P3 COMPONENT AS A POTENTIAL ENDOPHENOTYPE FOR CONTROL INHIBITION IN OFFSPRING OF ALCOHOLICS

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Running title: Go/No-Go task and P3 in offspring of alcoholics

Keywords: P3; Go/No-Go task, Inhibition; Alcohol; Offspring; Endophenotype.

ABSTRACT

Objective: To assess inhibitory processes and the on-going ERP activity of offspring of alcoholics (OA) during a Go/No-Go task, with the purpose of characterizing possible psychophysiological endophenotypes for alcohol-dependence vulnerability.

Methods: ERP measurements were obtained by EEG recordings of 65 participants divided into two groups: one group of 30 subjects with positive family history of alcoholism, and a control group of 35 subjects with negative family history of alcoholism. They performed a Go/No-Go task, where each individual was required to classify visual stimuli by colour (Go) and inhibit their response to a No-Go signal.

Results: OA have higher P3 amplitudes during the Go condition in all of the regions analysed and higher No-Go P3 amplitudes than control subjects in the frontal region. Unlike controls, OA have no differences between the P3 amplitudes across conditions.

Conclusions: The absence of differences between the P3 Go and No-Go observed in the OA group can be interpreted as a possible alteration related with inhibition, in a way that they may need to recruit similar resources for inhibitory and classificational processes for both conditions. Therefore, the P3 component may be considered as a useful endophenotype and a vulnerability marker to develop addictive behaviour.

Short summary:

EEG recordings and ERP measurements of young adults with positive and negative family history of alcoholism where obtained while they performed a Go/No-Go Task to assess inhibitory processes. Offspring of alcoholics showed a different ERP pattern compared to the control group and exerted greater effort than the control group.

Abbreviations: ERP, event related potentials; EEG, electroencephalogram; OA, offspring of alcoholics.

1. INTRODUCTION

Alcoholism is a highly prevalent disease with significant socioeconomic and health impacts (Anderson *et al.*, 2012). The neurotoxic effects of alcohol affect different cognitive functions. Distractibility and difficulties in inhibiting and sustaining attention are characteristics frequently present in alcohol dependent patients and in their offspring (Everitt *et al*., 2008). It has been hypothesized that alterations in inhibitory control could precede the problematic consumption of alcohol, constituting in these subjects a factor of vulnerability to alcohol consumption (Rangaswamy and Porjesz, 2008; Bari and Robbins, 2013) that can be added to vulnerability factors already known such as genetic and environmental factors. Therefore, the offspring of alcoholics (OA) may constitute a group with higher vulnerability to develop alcohol dependence (Tessner and Hill, 2010; Pandey *et al.,* 2012).

One of the methods used to verify the integrity of the cognitive processes mentioned is psychophysiological evaluation, since it allows direct measurement of the processes underlying cognitive activity. In this sense, the studies of event related potentials (ERPs) with the Go/No-Go paradigm have proved to be valuable for the assessment of the inhibitory processes (Aragues *et al.,* 2011). Normally these studies focus mainly on the No-Go condition, since it involves active inhibitory processes, whereas the Go condition involves response execution processes (Verbruggen and Logan, 2008).

The results of these studies have identified two main markers during the No-Go condition as an inhibitory response: the N2, a negative wave with a fronto-central distribution with a maximum peak between 200 and 300ms (No-Go N2), and the P3, a positive wave with a maximum peak between 300 and 600ms (No-Go P3), with a fronto-central-parietal distribution (Smith *et al.*, 2008). Low amplitudes reflected in

both components would reflect a deficit of the neural systems involved in inhibition, attention and orientation to infrequent stimuli (Lijffijt *et al.,* 2009; Gajewski and Falkenstein, 2013).

Two different alterations related to the effects of alcohol consumption in the psychophysiological activity in the inhibition process have been found. On one hand, numerous studies have detected a decrease in the amplitude of the P3 component during the No-Go condition in OA in comparison to control groups related with deficits in the inhibitory process (Kamarajan *et al.,* 2005; Kamarajan *et al.,* 2006; Kamarajan *et al.,* 2015). On the other hand, increased P3 amplitudes have been observed during the No-Go condition, in recent detoxified alcoholics and in young binge drinkers, interpreted as the reflexion of compensatory process, allowing them to achieve similar performances to controls (Lopez-Caneda *et al.,* 2012; Wetherill *et al.,* 2013; Petit *et al.,* 2014).

