Reduced brain processing of affective pictures in children with cerebral palsy

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ABSTRACT

Sensory and cognitive deficits are common comorbidities in children with cerebral palsy. This observational study examines if brain processing of affective information is also altered in children with cerebral palsy (CP) in comparison with typically developing peers (TDP).
Methods: Evoked-related potentials were recorded in 15 children with CP (age = 11.27 ± 4.53 yr, 6 girls) and 14 TDP (age = 10.14 ± 4.29 yr, 5 girls) when viewing pleasant, unpleasant and neutral pictures. The subjective perception of valence and arousal of each one of the pictures was examined.
Results: Children with CP showed a significant amplitude reduction of evoked potentials in the occipital region to the affective stimuli in early brain processing latencies (P100 and N200; all F > 2.9, all p < .05). Children with CP rated pictures with affective content (pleasant and unpleasant) as less arousing (F(2.25) = 46.71, p < .001), and neutral pictures as more pleasant, than their TDP (F(2.25) = 75.56, p < .001).
Conclusion: The pictures with emotional content produce less activation, both at the behavioral and brain processing levels in children with CP. These differences were found in early latencies of brain processing which could be related to alterations in the detection of emotionally relevant stimuli.

1. Introduction

Emotional disturbances are common in children with cerebral palsy (CP) (Sigurdardottir et al., 2010). From 48 to 65% of children with CP in preschool age have emotional and behavioral problems, such as aggressive behaviors, unhappiness and anxiety-depressive symptoms that compromised their daily life (Sigurdardottir et al., 2010). Children and adolescents with CP also display reduced behavioral and emotional regulation, low affective expression and externalizing behaviors in comparison with typically developing peers (TDP) (Hsieh, 2012; Whittingham, Fahey, Rawicki, & Boyd, 2010). In addition, children with CP frequently suffer from other comorbidities, such as pain, disability and fatigue (Riquelme, Cifre, & Montoya, 2011), which are associated with emotional difficulties, depression, anxiety and reduced quality of life (Colver et al., 2015). Further studies have reported that children with CP are impaired during the recogniton and expression of emotions (Amato et al., 2008; García-Navarro et al., 2000) and that adolescents with CP require external support to establish and to maintain social and affective relationships with peers (Colver et al., 2015). Given

that accurate perception of emotions is necessary for the organization of behavior and the development of social skills (Amato et al., 2008; García-Navarro et al., 2000; Jessen & Grossmann, 2015), the relationship between emotion and social functioning seems to be of particular importance in children and adolescents with CP (Mc Manus & Perry, 2008).

Despite previous literature reporting lower emotional competence in children with CP, little research has examined brain correlates of emotional processing in these individuals. A previous study demonstrated that negative affective stimuli elicited enhanced responses of the autonomic nervous system in children with CP (higher amplitude of skin conductance than that arose by positive affective stimuli, and higher low frequency/high frequency ratio of heart rate variability) as compared to TDP (Kirshner, Weiss, & Tirosh, 2016). Event-related potentials (ERP) elicited by affective pictures are particularly useful to examine brain correlates of emotional processing in TD children (Kujawa, Hajcak, Torpey, Kim, & Klein, 2012; Sabatinelli, Lang, Keil, & Bradley, 2006) and in other pathologies such as attention deficit and hyperactivity disorder (Singhal et al., 2012). In this sense, the International Affective Picture System (IAPS) (Lang, Bradley, & Cuthbert, 1997) is considered an optimal instrument for providing affective visual stimuli in neuropsychological studies. The IAPS is a standardized pool of color pictures ranging from smiling faces to human injury and surgical scenes, classified into emotional categories (i.e. pleasant – e.g. sport scenes, neutral – e.g. household objects- or unpleasant –e.g. threat images, mutilation-) according to their valence (pleasantness of the picture) and arousal (alertness).

