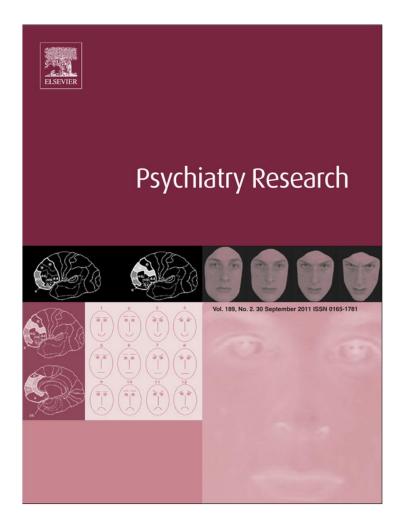
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# Sensitivity to expressions of pain in schizophrenia patients

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# ABSTRACT

Patients with schizophrenia tend to neglect their own pain and are known to have impairments in the processing of facial expressions. However, the sensitivity to dynamic expressions of pain has not been studied in these patients. Our goal was to test this ability in schizophrenia and to probe the underlying cognitive processes. We hypothesized that patients would have a reduced sensitivity to expressions of pain and that this impairment would correlate with deficits in attention, working memory, basic emotions recognition and with positive symptoms. We applied a battery of tests composed of the Comprehensive Affect Testing System (CATS), Sensitivity to Expressions of Pain (STEP), Toulouse-Pierón, Stroop and Digit Span tests to two groups of individuals, 27 patients with the diagnosis of schizophrenia and 27 healthy volunteers, matched on age, education and gender. Symptoms were assessed using Brief Psychiatric Rating Scale. The sensitivity to expressions of pain was found to be impaired in schizophrenia and a bias to attribute lower pain intensities may be present at some discrimination levels. STEP performance was correlated with working memory but not with Affect Naming or attention. These findings may contribute to the improvement of cognitive remediation strategies.

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## 1. Introduction

The recognition of basic emotions has been described as impaired in schizophrenia (for reviews, Kohler and Martin, 2006; Pinkham et al., 2007). This impairment has been mostly associated with deficits in the encoding of facial features at an early phase of processing (Combs and Gouvier, 2004; Bediou et al., 2007; Caharel et al., 2007; Namiki et al., 2007; Turetsky et al., 2007; Fakra et al., 2008; Wynn et al., 2008) and seems to be selective for emotions but not specific to any valence (Silver et al., 2009).

Although not so extensively studied, the facial expression of pain has been demonstrated as unique and distinct from the expressions of basic emotions (Prkachin and Solomon, 2008; Simon et al., 2008). At an early phase of processing, pain recognition seems to share with basic emotions a sensory analysis of stimulus information that is associated with amygdala activation (Frischen et al., 2008; Simon et al., 2008). This early phase has been regarded as strongly dependent on context and independent of task-demands (Fan and Han, 2008).

Behavioural and physiological responses to the perception of pain in others have been used to assess the "empathy for pain". A set of brain areas, referred to as "the pain matrix" is activated during selfreported pain and during the perception of pain in others (Singer et al., 2004; Gu and Han, 2007; Simon et al., 2008).

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Patients with schizophrenia have been described as impaired in several empathy domains not only at identifying emotions but also in the affective responsiveness, perspective taking (Derntl et al., 2009) and low-level facial mirroring (Varcin et al., 2010). Furthermore, several studies (Bonnot et al., 2009 for a review) have reported decreased reactivity to painful stimuli in these patients, probably resulting from a decreased expression of pain and not from physiological analgesia. In spite of these interesting facts, to our knowledge, no study has assessed if patients with schizophrenia have a decreased sensitivity to pain in others.

A test of Sensitivity to Expressions of Pain (STEP) has been recently developed (Prkachin, 2007). It is based on the attribution of pain intensity levels in dynamic facial expressions (Prkachin et al., 2004) and has been used to assess the perception of pain in others in normal and pathological groups. For example, patients with congenital insensitivity to pain are similar to controls in attributing intensity ratings (Danziger et al., 2006).

Dynamic expressions facilitate processing and lead to more efficient detection of emotional changes and intensity judgements (Kilts et al., 2003; Atkinson et al., 2004; Sato et al., 2004; Yoshikawa and Sato, 2008). However, it is not consensual if in schizophrenia dynamic expressions also lead to better judgements (Tomilson et al., 2006; Johnston et al., 2008). Furthermore, they have been related to different clusters of symptoms (positive), relatively to static expressions (Johnston et al., 2008).