Moreover, differences in event related oscillations during Go/No-Go tasks have been described; specifically a decrease in delta, theta and alpha band activity during the Go and No-Go condition, these results suggesting that OA may have dysfunctions in motor inhibition, as well as in the activations related to the motor response (Kamarajan *et al.,* 2006). There are also findings of neuroimaging studies with functional magnetic resonance imaging, which have shown an increase in the brain activation during the Go and No-Go conditions in OA compared to control subjects (Acheson *et al.,* 2014).

Taking these promising data into account, the use of the P3 component as an endophenotype for alcoholism has been suggested (Porjesz and Rangaswamy, 2007). Thus, it is possible to identify individuals that present a genetic risk for the development of a certain disorder, even in the absence of evident symptoms.

Therefore, it should be present in the alcohol dependent patients as well as in their non-affected family members.

Some studies, although scarce, have already proposed the use of psychophysiological measures as a marker for alcoholism (Porjesz and Rangaswamy, 2007; Petit *et al.*, 2014; Kamarajan *et al.,* 2015), and have concluded the P3 component during inhibition could be used a relevant marker. However, despite that the use of the P3 component as an alcoholism endophenotype has already been proposed, related data are still scarce. An ERP study where the main cognitive function involved in the correct execution task is the motor inhibition may be useful to confirm that alterations in these components may be related to a higher vulnerability to develop an addictive behaviour.

Thus, the aim of this research is to determine the presence of behavioural difficulties in motor inhibition in OA. We also aim to determine the existence of psychophysiological markers of vulnerability through the analysis of the P3 and the N2 components in a Go/No-Go paradigm.

2. METHOD

2.1 Participants

We have performed a cross-sectional study of subjects with an age-range of 16 - 29 years old. The experimental group included 30 subjects (31% males, 69% females) with a positive family history of alcoholism. To avoid possible cases of maternal alcohol abuse during pregnancy we only included offspring of fathers with DSM-5 alcohol dependence (American Psychiatric Association, 2013). Subjects were selected from among the relatives of patients who participated in the alcohol detoxification treatment program managed by the Psychiatry Unit at the 12th of October Hospital

(Madrid, Spain) and from the Association of Families of Alcoholics of the Province of Madrid. The control group included 35 subjects (18,2% males, 81% females) with a negative family history of alcoholism. Subjects were selected from high schools from the same hospital zone and from several Madrid universities. For both groups the inclusion criteria were the requirement that all subjects had to be right handed, and volunteer to participate in the study for which they had to sign an informed consent. In the case of the under-age participants the informed consent had to be signed by their legal representatives. As exclusion criteria for both groups, the subjects could not have any major medical or neurologic disorders, any visual or auditory deficits, or be currently or previously undergoing treatment with central nervous system-action drugs, or having any psychiatric disorder according to the DSM-5 (American Psychiatric Association, 2013). Experimental procedures and ethical guidelines were in accordance with approval from the institutional ethics review board (13/001).

2.2 Assessments tools:

2.2.1 Clinical evaluations

The clinical data of the sample was obtained using different instruments. The structured clinical interview for DSM-5 was used to determine family history of alcoholism and any psychiatric comorbidity (First *et al.*, 2015), whereas the alcohol use disorders identification test (AUDIT) (Rubio *et al.*, 1998) was conducted in order to identify any risk for damaging levels of consumption or alcohol dependence. The use of other substances was assessed through an open-interview with yes or no questions regarding cannabis, tobacco and coffee consumption.

Other clinical measures involved anxiety and depression self-informed questionnaires, since high anxiety and/or depression levels could have an effect on the cognitive

performance and the undergoing psychophysiological activity. Accordingly, several studies have found that anxiety and depression levels could influence the ERP activity during cognitive and emotional tasks (Huang *et al*., 2009; Yao *et al.,* 2010). Therefore we used the self-report questionnaire Beck Depression Inventory (BDI-II) (Sanz *et al.,* 2003) in order to assess the actual depressive symptomatology. Anxiety levels were evaluated using the self-report questionnaire STAI (Spielberger *et al*., 1970). Additionally, the Spanish adaptation of the Barrat Impulsiveness Scale (BIS)(Oquendo *et al*., 2001) was used to assess impulsivity. This scale provides three sub-scales: motor, cognitive, and non-planned impulsivity. To assess behavioural problems as externalising behaviours, scholar performance and social skills we used the youth self-report (YSR) (Achenbach and Edelbrock, 1987).