In healthy adults, ERPs elicited by affective pictures usually display a signal with different positive and negative peaks. An early negative peak can be observed between 150 and 200–300 ms after the stimulus onset over temporo-occipital electrode locations, and it is higher with higher arousing stimuli; it has been associated with early visual processing of the emotional stimuli (Schupp, Junghöfer, Weike, & Hamm, 2003; Schupp, Markus, Weike, & Hamm, 2003; Schupp, Junghöfer, Weike, & Hamm, 2004). A second positive peak is displayed between 200–300 ms after the stimulus onset over parietal electrode locations, giving information about stimulus salience and memory processes involved in affective processing (Kaestner & Polich, 2011). Finally, a late positive-going ERP component (starting around 300 ms and lasting few hundred milliseconds after stimulus onset), and also modulated by the emotional intensity of stimulus, seems to reflect top-down attention modulatory influences, with activation of the motivational systems that respond to salient information (Kujawa et al., 2012). In TD children, the ability to recognize the emotional content of daily situations is gradually developed at preschool and early school ages through the observation of others' behavior and the identification of the causes of a specific emotion in a specific context (Izard, Fine, Mostow, Trentacosta, & Campbell, 2002). ERP studies in TD children have shown identical peaks in the ERP signal (early negative peak, a second positive peak and a late positive-going component) and identical arousal-related emotional modulation in the amplitudes of the early negative peak and the late positive-going ERP component than in adults (Ravens-Sieberer et al., 2005; Sabatinelli et al., 2006). In contrast, brain activity in children is more located in occipital regions, reflecting a higher involvement of suboccipital regions in the emotional processing, compared to a higher involvement of executive prefrontal regions in adulthood; this could indicate a less elaborated cognitive processing of emotions in childhood (Hajcak & Dennis, 2009; Kujawa et al., 2012). Adolescents with attention and hyperactivity disorder displayed larger amplitudes of the positive peak and late positive ERP component in response to affective compared to neutral pictures (Singhal et al., 2012). The objective of this study was to examine brain activity in response to affective pictures in children with CP. It was hypothesized that children with CP would show significant abnormal amplitude in ERP components when compared to TDP, thus supporting the common emotional disturbances observed by using self-report measures.

2. Method

2.1. Participants

Children with cerebral palsy (CP) and typically developing peers (TDP) were recruited in primary schools in Mallorca (Spain) and matched on age and sex. Prior to the experiment, participants were identified by the Commission of Attention to the Diversity of the Department of Education of Mallorca Regional Government, and invited to participate after a meeting session with their parents. All participants (children and parents) were given detailed information about the experimental protocol. Inclusion criteria were: (1) age between 6 and 12 years, and (2) cognitive level that allowed to perform the experimental task (ability determined by the child's teacher). Exclusion criteria were: (1) insufficient cognitive level for the task, and (2) comorbilities preventing an adequate picture evaluation. Fifteen children with CP (age range = 8–12 yrs., mean age = 11.27 ± 4.53, 6 girls) and 14 TDP (age range = 8–12 yrs., mean age = 10.14 ± 4.29, 5 girls) met the inclusion criteria and agreed to participate in the study. Children presented different types of cerebral palsy (bilateral spastic n = 3, unilateral spastic n = 6, diskinetic n = 1, ataxic n = 2, other n = 3). Most of the children suffered from a severe motor impairment (eight children classified at the level 5 of the Gross Motor Function Classification System, two at the level 4, three at the level 3, one at the level 2 and one at the level 1) and were medicated with Baclofen (n = 12) or Dantrolene (n = 3). Five children suffered from visual problems, one from nistagmus and four from strabismus. All participants attended inclusive schools with the standard educational curriculum; children with CP had the cognitive capacity for following the normal school curriculum for their age and only received support for facilitating motor performance.

Parents and children signed informed consents. The study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Regional Government of the Balearic Islands (IB2247/14PI).