The assessment of the cognitive profiles associated with emotion recognition impairments in schizophrenia has been regarded as important because findings might influence the design of cognitive

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remediation strategies (Ochsner, 2008). It has been suggested that patients with schizophrenia have a less sharp categorization of facial emotions (Schneider et al., 2006; Vernet et al., 2008), an impairment that seems to be related with increased attention shifts while analyzing emotional faces (Combs and Gouvier, 2004; Chambon et al., 2006; Herrmann et al., 2006; Fakra et al., 2008; Russell et al., 2008) and with working memory deficits (Green et al., 2007; Fakra et al., 2008; Chen et al., 2009).

The main goal of our work is to assess if patients with schizophrenia are impaired in a task of sensitivity to expressions of pain (STEP). Since emotion recognition deficits seem to start at an early phase of processing common to the pain recognition pathway, our hypothesis is that STEP will be similarly impaired. Our second goal is to assess if working memory and attention are similarly related to STEP performance. Since emotion recognition deficits have been related to impairments in these two cognitive abilities, our expectation is to find similar correlations in STEP. Finally, since dynamic emotions' recognition has been related with positive symptoms, our third goal is to assess if STEP has a similar profile.

#### 2. Methods

#### 2.1. Participants

Twenty-seven patients with schizophrenia (SZ) (19 Male; 8 Female) and twentyseven healthy participants (HP) (19 Male; 8 Female) volunteered to participate in the study. Demographic characteristics are presented in Table 1. Patients were recruited among inpatients of the Santa Maria Hospital in Lisbon (n = 10) and occupational therapy institutions (n = 17). Healthy participants were faculty employees (n = 12), professionals (n=11) and undergraduate students (n=4). Patients were selected if they fulfilled the DSM-IV-TR (American Psychiatric Association, 2000) criteria for schizophrenia (18 were paranoid and 9 residual), with no other psychiatric co-morbidity on DSM-IV-TR Axis I. Participants with concomitant substance abuse, medical or neurological illness and head trauma were excluded. All patients were receiving antipsychotic medication and were clinically stable at testing time. The Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962) was used to obtain ratings for positive and negative symptoms. HP were age- education- and gender-matched with SZ patients and none reported any history of neurological diseases or psychiatric problems. All participants were between 18 and 65 years old and had reported normal or corrected-to-normal visual acuity. Participants received no financial reimbursement for taking part in the study and data was collected in one or two sessions within 48 h. This study was conducted in accordance to the declaration of Helsinki. Approval was obtained from the Ethics Committee of Santa Maria Hospital. Each participant gave informed consent before entering the study.

## 2.2. Methods

2.2.1. Comprehensive Affect Testing System (CATS)

Participants performed three subtasks of a validated Portuguese version (Fernandes SM, 2006) of the Comprehensive Affect Testing System, which presents face stimuli belonging to the Ekman collection (Ekman and Friesen, 1976):

 Identity Matching (IM) – subjects had to indicate whether 2 portraits displaying neutral emotions represented the same or different individuals.

#### Table 1

Demographic variables. S.D. - Standard deviation; M - Male; F - Female.

	Group		
	Healthy subjects	Schizophrenia patients	
Ν	27	27	
Age (years) $\pm$ S.D.	$40.2 \pm 13.7$	$41.5 \pm 10.9$	
Sex M:F	2.4:1	2.4:1	
Education (years) $\pm$ S.D.	$10.89 \pm 4.55$	$10.89 \pm 4.64$	
Duration of illness (years) $\pm$ S.D.		$14.7 \pm 11.3$	
Symptoms (mean $\pm$ S.D.)			
BPRS_Hostility		$2.7 \pm 2.0$	
BPRS_Grandiosity		$2.8 \pm 1.7$	
BRPS_Suspicioussness		$3.4 \pm 1.8$	
BPRS_Hallucinatiory Behaviour		$2.6 \pm 1.8$	
BPRS_Unusual Thought Content		$3.6 \pm 1.7$	
BPRS_Conceptual Disorganization		$2.1 \pm 1.1$	
BPRS_Blunted Affect		$2.2 \pm 1.2$	
BPRS_Emotional Withdrawal		$1.4\pm0.9$	
BPRS_Excitment		$1.8\pm1.1$	

- Affect Discrimination (AfD): two portraits displaying the same individual were shown simultaneously. Subjects were asked to indicate whether the same or different emotions were exhibited in both pictures.
- 3) Affect Naming (AN): a single picture with a face was shown. Participants had to match each face with the emotion that best described its expression: happy, sad, angry, surprised, disgusted, frightened or neutral state.

