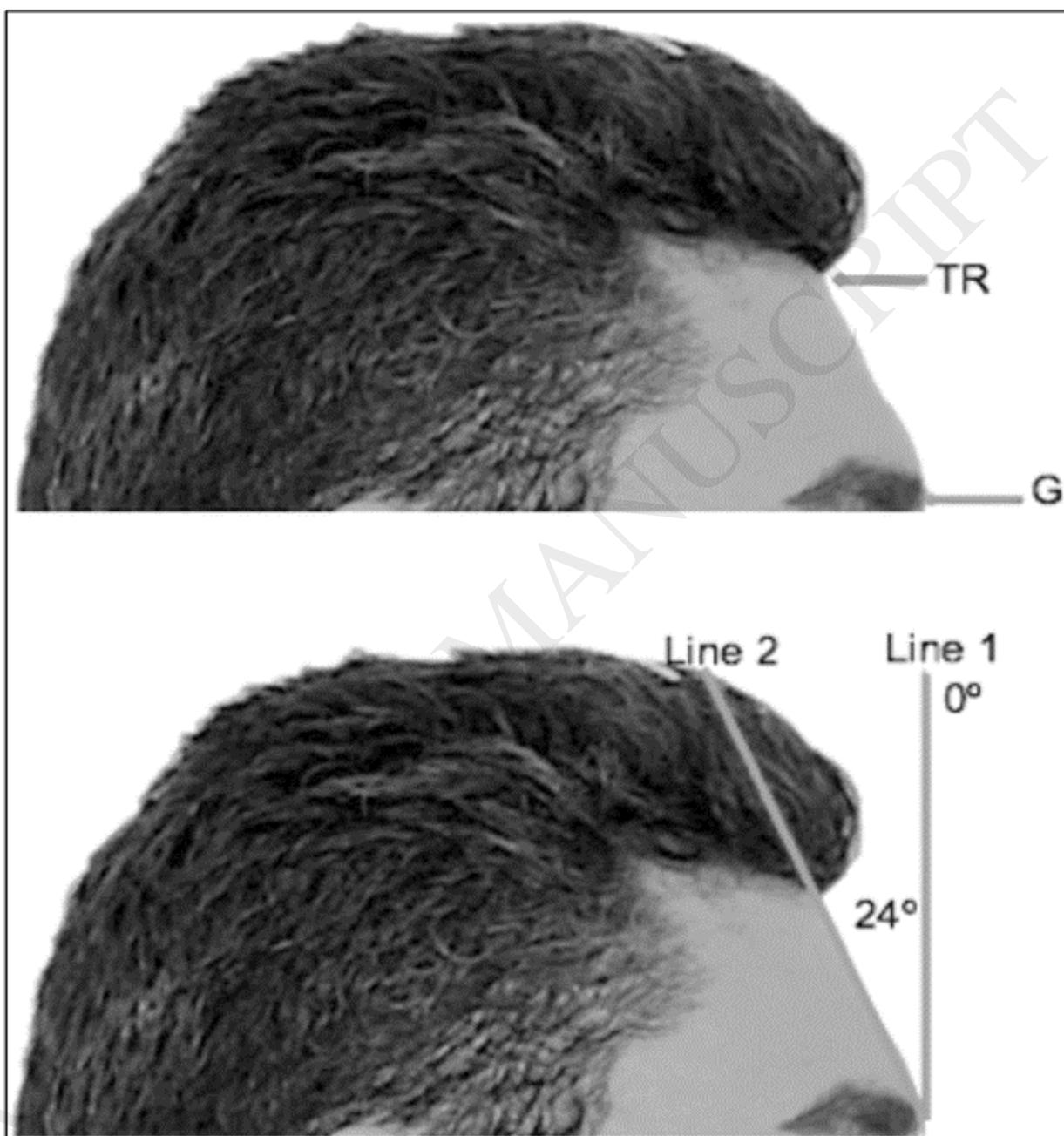
the forehead slant TR: triquion; G:

glabella.