2.2. Sociodemographic data and self-report of quality of life

Families provided demographic data such as age, sex and socio-economic situation. Type of cerebral palsy, level of gross motor function, medication and other possible medical problems were obtained from clinical histories provided by the families. Quality of

life was assessed by using the Spanish version of the KIDSCREEN-52 (Ravens-Sieberer et al. 2005). This questionnaire provides information about quality of the daily life in 10 dimensions: physical well-being, psychological well-being, mood and emotions, self-perception, autonomy, parent relation and home life, social support and peers, school environment, social acceptance-bullying and financial resources. Raw scores were transformed into t-scores with higher values indicating higher quality of life.

2.3. Affective stimuli

Ninety developmentally appropriate affective stimuli were selected from the International Affective Picture System (IAPS) (Lang et al., 1997). Stimuli were identical to those already used in a previous study with TD children (Hajcak & Dennis, 2009). Stimuli were similar to those that children might view on television, and grouped into three affective categories according to valence ratings from normative adult data: 30 pleasant (e.g. happy faces, scenes with sports, family or wildlife), 30 neutral (e.g. domestic objects), and 30 unpleasant (e.g. sad and angry faces, scenes with people crying). Pleasant and unpleasant pictures were comparable in arousal and valence levels.

A computer using Presentation software (Neurobehavioral Systems, Inc.; Albany, CA) controlled stimulus timing and presentation order. Stimuli were displayed in color on a curved screen (120 cm width x100 cm height) at a viewing distance of 100 cm, each picture occupying a visual angle of 61° (horizontally) and 53° (vertically). Each picture was presented for 6000 ms (stimulus duration), followed by a white fixation cross on a black screen for 1000 ms (pause between stimuli). The order of picture presentation was completely random, and each participant received a different sequence of presentation order.

2.4. EEG recording, data reduction and analysis

Electroencephalography (EEG) was recorded from 32 scalp electrodes placed following the international 10/20 system and with mastoids electrodes as reference. Eye movements (EOG) were recorded by placing one electrode above and one below the left eye. All EEG and EOG electrode impedances were kept below 10kΩ. Signals were acquired by using a Brain Amp amplifier (Brain Products, Inc, Gilching, Germany) with a sampling rate of 1000 Hz, a high-pass filter at 0.10 Hz, a low-pass filter at 70 Hz, and a 50 Hz notch filter. EEG was continuously acquired when participants were viewing the affective pictures. Data acquisition always started 5 min (baseline) before the presentation of the first stimulus. EEG acquisition was externally triggered from the presentation software for baseline and stimulus onset.

EEG and EOG waveforms were segmented offline in epochs of 1000 ms duration (from -100 ms to 900 ms relative to stimulus onset). EEG epochs were digitally filtered (0.05 Hz low pass and 30 Hz high pass) and corrected for eye-movement artifacts by using the regression method by Gratton, Coles, and Donchin (1983). Furthermore, EEG epochs containing artifacts (maximal allowed voltage step/sampling point = 100μV, minimal allowed amplitude = -100μV, maximal allowed amplitude = 100μV, or maximal allowed absolute difference in the epoch = 100μV) were automatically and manually rejected. Finally, EEG waveforms were averaged separately for each condition (pleasant, neutral, and unpleasant). ERP data from two children with CP and one TDP had to be eliminated from statistical analyses because their EEG recordings did not meet the criteria specified above.

Derived from inspecting grand average data, amplitudes of two ERP components were computed for each condition. The first component was an early positive peak around 100 ms after stimulus onset and termed P100 component. Enhanced P100 amplitudes have been usually related to the automatic detection and encoding of stimuli emotionally relevant (Kaestner & Polich, 2011). In the current study, P100 peak amplitudes were defined as major positive peak at Oz electrode in latency range 100–200 ms after stimulus onset. A second negative component was the N200, a characteristic negative shift over occipital sites that has been related to the early visual processing of emotional pictures. Here, N200 amplitudes were defined as major negative peak at Oz electrode in latency range 200–300 ms after stimulus onset. Finally, the area of ERP ongoing waveforms from 300 to 400 ms (P300) and from 400 to 1000 ms (late positive potential) were examined.