In all tests the written labels were visible throughout testing (in a multiple choice format) and there was no time limit. No feedback was given regarding the appropriateness of any response. The total number of stimuli was 22 in each test except in the Affect Naming task that included 16 stimuli (2 for each emotion and 4 for neutral expressions).

# 2.2.2. Sensitivity to Expressions of Pain Test (STEP)

Participants viewed videotaped excerpts of the facial expressions of patients undergoing assessment of their shoulder injuries by active and passive range of motion tests. The excerpts were sampled from records taken in a previous study (Prkachin and Mercer, 1989), which have been coded for the intensity of pain expressed using Ekman and Friesen's (1976) Facial Action Coding System (FACS). Extensive research has demonstrated that the specific facial actions of brow lowering, orbit tightening and contraction of the levator muscle that wrinkles the nose and raises the upper lip encode pain (Prkachin and Solomon, 2008). Each of these actions varies on a six-point (0-5) intensity dimension. Sixty 1-s-long filmed sequences 20 depicting no pain, 20 depicting strong pain and 20 depicting moderate pain were presented. The sequences were selected from a larger archive according to a FACS-based pain score derived from previous research (Prkachin, 1992; Rocha, et al., 2003). Stimuli in the no pain category displayed no facial actions indicating pain. Stimuli in the moderate pain category showed at least one pain-related action receiving a score of 2 or 3 on the FACS intensity scale. Stimuli in the strong pain category displayed at least one pain-related action receiving a score of 4 or 5. The sixty stimuli were arranged in a random order. Participants were asked to determine whether each stimulus depicted 'no pain' (score 0), 'moderate pain' (score 1) or 'strong pain' (score 2). Answers were scored using a computerized scoring system based on a non-parametric signal detection theory model and probabilities were calculated by treating the patients' ratings as a three-category scale, using methods described by McNicol (1972). In this way, three indices were calculated, one reflecting the ability to discriminate no pain from moderate pain (PANM), one reflecting the ability to discriminate no pain from strong pain (PANS) and one reflecting the ability to discriminate moderate pain from strong pain (PAMS). PA values can range from 0 to 1. A value of .5 represents chance performance or "guessing".

Response bias (B) was estimated according to McNicol method (McNicol, 1972). Scores vary between 1 and 3, with higher scores representing a more "liberal" bias, or greater willingness to impute pain to the patient. Three bias indices (BNM, BNS and BMS) were calculated.

Finally, Average Discrimination (AvD) = (PAMS + PANM + PANS)/3 and Average Bias (AvB) = (BMS + BNM + BNS)/3 were calculated.

# 2.2.3. Neuro-cognitive assessment

We used standard cognitive measures for attention and working memory: 1) working memory was assessed with Digit Span (DS) forwards, backwards and total score (Richardson, 2007); 2) attention assessment was performed using Toulouse Piéron (TP) 'work-efficiency' (which gives us a measure that is highly dependent on the speed of performance), 'dispersion index' (dependent on the resistance to distraction) (Toulouse and Piéron, 1986) and Stroop test (Golden, 1978) which measures inhibitory control.

#### 2.3. Statistical analysis

To assess the differences between groups in STEP, CATS and neuro-cognitive variables, we first addressed which parameters were normally distributed using a one-sample Kolmogorov–Smirnov (K–S) test (P>0.05). Independent samples t-tests were then performed for comparisons involving scale variables considered to be normally distributed. For the variables not normally distributed (K–S P=0.05) we used the non-parametric Mann–Whitney test. Cohen's *d* was used to calculate effect sizes.

Correlations were assessed using parametric methods (Pearson) when variables were normally distributed. Otherwise we used the Spearman coefficient. Post-hoc adjustments of significance levels were performed using the Bonferroni–Holm method.

