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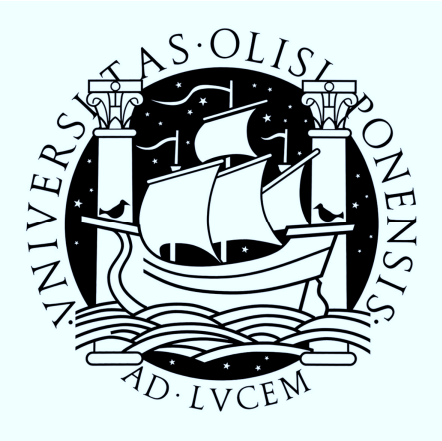

ANALYSIS OF THE UNPLEASANTNESS OF SOUNDS BY SCHIZOPHRENIC PATIENTS

Carina Patrícia de Barros Freitas

Mestrado em Neurociências

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“Men ought to know that from the brain, and from the brain only, arise our pleasures, joys, laughter and jests, as well as our sorrows, pains, griefs and fears.
Through it, in particular, we think, see, hear and distinguish the ugly from the beautiful, the bad from the good, and the pleasant from the unpleasant”

On the sacred disease

Hippocrates - 400 B.C.

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Resumo

No presente trabalho estudámos o processamento emocional de sons desagradáveis em doentes esquizofrénicos, em fases iniciais da doença.

O estudo decorreu em doentes pertencentes à consulta externa dos Serviços de Psiquiatria do Hospital de Santa Maria e Hospital Júlio de Matos e a amostra consistiu em 29 doentes e 29 controlos emparelhados para o sexo e idade.

As avaliações realizadas incluíram uma escala de Avaliação Breve do Estado Mental (MMSE), uma escala de gravidade dos sintomas positivos e negativos da esquizofrenia (PANSS) e uma bateria de sons desagradáveis desenvolvida para este estudo, intitulada de Newcastle Battery of Unpleasant Sounds (NBUS).

Os resultados mostraram que os doentes esquizofrénicos têm uma percepção emocional preservada dos sons desagradáveis, na fase inicial da doença. Não se observaram correlações significativas entre medidas de gravidade clínica (duração da doença e sub-escalas da PANSS) e os valores da avaliação dos referidos sons.

Observou-se ainda que a bateria de sons apresentada revelou grande variabilidade nos valores obtidos na avaliação. Associações semânticas, assim como certas características acústicas dos sons poderão ter influenciado a percepção e avaliação emocional dos mesmos.

Palavras-chave: esquizofrenia, sons desagradáveis, processamento emocional

Abstract

In the present study, we evaluated the emotional processing of unpleasant sounds in schizophrenic patients in early stages of the disease.

This study was performed on schizophrenic outpatients from the Psychiatry Departments of Hospital Santa Maria and Hospital Júlio de Matos. The sample group comprised 29 schizophrenic patients and 29 matched healthy controls, equal in sex and age.

Evaluations included the Mini Mental State Examination, the Positive and Negative Syndrome Scale (PANSS) and the Newcastle Battery of Unpleasant Sounds, which we developed to study this issue.

Results showed that schizophrenic patients in early stages of the disease have a preserved emotional perception of unpleasant sounds. No correlation was found between clinical severity measures (disease duration, PANSS total and sub scores) and mean unpleasantness rating, which suggests that the emotional processing of unpleasant sounds is rather stable during the first five years of illness.

We observed that the sound set presented varied widely in perceived unpleasantness. Semantic associations as well as certain acoustic features may have had an effect upon unpleasantness ratings of sounds.