2.2.2 EEG Data Acquisition

EEG continuous data was recorded with Vision Recorder software (BrainProducts. GmbH. Munchen. Germany), from 32 monopolar derivations (International 10-20 system) distributed in a cap (Actycap), at a sampling rate of 500 Hz and a band-pass filter of 0.5-100 Hz, with a 50 Hz notch filter. A left mastoid (TP9) channel was used as an online reference and two active electrodes recorded the horizontal and vertical eye activity. Impendances were kept under 5KΩ.

2.2.3 Go/No-Go Task

During the EEG recordings, subjects carried out a Go/No-Go task (designed and implemented with Presentation software, Neurobehavioral systems). The task was designed using the methodology proposed by Barcelo *et al.* (2008) for the Go/No-Go task. The participants were seated in front of a screen where the images were presented. The images consisted of four frequent colour figures (blue and red circles and squares) and two infrequent black figures (“+” and “x”). For the Go trials the

subjects had to classify the stimulus by colour, pressing the right key for the red figures (“Z”) and the left key for the blue figures (“-“), and for the No-Go trials they where instructed to inhibit their response, not executing any motor response to the black figures.

All stimuli had the same dimensions (6.5 x 6.5 cm) and presentation time of 150ms, and each trial had asynchronous and random start times between 1500 and 1600ms, in order to avoid the subject predicting when the next image would appear. Each block of stimuli had different numbers of coloured figures and had between 6and 8 colour figures placed in between two black symbols, thereby preventing subjects from being able to predict the order of the images.

Before the experimental session, subjects carried out a training block of 50 trials to make sure they understood the instructions. During the experimental task each subject carried out a total of 780 trials with a total duration of 24 minutes without break. All subjects received the same visual stimuli trials sequence. Response time, classifications errors, No-Go commission errors and Go perseverations answers were recorded. It is considered that the Go perseveration error occurs when a subject responds more than once to a Go stimulus.

2.3 Procedure

Data assessments were compiled in two different sessions. In the first session all the clinical data was obtained, with a total duration time of 45 minutes. In the second session the EEG data was recorded, with a total duration time of 1 hour and 30 minutes.

2.4 Analysis

2.4.1 EEG preprocessing:

Data preprocessing was performed using Vision Analyzersoftware (BrainProductsGmbH. Munich, Germany). Raw EEG continuous data was re-referenced to left and right mastoids (TP9-TP10) average activity. ERPs were time-locked to the onset of black symbols (“x” and “-“) (No-Go trials) as well as to target stimuli (Go trials). Each epoch was 1-second length, including a 200ms baseline. A semi-automatic artefact-rejection step was completed, rejecting both activity outside the +/- 45mV range and trials containing eye movements, ambient or muscular noise through visual inspection method. A minimum of 50% No-Go and 60% Go trials of the total epochs contributed to individual average ERP waveforms for each condition. Grand averages were computed for each group and conditions.

For the P3 Go and No-Go latency a semi-automatic peak detection was performed, with a280-500ms time-window at F3, Fz, F4, C3, Cz, C4, P3, Pz, P4 electrodes. For the latency of N2 component, a semi-automatic peak detection was performed, with a time-window of 180-300ms at F3, Fz, F4, FC1, FC2, Cz electrodes. For both components, the mean amplitude was computed in a 10 ms window around its peak latency.

2.4.2 Statistical Analyses:

The quantitative variables are described by their mean values and their standard deviations, and the nominal variables are described by their frequency. A parametric comparison between groups with the Student's T-test was performed for those variables with normal distribution. For the psychophysiology data, repeated measurement ANOVA (RM ANOVA) with the number of years of education as a co-variable was used. In the case of the P3 component (amplitude and latency) analysis, a 2x3x3 ANOVA was used with condition (Go and No-Go), region (frontal, central and parietal) and electrode (F3, Fz, F4, C3, Cz C4, P3, Pz and P4), and group (Control

and OA) as an inter-subject factor. The number of years of education did not have a significant effect neither for the P3 amplitude [F (1,59)= .993; *p*= .323] or P3 latency [F (1,59)= .422; *p*= .512] and therefore was excluded from the model, For the N2 component, a 2x2x3 ANOVA was used with condition (Go and No-Go), region (Frontal and central) and electrode (F3, Fz, F4, FC1, FC2 and Cz), and group (Control and OA) as an inter-subject factor and the number of years of education as a co-variable, as it did have a significant effect for both N2 amplitude [F (1,58)= 13.332; *p*= .001] and latency [F (1,58)= 5.035; *p*= .029]. Greenhouse-Geisser correction was used for those factors that violated the sphericity assumption. The effects were assessed using Bonferroni post-hoc analysis. The correlation analysis between quantitative variables was computed using a parametric Pearson correlation. All statistical analysis was performed using the SPSS version 22 software.