2.5. Procedure

After written informed consent was obtained from children and parents, children participated in one EEG recording session and one session for subjective ratings of affective pictures. In addition, parents provided sociodemographic and clinical data, and completed the KIDSCREEN-52 questionnaire of quality of life in an extra session. All data were collected from September 2014 to June 2015.

After EEG acquisition, pictures were new randomly projected and the Self-Assessment Manikin was applied to examine subjective ratings of valence and arousal (Bradley & Lang, 1994). Children were asked to rate the pictures for valence and arousal on a numerical scale ranging between 1 (low pleasantness, or low arousal) and 9 (high pleasantness, or high arousal).

2.6. Statistical analysis

Data were statistically analyzed using the SPSS (version 22.0). Before statistical analyses, electrodes were pooled according to the following scalp sites: frontal (F3-Fz-F4), central (C3-Cz-C4), parietal (P3-Pz-P4), and occipital (O1-Oz-O2). EEG data were statistically analyzed using multivariate analyses of variance (MANOVA) for repeated measures with CONDITION (pleasant, unpleasant, neutral) and BRAIN REGION (frontal, central, parietal, occipital) as within-subjects factors and with GROUP (children with CP vs. TDP) as between-subject factor. To analyze scores of valence and arousal, only the factor in intra-subject factor CONDITION and the between-

Table 1

Mean and standard deviations of the dimensions of the *Kidscreen-52 for* children with cerebral palsy (CP) and their typically developing peers (TDP). Physical wellbeing (PHY), psychological wellbeing (Psy), moods and emotions (M&E), self-perception (Sel), autonomy (Aut), parents relation and home life (Couple), social support and peers (Pee), School Environment (Sch), social acceptance-bullying (BUL), finantial resources (ER).

	Phy	Psy	M&E	Sel	Aut	Couple	Pee	Sch	Bul	FR
TDP	53.91	47.80	35.60	42.06	48.77	46.53	53.50	59.47	38.90	34.75
	(3.74)	(4.75)	(1.46)	(5.57)	(7.07)	(5.54)	(3.99)	(6.88)	(3.03)
CP	33.30	41.72	22.60	36.15	27.15	39.76	47.71	63.87	32.92	40.11
	(3.48)	(8.50)	(2.84)	(3.87)	(6.02)	(1.58)	(11.1)	(3.14)	(2.31)	(10.2)
t-values	15.37	6.05	9.88	3.34	8.89	1.07	5.57	3.26	3.09	1.95
Significance level	< .001	< .001	< .001	.002	< .001	.305	< .001	.003	.007	.068

subjects factor GROUP were used. The degrees of freedom were corrected using the Greenhouse-Geisser epsilon and post-hoc analyses were based on pairwise mean comparisons with Bonferroni adjustment. Sociodemographic data and quality of life domains were compared between groups using t-tests for independent samples. Spearmann correlations were used to explore associations among Kidscreen domains and scores of valence and arousal.

3. Results

3.1. Sociodemographic data and quality of life

Children with CP and their TDP were similar in age, sex and socioeconomic situation. Nevertheless, significant differences arose between the groups in quality of life, with children with CP showing lower quality of life than their TDP in most of the domains (all t > 3.3, all p < .01), except for the domain *school environment*, where children with CP showed higher scores than the TDP (t = 3.26, p = .003), and for the domains *parent relations and home life* and *financial resources*, which were similar for both groups (both t > 1.07, p < .068). Table 1 displays the quality of life scores in the different domains for the two groups of children.