Keywords: Schizophrenia, unpleasant sounds, emotional processing

1. Introduction

1.1. About unpleasant sounds

Unpleasant sounds, referred to by Aristotle as "hard sounds", have been bothering scientists for at least 2,300 years. These sounds exist in everyday life and can sometimes induce such psychological aversion, as well as the intense involuntary physiological response reaction known as "a shiver down the spine", that even thinking about them can be unpleasant. Nevertheless, little is actually known about this phenomenon. It has been suggested that this strong visceral/somatic response, often described as a "tingling sensation" running down the spine or along the sides of the body, like a synastesia (somatic sensation), harks back to our early fish-like ancestors. These had lateral-line organs consisting of horizontal rows of hair cells on either side of the body, which were thought to be used for detecting vibrations in the water, which might help with schooling, as well as for detecting obstacles and predators (Ramachandran, 1996). The same author also suggested that this lateral line system could have become "internalized", becoming the cochlea in the higher vertebrates and still present in vestigial form in humans. Other authors have suggested that the visceral reaction to these sounds mimics some "naturally occurring, innately aversive event" (Green, 1975) or is a reaction to sounds similar to the vocalizations of some predators (Halpern, Blake et al., 1986). Audition, especially the ability to quickly identify environmentally salient information, including danger and reward, and to react rapidly, has always been critical for survival (Darwin, 1872/1965).

Neuroimaging studies have shown that the amygdala is involved in evaluating and/or responding to a sensory input of aversive stimuli, not only for auditory, but for other

sensory modalities (visual, olfactory, and gustatory) (Zald and Pardo, 2002). Some inconsistency in amygdala responses has been found in previous studies of unpleasant sounds , and contributing factors might have been the use of a mildly unpleasant sound or an extremely rapid habituation of the amygdala (Bordi, LeDoux et al., 1993). Other structures are also triggered in reaction to aversive stimulus, such as the limbic/paralimbic areas (Zald and Pardo, 2002).

In normal subjects, unpleasant sounds provoke autonomic responses and musculoskeletal tension (Davis, 1997).

1.2. Neural substrates triggered by auditory emotionally salient stimuli

It has been suggested that emotionally-charged stimuli produce preferential rapid routing of the impulse which bypasses the cortical route via the amygdale. Studies in the rat showed that thalamic sensory nuclei relay afferent signals to subcortical as well as cortical areas (LeDoux, Ruggiero et al., 1985; LeDoux, Farb et al., 1990). Auditory information from the posterior thalamus reaches the lateral nucleus of the amygdala (LA) by means of two pathways: a direct thalamo-amygdala projection (classical auditory pathway, “low route”) and a polysynaptic thalamo-cortico-amygdala projection (non–classical auditory pathway, “high route”). The medial division of the medial geniculate body (MGm), the suprageniculate nucleus (SG) and the posterior intralaminar nucleus (PIN) are the thalamic areas that receive input from both the inferior collicullus and the spinal cord and project it to the lateral nucleus of the amygdale (LeDoux, 2000). Many of these mechanisms have been best studied in auditory fear conditioning conditions. Recent research in this field has suggested that the thalamo-cortico-amygdala is the principal CS pathway route when the

brain is intact, contrary to several lines of evidence in favour of the direct thalamo-amygdala pathway (Boatman and Kim, 2006).

In humans, these pathways have been studied in tinnitus patients, in whom there seems to be a cross-modal interaction between the auditory and the somatosensory system. Normally, this interaction occurs in young children and decreases with age, and is rare in individuals above the age of 20 years who do not have tinnitus (Moller, 2003). One main difference between these two auditory pathways is that neurons in the classical pathway only respond to sound, while neurons in the non-classical pathway respond to sound and other sensory modalities, such as touch and light. It has been suggested that non-classical auditory pathways may be abnormally active in some tinnitus patients, which would allow the conduction of auditory information to the amygdala through the subcortical route. This may explain the affective symptoms that often accompany severe tinnitus, such as depression and phonophobia.