3. RESULTS

3.1 Socio-demographic Data

The initial sample (65) was reduced to 62. In the OA group one subject was excluded due to a family history of heroin dependence as well as alcohol dependence. In the control group the initial sample (35) was reduced to 32; three subjects were excluded for having outlier values for the psychophysiological and psychological measurements. No intergroup differences were found in terms of mean age (T=1.400, *p*=167), gender (chi-square= 1.398; *p*=.238), occupation (chi-square=5.119; *p*=.163) or alcohol (t=3.327; *p*=.163), tobacco (t=0.345; *p*=.344), coffee (t=3.240; *p*=.070) or cannabis (t=0,042; *p*=.838) consumption. There are differences in the number of years of education (t=2.358; *p*=.022), with the control subjects having more years of education [X=14.91 (1.25)] than OA [X= 13.97 (1.80)].

3.2 Psychological Assessments and Behavioural Results

Both psychological and behavioural outcomes did not show any statistical groups differences. (For mean, standard deviation, T and *p* values for the psychological and behavioural assessments see table 1).

3.3 ERP Results

P3 amplitude main and interaction effects in the RM-ANOVA are listed in table 3. They showed a significant main effect for Region and Electrode, and significant 2-way interaction effects between: Condition*Group, Region*Group, Condition*Region, Condition*Electrode, Region*Electrode; and a significant 3-way interaction effects between: Condition*Region*Group and for Condition*Region*Electrode (to see P3 mean amplitudes see figure 1). These results are explained as follows:

----------Figure 1----------

*Condition*Region*Group:* The interaction between the different Conditions, Regions and Groups imply differences for the P3 amplitudes during the Go condition in frontal ($p<.001$), central ($p<.001$) and parietal ($p<.001$) regions between groups. The OA group shows higher amplitudes in all of the regions than the control group. During the No-Go condition there have also been found higher amplitudes for the OA P3 amplitudes in frontal areas ($p<.010$), but not in central ($p=.713$) or in parietal ($p=.250$) regions.

Further *posthoc* comparisons of the interaction by region has shown intragroup differences for control subjects regarding P3 amplitudes, between Go and No-Go conditions, in frontal ($p<.050$) and central ($p<.010$) regions, but not in parietal regions ($p=.250$). Meanwhile, OA subjects did not show any statistical difference for P3 amplitudes in any region during the different conditions.

We have also found that inside the control group that P3 amplitudes during the Go condition are lower in the frontal region than in the parietal (p<.001) and central (p<.001) regions, and the P3 amplitudes are also lower in central than in parietal regions (p<.001) (frontal <central < parietal). During the No-Go condition the P3 amplitudes are also lower in the frontal region than in parietal (p<.001) or central (p<.001) regions, and the amplitudes between parietal and central regions are not different (p=.1) (frontal <central < parietal).

In the OA group we have found that the P3 amplitude is also lower in the frontal area than in central (p<.001) and parietal (p<.001) regions during the Go condition (frontal <central < parietal), but during the No-Go condition we found higher amplitudes in frontal and central regions than in the parietal (p<.010) region, and that the P3 amplitudes in frontal and central regions are not different (frontal=central >parietal).

Regarding **P3 component latencies** main and interactions effects in the RM-ANOVA are listed in table 3. They showed significant main effects for Condition and Region factors, and a significant 2-way interaction effects between Condition and Group (mean P3 latencies are display in figure 1).

*Condition*Group:* Regarding the significant interaction found between the Condition and Group the OA had longer No-Go P3 latencies (p<.001) than the control group, with no group differences in the Go P3 latencies (p=.460).

N2 amplitude RM-ANOVA showed significant main effects for Electrode factor [F(1, 82)=10.297; P=.002] and a significant 2-way interaction between Condition and Electrode [F(1.68,76)=49.543; p<.0001]. Regarding N2 **latency**, RM-ANOVA did not show any significant main or interaction effects (to see ERP and mapping view see figure 2).