Figure 2. Statistically significant correlations between slant of the forehead degree and cortical gray matter volume. Adjusted by academic level and age.
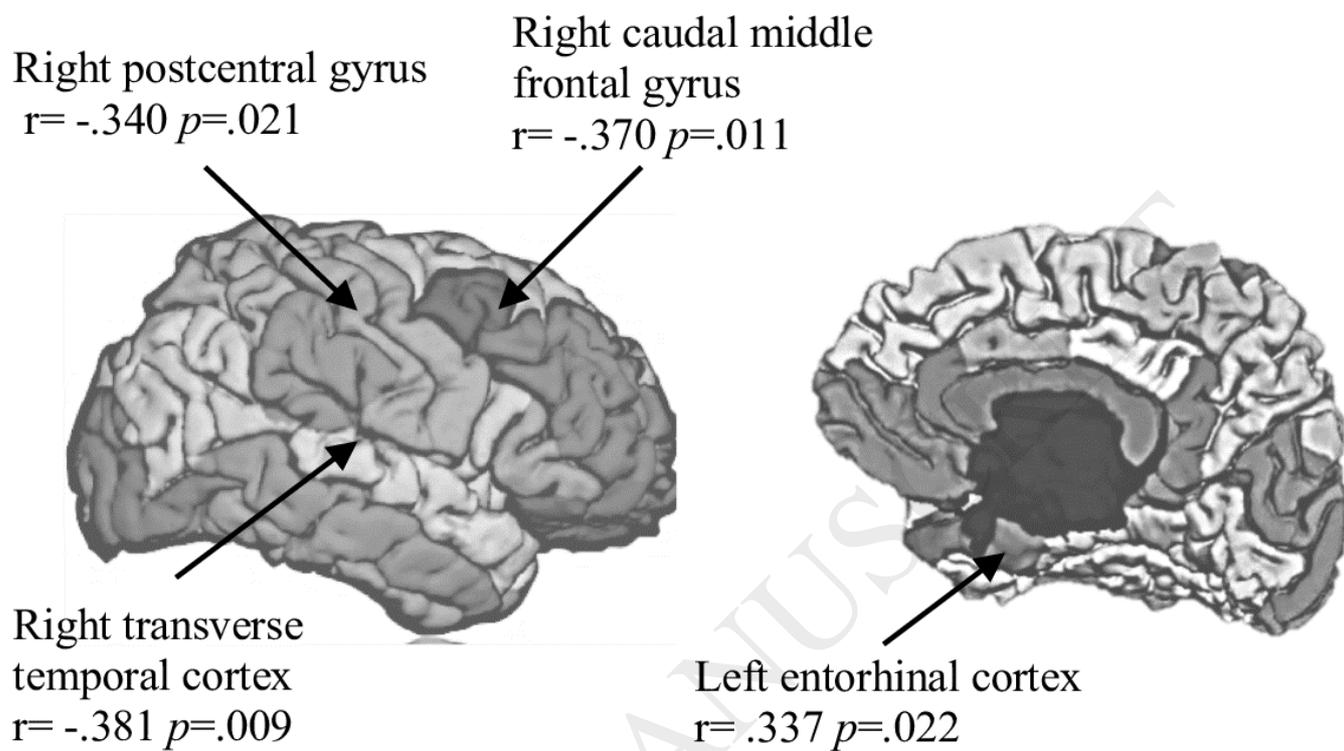
Right postcentral gyrus
r= -.340 p=.021

Right caudal middle frontal gyrus
r= -.370 p=.011

Right transverse temporal cortex
r= -.381 p=.009

Left entorhinal cortex
r= .337 p=.022

Table 1. Description of slant of the forehead degree and BIS 11 measures

N=48	Mean	SD	Minimum	Maximum
Slant of the forehead degrees (SFD)	17.73	5.49	10	34
Total score (0-120)	44.35	15.62	21	91
Attention impulsiveness (0-32)	13.77	4.55	6	27
Motor impulsiveness (0-40)	14.75	6.50	3	32
Non-planning impulsiveness (0-48)	15.83	7.04	1	34

Between brackets range of possible values.

Table 2. Correlations between BIS 11 scores, cortical grey matter volume and slant of the forehead degree (SFD)

for areas with at least one statistically significant result.

N=48	Total score	Attention impulsiveness	Motor impulsiveness	Non-planning impulsiveness
Right caudal anterior cingulate cortex	.218	.131	.087	**.317**
	.145	.384	.563	**.032**
Right parsopercularis gyrus	-.189	.017	-.121	**-.316**
	.208	.910	.424	**.032**
Right postcentral gyrus	-.231	-.010	-.222	**-.298**
	.122	.948	.138	**.044**
Right transverse temporal cortex	-.286	-.029	-.255	**-.375**
	.054	.848	.087	**.010**
Right fusiform gyrus	.121	**.340**	.038	.015
	.423	**.021**	.800	.919
Right lingual gyrus	**.393**	.258	**.408**	.324
	.007	.084	**.005**	.028
Left rostral anterior cingulate cortex	-.236	-.078	**-.310**	-.185
	.114	.608	**.036**	.220
Left caudal anterior cingulate cortex	-.258	-.018	-.262	**-.315**
	.084	.905	.079	**.033**
Left posterior cingulate cortex	**.332**	**.393**	.170	**.325**
	.024	**.007**	.260	**.027**
Left precentral gyrus	.218	.131	.087	**.317**
	.145	.384	.563	**.032**
SFD	**.442**	**.461**	**.361**	**.349**
	.002	**.001**	**.012**	**.015**

In each cell: Pearson correlation (adjusted by academic level and age), *p* value.

In bold statistically significant correlations.