3.2. Subjective ratings

Fig. 1 displays the average ratings of valence and arousal for each type of picture (pleasant, unpleasant and neutral) for the two groups of children (children with CP and TDP). In v*alence*, a significant interaction GROUP x CONDITION (F(2.25) = 75.56, p < .001) showed that children with CP valued neutral pictures as more pleasant than their TDP (p < .001), while no significant differences between groups were found in pleasant and unpleasant pictures. Both groups rated with higher scores the valence in pleasant pictures, followed by the neutral and unpleasant pictures (all p < .001). Significant main effects were found in CONDITION
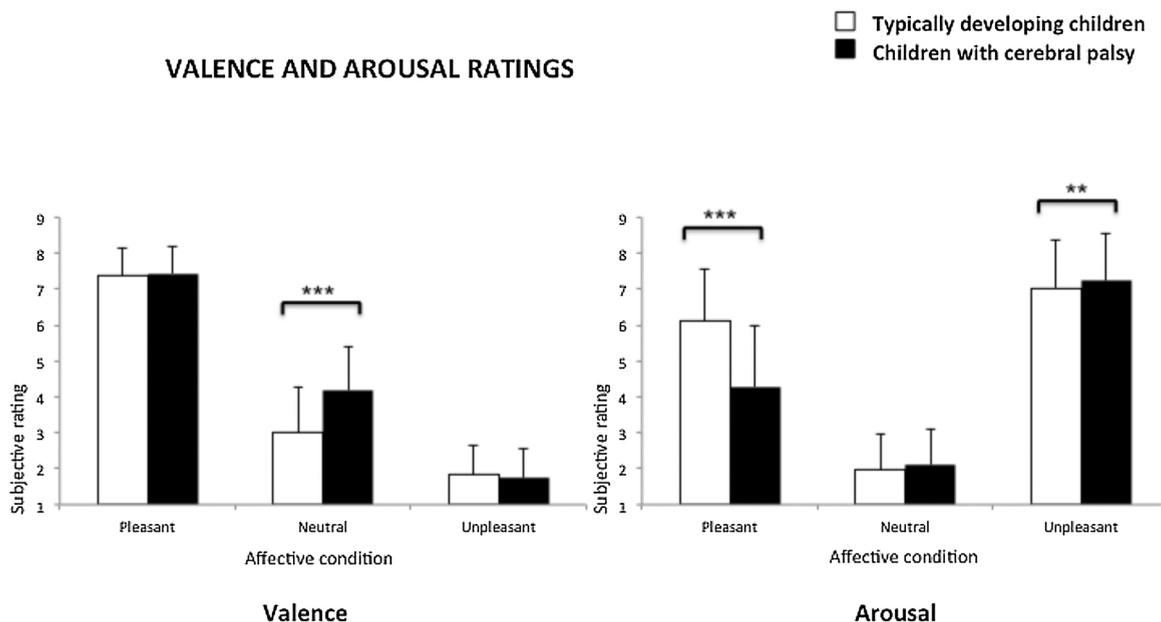
Fig. 1. Means of valence and arousal rated by children with cerebral palsy and their typically developing peers to pleasant, unpleasant and neutral pictures. ** p < .01, *** p < .001.
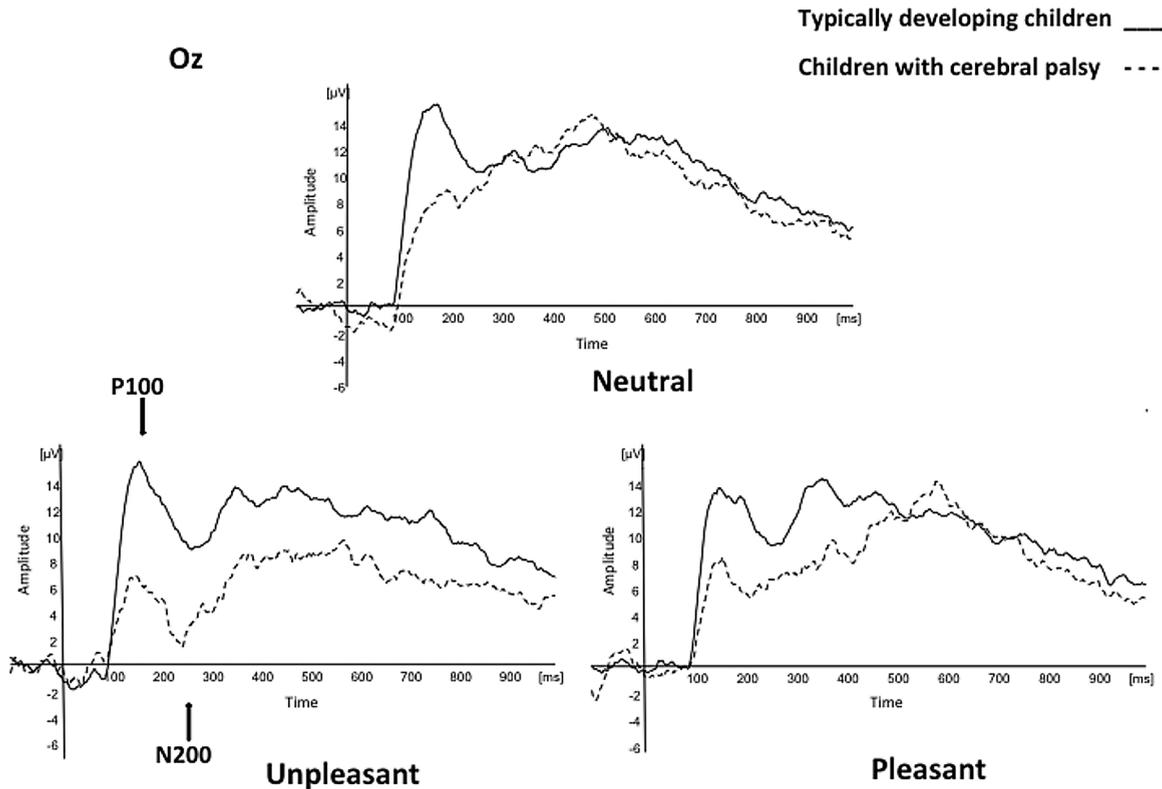
Fig. 2. Event-related potentials in the occipital region in children with cerebral palsy and typically developing children for each of the three conditions: pleasant, unpleasant and neutral pictures.