----------Figure 2 ----------

3.4 Correlations between self-informed impulsivity (BIS) and psychophysiological data

The correlation between the P3 amplitude and the BIS scores are displayed in table 3. Inside the control group, an inverse correlation was observed between the BIS Motor Impulsivity sub-scale with P3 amplitudes at F3 and C3 channels, between the BIS Non Planned Impulsivity sub-scale and P3 mean amplitudes at F3, F4 and C3 and between the BIS total scores and P3 amplitudes at F3, F4 C3, CZ and C4 sites. In the OA group, however, an inverse correlation between the BIS Motor Impulsivity sub-scale with the P3 amplitudes at Cz and P4 sites was observed.

4. DISCUSSION

The aim of this study was to assess the motor inhibition in OA using a Go/No-Go task and psychophysiological measures in order to assess inhibitory processes. Our results indicate that OA have a different psychophysiological activation pattern related to inhibition, reflected in the significant differences in P3 amplitudes and latencies, in spite of having similar performance at a behavioural level as the control group.

Regarding the psychological assessment and contrary to expectations, the OA did not have significantly higher scores in the self-informed impulsivity (BIS). This finding differs from previous researchers' observations, which have reported an increased impulsivity in OA, considered one of the main characteristics involved in the etiology of substance abuse (Dougherty *et al*., 2015; Kamarajan *et al.,* 2015). This may be due to the fact that all of the subjects included in this study are healthy and don't have any psychological illnesses. Additionally, the self-informing questionnaires incite the subjects to discuss their perception of their impulsivity, and since they are healthy they might not experience any impulsivity problems in their everyday life, resulting in

the misinterpretation of some behaviour as normal and thus failing to report it. Furthermore, self-informative measurements may imply a meta-cognitive bias, such that behavioural or psychophysiological measurements may not correlate directly with them (Aragues *et al.*, 2011).

At a behavioural level no intergroup differences were found, but the psychophysiological correlates analysis have shown clear differences in the way OA execute a Go/No-Go task.

Firstly, OA have higher P3 amplitudes during the Go condition in all of the regions analysed, and they also have higher P3 amplitudes than control subjects in the frontal region during the No-Go condition.

Previous research has described decreased amplitude in the No-Go P3 component for the OA in comparison with the control subjects, especially in frontal regions, while in the Go trials the P3 amplitudes are the same for both groups (Kamarajan *et al.*, 2005). However, our results indicate the opposite. Notwithstanding, the methodology used by Kamarajan *et. al*. (2015) is based on inhibitory processes influenced by monetary reward. Therefore, the psychophysiological activity associated with the cognitive processes, although related, is different to the one assessed in this study. They also included subjects with actual and past history of externalizing disorders, while the present study did not. What can be considered the same is the presence of psychophysiological alterations related with inhibitory responses in the offspring of alcoholics. The differences in the No-Go P3 amplitude in frontal areas may be in line with the theory that the cognitive functions related with the prefrontal cortex may be considered as a marker for alcoholism (Cohen *et al.*, 1993; Claus *et al.*, 2011; *Ding et al.*, 2014).

Secondly, it was observed that the OA have no differences between the P3 amplitudes

across the Go and No-Go conditions, maintaining higher amplitudes throughout the whole task. Traditionally, the No-Go P3 component amplitude is considered a reflection of the motor inhibition neural substrate, and is a more demanding cognitive function than the one required to classify stimuli in the Go condition. Its correct execution, therefore, usually requires higher cognitive resources and higher neural recruitment, which can be translated into higher amplitudes for the No-Go P3 component in relation with the Go P3 (Enriquez-Geppert *et al.*, 2010; Gao, *et al.*, 2017).

This expected ERP morphology occurs in the control group but not in the OA, which may be interpreted as a possible alteration in the information processing and execution of the task, in such a way that the OA may need to recruit similar resources to execute inhibitory and classification processes, sustaining constant neural activation throughout the task.

In line with these results, there are some studies that have described increased No-Go P3 amplitude in subjects with binge drinking (Lopez-Caneda *et al.*, 2012) and in recovering alcoholics (Petit *et al.*, 2014) and have interpreted these increases as a reflexion of compensatory mechanism. Even though the samples differ from the present study in terms of clinical characteristics, their results can sustain the possibility that the increased P3 amplitude may be a reflexion of compensatory mechanism resulting from inhibition alterations, which can result in higher vulnerability to developing problematic consumption.