# 3. Results

# 3.1. Sensitivity to expressions of pain

SZ patients had significantly lower discrimination scores between all pain categories tested (Table 2): a) No pain vs. Strong pain (PANS; z = -3.061; P = 0.002, r = 0.94), b) No pain vs. Moderate pain (PANM; t(51) = -3.174; P = 0.013, r = 0.89) and c) Moderate pain vs. Strong pain (PAMS; t(46) = -2.795; P = 0.019, r = 0.78). Patients also had a significantly lower Average Discrimination (AvD) score (z = -3.363; P = 0.001, r = 0.94). Relative to bias scores, patients were less likely to attribute 'Strong Pain' to 'Moderate Pain' (BAMS;

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#### Table 2

STEP performance scores. S.D. – Standard deviation \*P<0.05; \*\*P<0.01.

	Group	Group		t-test/Mann-Whitney	
	Healthy subjects	Schizophrenia patients	t/z	P-value	
Pain Intensity Discrimination (mean $\pm$ S.	D.)				
No pain-Strong pain	$0.95\pm0.08$	$0.85 \pm 0.13$	- 3.061	**0.002	
No pain-Moderate pain	$0.75\pm0.09$	$0.65 \pm 0.12$	-3.176	**0.003	
Moderate pain-Strong pain	$0.82\pm0.08$	$0.75 \pm 0.11$	-2.795	**0.008	
Average Discrimination	$0.84 \pm 0.07$	$0.75 \pm 0.11$	- 3.363	**0.001	
Biases (mean $\pm$ S.D.)					
No pain-Strong pain	$1.50 \pm 0.35$	$1.34 \pm 0.39$	-1.542	0.129	
No pain-Moderate pain	$1.05 \pm 0.32$	$1.01 \pm 0.33$	-0.478	0.634	
Moderate pain-Strong pain	$2.78 \pm 1.05$	$2.12 \pm 1.00$	-2.325	*0.024	
Average Bias	$1.77 \pm 0.36$	$1.49 \pm 0.45$	-2.572	*0.013	

t(51) = -2.325; P = 0.024, r = 0.65) than control subjects and more likely to attribute lower pain intensities in general (t(49.3) = -2.572; P = 0.013, r = 0.72). There was no significant difference between groups on the remaining on bias scores (BNS and BNM).

# 3.2. Comprehensive affect testing system

Raw scores of Identity Matching (IM), Affect Discrimination (AfD) and Affect Naming (AN) are presented in Table 3. We found a significant difference on IM (t(51) = -2.406; P = 0.020, r = 0.67) and a trend difference on AN (t(46) = -1.968; P = 0.055, r = 0.55) between controls and SZ patients. When we removed 'Happy' expression (identified correctly 100% of the times in both groups) from the AN analysis, the difference between groups became significant (t(316) = -2.047; P = 0.041, r = 0.57). There was no significant difference on the AfD or on the naming of any particular emotion (happy, sad, disgust, surprise, fear, disgust and neutral).

#### 3.3. Correlations between STEP and emotion recognition

In the control group, Affect Naming was correlated with STEP PANS (r = 0.559; P = 0.003), PANM (r = 0.414; P = 0.036), PAMS (r = 0.539; P = 0.004) and Average Discrimination (AvD; r = 0.580; P = 0.002). In the patient group, STEP AvD correlated with the CATS Affect Discrimination (r = 0.534; P = 0.005) but not with Affect Naming (P > 0.05). After post-hoc corrections, all correlations remained significant.

# 3.4. Correlations between CATS and neuro-cognitive variables

Patients performed worse than controls in almost all the neuro-cognitive tasks (Table  $5^1$ ).

Affect Discrimination correlated with DS forwards (r=0.485; P=0.012), backwards (r=0.421; P=0.032) and total (r=0.540; P=0.004); Stroop interference (r=0.412; P=0.037) and Stroop Errors ( $\rho$ =-0.549; P=0.010). On the other hand, Affect Naming was correlated with TP work-efficiency (r=0.520; P=0.008), dispersion index ( $\rho$ =-0.505; P=0.010), DS inverse (r=0.619; P=0.001), DS total (r=0.596; P=0.001), the number of Stroop Errors ( $\rho$ =-0.729; P<0.001) and with the Stroop interference score (r=0.657; P<0.001).