(F(2.25) = 4585.29, p < .001) and GROUP (F(1.26) = 66.20, p < .001), in the same sense of the interaction.

A significant interaction GROUP x CONDITION (F(2.25) = 46.71, p < .001) showed that children with CP rated the pictures with affective content as less **arousing** than their TDP (pleasant p < .001, unpleasant p = .007), while there were no differences between the groups in neutral pictures. Both groups rated unpleasant pictures as the most arousing, followed by pleasant and neutral pictures (all p < .01). Significant main effects were found for CONDITION (F(2.25) = 747.69, p < .001) and GROUP (F(1.26) = 46.60, p < .001).

3.3. Visual ERPs elicited by affective pictures

EEG waveforms obtained during the display of the affective pictures showed an early positive peak at 100 ms (P100) followed by a negative peak at 200 ms (N200). Fig. 2 displays the amplitudes of ERP in the three types of affective pictures in each of the groups.

The analysis of amplitudes in **P100** produced significant effects CONDITION (F(2.22) = 4.32, p < .029) and BRAIN REGION x GROUP (F(321) = 4.29, p < .037). Post-hoc pairwise mean comparisons indicated that unpleasant pictures elicited lower P100 amplitudes than neutral pictures (p = .068). Moreover, children with CP showed reduced P100 amplitudes in comparison to TDP in occipital regions, regardless of the emotional content of the pictures (p = .033).