Supporting the link between the No-Go P3 amplitude and the inhibition, and therefore its possible utility as an endophenotype, is the observed negative correlation between the No-Go P3 and the BIS Motor Impulsivity subscale observed in both groups. Nevertheless, these correlations are not the same for both groups; in the case of OA,

the BIS Motor subscale correlates with P3 amplitudes at central and right parietal sites, whereas in the control group all three susbscales (Motor, Non-planned and Cognitive impulsivity) and total BIS scores correlated negatively with P3 amplitudes at frontal and central regions.

These results may serve as further evidence that underlying psychophysiological inhibition correlates may be different for the OA, and as result they need to recruit more resources in order to regulate their response to environment.

A possible limitation for these results is the difference in the number of years spent in education between the groups. Although the controls are slightly more educated than OA, this variable has not had a consistent influence in the psychophysiological measurements (Kamarajan *et al*., 2005; Begum *et al., 2014*). Furthermore, our results do not indicate a significant interaction between the number of years of education and the P3 amplitude and latency analysis. Thus, we consider that the number of years of education has a reduced effect on the psychophysiological measures obtained.

5. CONCLUSION

Our results provide new data regarding control inhibition as a vulnerability marker for developing addictive behaviour. It would appear that despite showing similar psychological and behavioural characteristics as the control group, a distinct psychophysiological profile was observed for the OA group. Particularly, OA participants would need to recruit more cognitive resources than controls throughout the whole task, when executing a Go/No-Go task. They also seem to activate different brain regions in order to inhibit a preponderant response, having higher P3 amplitudes in the frontal region than in central or parietal sites.

It is suggested that the use of P3 component during inhibition may be considered as

an endophenotype and vulnerability marker to identify the development of addictive behaviour. The utilization of these markers will not only be useful in gaining a better understanding of this study group but also as an early detection tool, allowing for the development of early intervention treatments.

To date there are few studies that support the use of endophenotypes in OA (Kamarajan *et al.*, 2005; Porjesz and Rangaswamy, 2007; Kamarajan *et al*., 2015). For future research in this field, it would recommendable to replicate these studies in OA of different ages and control variables such as the actual state of recovery of the alcohol-dependent parent and the level of exposure of the subject to the addictive behaviour. It would also be pertinent to perform a follow-up study of OA consumption behaviour through longitudinal studies.

Acknowledgments:

We would like to thank Dr. José Antonio Periañez for his contribution developing the paradigm for this study. This work was supported by the government's delegation for the National Drug Plan of the Ministry of Health and the Social Services and Equality granted to I. Martinez-Gras.R,Jurado-Barba, G. Castillo-Parra, F. Lopez-Muñoz, G. Rubio [Grant number 2012/053]. The funding source was not involved in the study design, collection of the data, analysis or interpretation of the data. All authors participated in designing the study, in the analysing and interpretation of the data and in writing the manuscript. All authors have approved the final article.

Conflict of interest: None of the authors has potential conflicts of interest to be disclosed.

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Tables and Figures

Table 1: Psychological and behavioural assessment means scores and SD categorized by groups (Offspring of alcoholics and control group). Mean scores have been compared using t-test.

		OA	Control	T-test	
		Mean (SD)	**Mean (SD)**	**T**	***p***
AUDIT		2.38 (3.04)	3.48 (2.50)	-0.487	0.628
STAI	State	19.11 (10.93)	14.74 (9.58)	1.429	0.159
	Trait	23.52 (11.74)	18.93 (12.6)	-1.544	0.129
	Total	42.19 (20.01)	33.3 (20.94)	-1.386	0.172
YSR	Total activities sum	18.04 (6.41)	14.56 (7.26)	-1,599	0.116
	Social behaviour sum	12.56 (4.04)	14.32 (2.82)	-1,823	0.075
	Mean scholar performance	2.85 (5.44)	1.2 (3.04)	1,836	0.073
	Global social skills	33.44 (7.82)	27.96 (10.78)	-1,294	0.202
	Problem behaviour	58.54 (18.86)	51.44 (18.21)	-2,085	0.043
	Socially desired behaviour	11.88 (3.03)	12.4 (7.68)	-1,367	0.178
Beck		9.89 (8.70)	7.48 (7.07)	0,337	0.738
WURS		59.78 (21.48)	59.19 (18.93)	-0,108	0.915
BIS	Cognitive	14.48 (4.49)	15.3 (5.44)	0.6	0.551
	Motor	16.33 (7.34)	15.93 (5.96)	-0.224	0.824
	No planned	14.52 (6.72)	13.37 (7.67)	-0.585	0.561
	Total	45.7 (15.66)	43.7 (14.46)	-0.487	0.628
RT		594.54 (80.68)	577.19(69.20)	-0.872	0.387
Nogo comisión Errors		2.46 (3.62)	1.55 (2.56)	-1.11	0.272
Perseveration Errors		2.55 (2.79)	2.18 (2.19)	-0.563	0.575
Clasification Errors		2.60 (2.74)	2.54 (2.46)	-0.08	0.936