Since education correlated with Affect Discrimination (r = 0.460, P = 0.018) and Affect Naming (r = 0.637, P < 0.001) and can have effects on both emotion recognition and cognitive tasks (Fernandes SM, 2006), we repeated the analysis controlling for this variable. Only the negative correlation between Stroop Errors and Affect Naming remained significant (r = -0.832; P < 0.001) even after post-hoc adjustments.

## 3.5. Correlations between STEP and neuro-cognitive variables

Correlations between STEP parameters and Stroop, TP and DS were assessed for the SZ group. Results are depicted on Table 4 (for a more detailed version access supplemental material). DS forward correlated with the ability to discriminate between no pain vs. Moderate pain (PANM; r = 0.580, P = 0.002), No pain vs. Strong pain (PANS; r = 0.400, P = 0.039) and Average Discrimination score (AvD; r = 0.425, P = 0.027). However, after post-hoc adjustments only the PANM and AvD correlations remained significant.

Age and education were not significantly correlated with any of the STEP parameters (P>0.05). However, when we controlled for education, the correlation between PANM and DS forward remained significant (r=0.507; P=0.027) even after post-hoc correction.

# 3.6. STEP and symptoms

To assess correlations between BPRS symptoms scores and STEP parameters we calculated non-parametric Spearman coefficients. We found that higher severity on the symptom 'Unusual Thought Content' negatively correlated with the ability to discriminate between No pain vs. Moderate Pain (PANM;  $\rho = -0.434$ ; P = 0.030). Furthermore, higher 'Suspiciousness' severity positively correlated with a higher bias to attribute Strong pain to neutral faces (BNS;  $\rho = 0.413$ ; P = 0.040) and to attribute stronger pain in general (AvB;  $\rho = 0.463$ ; P = 0.020). After post-hoc adjustments none of these correlations did remain significant.

# 4. Discussion

# 4.1. Sensitivity to Expressions of Pain (STEP)

Our results seem to indicate that patients with schizophrenia are impaired, relatively to healthy subjects, in categorizing pain intensity from facial expressions. Although these results may reflect a general impairment in the early processing of emotional expressions, other factors may be involved. For example, patients seem to have a bias to attribute lower pain intensities, especially when discriminating between moderate vs. strong pain. Interestingly, this bias is weaker in the discrimination between 'no pain' and other intensity levels.

Our interpretation is that different discrimination levels may be related to different mechanisms: 1) the discrimination between 'pain vs. no pain' may be essentially limited by the early detection of emotional signals (Combs and Gouvier, 2004; Bediou et al., 2007; Caharel et al., 2007), by the ability to use contextual cues (Fan and Han, 2008) and by the ability to maintain information 'online' until the judgment phase (Green et al., 2007); 2) in the judgement phase, once pain is detected, the decision to attribute a certain intensity (moderate vs. strong) may be influenced by other factors such as a degraded affective processing of pain (Bonnot et al., 2009).

<sup>&</sup>lt;sup>1</sup> Available as supplemental material.

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# Table 3

Percentage of correct answers on CATS subtests in schizophrenia patients and healthy subjects. § After removing 'Happy' expression from the analysis. S.D. – Standard deviation \**P*<0.05; \*\**P*<0.01.

	Group		<i>t</i> -test/Mann-Whitney	
	Healthy Subjects	Healthy Subjects	t/z	P-value
Identity Matching (mean $\pm$ S.D.)	$95.0\pm7.8$	88.6±11.1	-2.406	*0.020
Affect Discrimination (mean $\pm$ S.D.)	$90.9 \pm 9.43$	$90.9 \pm 8.3$	-0.354	0.723
Affect Naming Total (mean $\pm$ S.D.) §	$72.2\pm16.0$	61.8±22,0	-2.047	*0.041

## 4.2. Cognitive associations

We replicated the findings of basic emotions recognition deficits (CATS) in schizophrenia (for reviews, Kohler and Martin, 2006; Pinkham et al., 2007). However, although Affect Naming and Discrimination strongly correlate with pain intensity discrimination in healthy subjects, they dissociate (especially Affect Naming) in the patient group. If patients use cognitive strategies to compensate for an early processing deficit of emotional faces (Fakra et al., 2008), this dissociation probably reflects the recruitment of different cognitive resources in tasks that differ in more than one domain: categorization (CATS) vs. intensity discrimination (STEP), basic emotions (CATS) vs. pain (STEP), and static (CATS) vs. dynamic expressions (STEP). Interestingly, a correlation was found between Affect Discrimination and Average (pain intensity) Discrimination. This could mean that STEP judgements might be more implicit and less abstract than Affect Naming.