In **N200,** significant effects BRAIN REGION (F(3.21) = 16.01, p < .001) and GROUP x CONDITION x BRAIN REGION (F (6.18) = 2.94, p = .05) were observed. Post-hoc comparisons showed higher activity in occipital brain region (p < .001). Moreover, unpleasant pictures elicited reduced N200 amplitudes in children with CP than in TDP in occipital areas (p < .022). In addition, only children with CP showed lower amplitudes in unpleasant pictures than in neutral pictures in the occipital area (p = .022). No significant effects were found for **P300** or the **late positive potential**.

4. Discussion

The aim of our study was to examine brain processing of affective pictures in children with CP compared with TDP of the same age. The reduced arousal ratings and ERP amplitudes in response to affective stimuli in children with CP could indicate deficits in the detection of emotionally significant stimuli in comparison to TDP. As emotion perception is a key factor for social functioning and emotional health, interventions addressed to enhance emotion knowledge and regulation may have a positive influence in improving quality of life in children with CP.

In accordance with previous results in TD children, we found that valence and arousal ratings of affective stimuli in our TD

children were similar to those already reported in adults (valence: pleasant pictures > neutral > unpleasant; arousal: unpleasant and pleasant pictures > neutral) (Hajcak & Dennis, 2009). Furthermore, amplitudes of ERP components followed the same temporal patterns and anatomical locations (maxima at occipital regions) as in previous studies conducted in pediatric population (Hajcak & Dennis, 2009; Kujawa et al., 2012).

Children with CP showed an identical valence and arousal rating pattern than TD children, and the ERP signal showed the same temporal peaks located at occipital locations, likewise their TDP. These data support the validity of the current task for the study of affective modulation in children with CP. Nevertheless, when children with CP were compared with their TDP, we observed significant differences in subjective ratings and early ERP amplitudes. In particular, we found that children with CP rated both affective pictures (pleasant and unpleasant) as less arousing than TDP. Moreover, all types of affective pictures (pleasant, unpleasant and neutral) elicited lower amplitudes in children with CP than in TDP. There were significant group differences in P100 amplitudes for all types of affective pictures and N200 amplitudes for unpleasant pictures. These middle-latency components of the event-related potentials (less than 300 ms after stimulus onset) are linked to automatic detection and fast encoding processes of emotionally relevant stimuli (Kujawa et al., 2012). These components have been related to a kind of feed-forward mechanism that would trigger the connections among brain regions implied in emotional, sensory, pre-frontal and subcortical processing. The stimulus arousal properties seem to mediate the rapid recruitment of selective attention mechanisms, facilitating the subsequent processing (Bekhtereva, Craddock, & Müller, 2015). The decline in both arousal and the amplitude of early-evoked potentials in children with CP might suggest a reduced ability to detect emotionally relevant stimuli and lower attention recruitment. In addition, our children with CP seemed to give an emotional value to neutral pictures; rating their valence higher than TDP and showing higher amplitudes in N200 in neutral pictures compared to unpleasant pictures. Early adverse experiences may alter early neural responses to the perception of negative facial expressions (Hajcak & Dennis, 2009). On the other hand, emotional stimuli subtracted attention resources to cognitive tasks (Bekhtereva et al., 2015). Numerous studies have shown attention problems in children with CP (Poole et al., 2015; Weber, Depoorter, Hetzel, & Lemola, 2016) that produced a decrease of early-evoked potentials to cognitive and visuo-spatial task (Zielinski, Jongsma, Baas, Aarts, & Steenbergen, 2014). Therefore, it might be considered that whether early adverse experiences, such as pain, or attention deficits could be compromising the detection of emotional stimuli in children with CP. Future studies are needed to elucidate the influence of these factors in the emotional processing of individuals with CP.