Table 2.Main interaction effects of the RM-ANOVA for the P3 amplitude with several between-subjects factors. The significant effects have been highlighted.

*p<.050, **p<.010, ***p<.0001

P3 Amplitude				P3 Latency			
Effect	**df**	**F**	***p***	**Effect**	**df**	**F**	***p***
Condition	1	0.734	.395	**Condition**	**1**	**55.486**	**<.0001**
Condition*group	**1**	**5.294**	**.025**	**Condition*group**	**1**	**8.991**	**.004**
Region	**2**	**33.497**	**<.0001**	**Region**	**1.648**	**20.91**	**<.0001**
Region*Group	**2**	**4.768**	**.010**	Region*Group	1.648	1.648	.070
Electrode	**2**	**36.591**	**<.0001**	Electrode	1.734	0.449	.612
Electrode*Group	2	0.983	.377	Electrode*Group	1.734	0.73	.466
Condition*Region	**1.21**	**9.55**	**<.0001**	Condition*Region	1.719	2.315	.112
Condition*Region*Group	**1.21**	**7.094**	**.006**	Condition*Region*Group	1.719	0.656	.499
Condition*Electrode	**2**	**8.989**	**<.0001**	Condition*Electrode	2	1.769	.175
Condition*Electrode*Group	2	1.006	.369	Condition*Electrode*Group	2	0.514	.600
Region*Electrode	**3.28**	**11.018**	**<.0001**	Region*Electrode	3.416	1.974	.111
Region*Electrode*Group	3.28	1.949	.117	Region*Electrode*Group	3.416	0.530	.685
Condition*Region*Electrode	**3.59**	**2.805**	**.026**	Condition*Region*Electrode	3.247	0.488	.706
Condition*Region*Electrode*Group	3.59	1.94	.112	Condition*Region*Electrode*Group	3.247	1.012	.393

Table 3. Correlations between the scores in the BIS with the P3 amplitudes per group. (*r* represents the correlation value and p level of significance)

	OA Group								**Control Group**							
	Barrat Impulsivity Scale								Barrat Impulsivity Scale							
Electrode P3 Nogo	Cognitive		Motor		Not Planned		Total		Cognitive		Motor		Not Planned		Total	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
F3	-.066	.742	-.085	.674	-.058	.774	-.021	.915	-.293	.137	**-.468**	**.014**	**-.538**	**.004**	**-.523**	**.005**
Fz	-.041	.840	-.194	.333	-.028	.890	-.141	.483	-.151	.453	-.246	.217	-.361	.064	-.285	.150
F4	-.074	.712	-.173	.390	-.071	.724	-.123	.541	-.200	.316	-.336	.086	**-.449**	**.019**	**-.384**	**.048**
C3	-.070	.729	-.291	.141	-.054	.789	-.182	.363	-.194	.333	**-.469**	**.014**	**-.407**	**.035**	**-.515**	**.006**
Cz	-.190	.342	**-.407**	**.035**	-.136	.500	-.306	.121	-.168	.401	-.379	.051	-.380	.051	**-.469**	**.014**
C4	-.109	.588	-.369	.058	-.157	.434	-.281	.156	-.213	.286	-.268	.177	-.350	.073	**-.417**	**.031**
P3	-.038	.849	-.284	.151	-.021	.919	-.129	.522	-.175	.383	-.351	.073	-.236	.236	-.359	.066
Pz	-.124	.539	-.351	.073	-.048	.813	-.213	.286	-.132	.512	-.248	.212	-.226	.258	-.326	.097
P4	-.106	.598	**-.418**	**.030**	-.033	.872	-.239	.229	-.137	.496	-.251	.206	-.236	.236	-.305	.122