While we replicated previous results regarding associations between attention, working memory and emotion recognition in static expressions (Combs and Gouvier, 2004; Chambon et al., 2006; Fakra et al., 2008; Russell et al., 2008; Chen et al., 2009), these correlations were highly influenced by education. This means that the general cognitive status might explain the variation of performance within the patient group.

Interestingly, a different cognitive profile was found in STEP: 1) education and attention did not correlate with STEP performance and 2) DS direct correlated with the ability to discriminate between 'No pain' and other intensity levels. Several factors might contribute to this finding. First, STEP might be less abstract and because it's dynamic it might facilitate attention mechanisms (Yoshikawa and Sato, 2008). On the other hand, even if dynamic expressions enhance signal detection, and because they might imply a delay between stimuli and response, if these changes were not kept online in order to make explicit judgments, then the inference about pain would still be poor.

#### Table 4

Correlations between neuro-cognitive variables and both CATS and STEP. DS – Digit Span; TP WE (Toulouse–Pieron Working Efficiency). \*P<0.05; \*\*P<0.01.

		Working Memory		Attention	
		DS forwards	DS backward	Stroop Errors	TP WE
STEP (Discrimination)					
No pain-Strong pain	r/ρ	0.400	-0.147	-0.328	0.166
	Sig.	*0.039	0.463	0.147	0.428
No pain-Moderate pain	r/ρ	0.580	-0.088	-0.240	0.211
	Sig.	**0.002	0.663	0.294	0.312
Moderate-Strong pain	r/ρ	-0.089	-0.182	-0.396	-0.022
	Sig.	0.659	0.364	0.076	0.915
Average Discrimination	r/ρ	0.425	-0.16	-0.226	-0.159
	Sig.	*0.027	0.426	0.277	0.447
CATS					
Naming	$r/\rho$	0.346	0.619	-0.729	0.520
	Sig.	0.083	**0.001	**0.000	**0.008
Discrimination	$r/\rho$	0.485	0.421	-0.549	0.114
	Sig.	*0.012	*0.032	**0.010	0.587

It could be speculated that this association between working memory and STEP might reflect the ability to maintain coherence of judgement across the 60 stimuli (and compare present and previous stimuli). However, the dimension of working memory that is correlated with PANM is the ability to repeat a stream of numbers (DS forward) and not the ability to manipulate them (DS backwards). So we believe that since patients have a slower processing of emotional expressions (Onitsuka et al., 2006; Caharel et al., 2007; Turetsky et al., 2007; Combs et al., 2008; Wynn et al., 2008), it is more likely that this memory association reflects a higher dependency of performance on the ability to maintain facial motion information online until the decision is made.

# 4.3. STEP and symptoms

Although positive symptoms have been associated with poor recognition of dynamic emotions (Johnston et al., 2008), in our study this association was rather weak. Although we did find a correlation between poor pain detection and higher levels of 'unusual thought', the significance level was not adequate. Maybe a clustering analysis of the symptoms would reveal a stronger relationship. On the other hand, although patients have, in general, a bias towards attributing lower pain intensity levels, it seems that patients with higher suspiciousness levels might be more likely to attribute stronger pain. This might be explained by a higher vigilance and/or a bias towards attributing negative valences to neutral stimuli (since the strongest relation was found for attributing 'Strong pain' to 'No pain').

# 4.4. Conclusions and clinical implications

This was the first study to show that patients with schizophrenia are impaired in the recognition of facial expressions of pain. We used dynamic expressions, which increase the ecological validity. Since some studies have suggested that emotion recognition may be more impaired in dynamic than in static expressions (Johnston et al., 2008) in spite of the attention facilitation (Yoshikawa and Sato, 2008), we think that the focus given to attention in cognitive remediation strategies may be misguided. Furthermore, factors such as a degraded affective processing of pain and the severity of suspiciousness may play a role in the empathy for pain in patients with schizophrenia.

# 4.5. Limitations

Our sample was not large or heterogeneous enough to allow for a comparison of different schizophrenia subtypes. On the other hand, a very directed cognitive assessment was performed decreasing the power of our interpretations. Controlling for general intelligence, medication and socio-cultural background will be necessary in following studies.

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# Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.psychres.2011.03.007.

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