No differences were found on amplitudes of P300 and the late positive potential, and they were not modulated by the affective content of the pictures in any of the groups (not effects GROUP or CONDITION). This result contradicts previous studies showing enhanced P300 and late positive potential amplitudes to arousing pictures (both pleasant and unpleasant) in comparison to neutral ones in healthy adults. (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Foti & Hajcak, 2008; Hajcak & Olvet, 2008). However, previous studies have shown that the emotional reactivity in children is mainly mediated by the activation of visual processing areas, with less involvement of attention fronto-parietal networks. Therefore, it is thought that the emotional processing in children is based on visual attention scan instead of on more elaborate processing, which is the one that would reflect the component late positive potential (Kujawa et al., 2012).

Children with CP showed decreased quality of life in 8 dimensions of the Kidscreen questionnaire. Emotional difficulties have been previously associated with a reduction of the quality of life in children with CP (Mc Manus et al., 2008). Brain processes related to emotion perception have been considered a key factor for social functioning (Jessen & Grossmann, 2015) and people with higher emotional intelligence have shown higher amplitudes in early-evoked potentials to affective faces (Raz et al., 2016). Thus, the emotion processing anomalies in children with CP might be highly influencing quality of life dimensions such as psychological well-being, self-perception, social support and social acceptance. Interventions addressed to alleviate psychological difficulties and pain have been suggested for enhancing quality of life of children and adolescents with CP and could be useful in normalizing emotional processing by regulating high-influencing comorbilities (Colver et al., 2015; Amato et al. 2008; García-Navarro et al., 2000). In these sense, some specific interventions based on adaptive pretend play (Hsieh, 2012) have shown to increase the frequency of positive affective expression in children with CP. A better understanding of the relationships between emotion processing, quality of life, and other comorbilities would help develop adequate intervention programs.

Limitations. Although visual problems of the participants were checked in their medical history, no specific test was performed to detect possible visual deficits that might interfere with the processing of the pictures. Although all participants with CP attended to inclusive schools and followed the standard curriculum according to their age, no cognitive test was performed to assess the cognitive level. No preference screening of the stimuli was performed, and although we used standardized pictures suitable and validated for the pediatric population, we can not discard that an individual high preference could affect the emotional response in some specific pictures.

Future research perspective. To our knowledge, this is the first study using evoked potentials to examine the emotional regulation in children with CP. Our results suggest that children with CP have deficits in the detection of emotionally significant stimuli in comparison to TDP. Future studies should investigate the causes of this alteration of emotion regulation, and their influence on the psychological, emotional and social needs of individuals with CP. Specifically, neurophysiological research should address brain functioning of selective attention recruitment in children with CP and the processing of other common daily affective stimuli, such as emotional faces. On the other hand, broader studies exploring the relationship between emotion processing and CP comorbidities could detect risk factors leading to an altered emotion regulation. Finally, studies on the efficacy of interventions for improving emotional competence in this population are warranted.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Funding

Annex 1 Codes of IASP system pictures used in the study

Unpleasant pictures: 1050, 1120, 1201, 1300, 1321, 1930, 2120, 2130, 2688, 2780, 2810, 2900, 3022, 3230, 3280, 5970, 6190, 6300, 7380, 9050, 9250, 9404, 9421, 9470, 9480, 9490, 9582, 9593, 9600, 9611.

Neutral pictures: 5220, 5711, 5740, 5750, 5800, 5820, 7000, 7002, 7004, 7006, 7009, 7010, 7025, 7031, 7035, 7041, 7050, 7080, 7090, 7100, 7140, 7150, 7.175, 7190, 7224, 7233, 7235, 7236, 7595, 7950

Pleasant pictures: 1460, 1463, 1601, 1610, 1710, 1750, 18111460, 1463, 1601, 1610, 1710, 1750, 19201460, 1463, 1601, 1610, 1710, 1750, 1999, 2070, 2091, 2165, 2224, 2311, 2340, 2345, 2791, 4603, 5831, 7325, 7330, 7400, 7502, 8031, 8330, 8380, 8461, 8490, 8496, 8620.

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