Figure 1. P3 amplitude and latency. P3 amplitude (top) and latency (down) mean and standard deviations, divided by group and condition. (p<.050*)

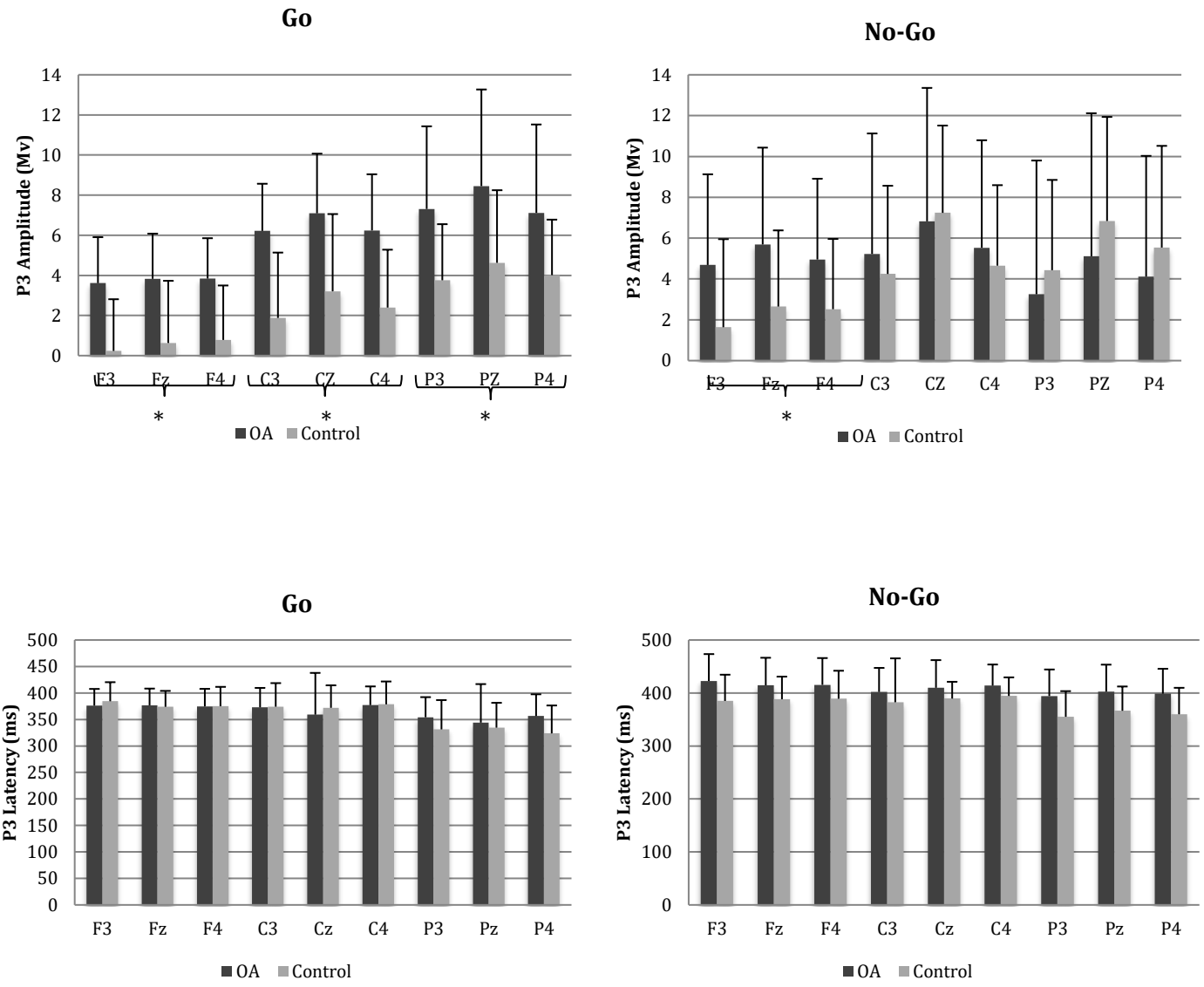

Figure 2: P3 Activity during Go Condition in the OA group and in the control group. ERP at frontal, central and parietal location and mapping view of the psychophysiological activity during Go and No-Go condition.