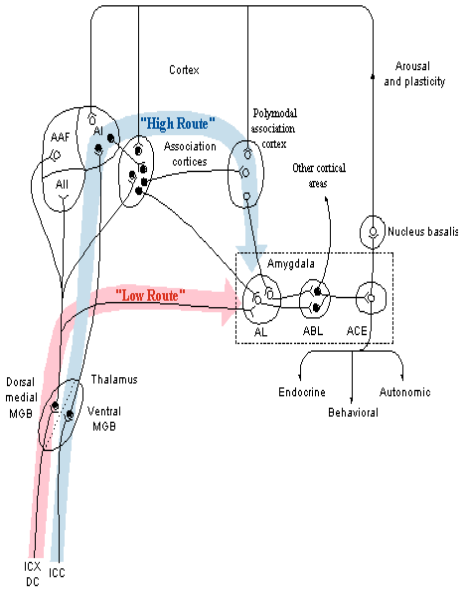


Figure 1: Connections from the auditory system to the amygdala, through the high route and the low route. AL: lateral nucleus of the amygdala, ABL: basal nucleus of the amygdala, ACL: central nucleus of the amygdala (Moller, 2003).

This mechanism is not well understood but there are indications that neural plasticity expression is involved. The non-classical auditory pathways might be activated through the expression of neural plasticity by which "dormant" synapses could be "unmasked" , thereby opening connections that are normally blocked by non-conducting (masked) synapses (Moller, 2003).

1.3. About emotion

Our motivational organization of emotions has a simpler, biphasic structure. Circuits are activated by unconditioned appetitive and aversive stimuli. Pleasant emotions are associated with an appetitive system, whereas unpleasant emotions are driven by a defensive system. These neural circuits were laid down early in our evolutionary history, in the primitive cortex, sub cortex and mid brain areas, and mediate behaviour which is fundamental to the survival of individuals and species. They mediate a broad range of physiological and behavioural events: changes in the facial musculature, skin conductance, heart rate and cortical event-related potentials recorded from the scalp surface. All are valuable measures of emotional expression.

An emotion begins with appraisal of an emotional stimulus, and signals evoked by that stimulus are carried from sensory areas to a number of emotion-triggering sites in the brain, including the amygdala and orbitofrontal cortex: the amygdala is more engaged in triggering emotions when the emotional stimulus is present; the orbitofrontal cortex is more important when it is recalled from memory. To create an emotional state, activity must propagate to the execution sites, which include the hypothalamus, the basal forebrain and nuclei in the brainstem tegmentum (Lang, Bradley et al., 1998; Lang, Davis et al., 2000; Phillips, Drevets et al., 2003). However, studies on emotion are far from exhaustive.

Damasio distinguishes emotions from feelings. Emotions are changes in body and brain states triggered by a dedicated brain system which responds to the content of one's perceptions, whether actual or recalled. Body responses range from changes in heart rate or smooth muscle contraction to changes which are perceptible to an external observer (such as those of posture or facial expression). The signals generated by these body responses produce brain changes that are perceptible mostly to the individual and provide the essential ingredients for what is ultimately perceived as a feeling. Emotions are what an outside observer can see; feelings are what the individual subjectively experiences (Damasio, 1994; Damasio, 1998; Lang, Bradley et al., 1998; Damasio, 1999; Bechara and Naqvi, 2004).

1.4. Emotional disturbances in schizophrenia

Since its original description, emotional dysfunction has been regarded as a hallmark of the disease (Bleuler, 1911). Bleuler considered that affective symptoms belong to the primary symptoms of schizophrenia and even raised the question as to whether emotional disturbances are a cause or an effect. In the past, researchers and clinicians have seen emotional disturbance more as a reaction to the illness. Nevertheless, some authors argue that the dysfunction of emotional brain systems may be very important in understanding this disorder. Recent theoretical proposals incorporate the growing body of evidence that emotional disturbances and dysfunction of the corresponding brain circuits may be at the core of schizophrenia, more specifically, the role of amygdala abnormalities in dysregulating the emotional brain as well as the medial prefrontal and orbitofrontal cortex, anterior cingulate, and insula (LeDoux, 1995; Aleman A. and Kahn R., 2005). Furthermore, MRI studies in schizophrenic patients have demonstrated volume reductions of the

amygdala (Joyal, Laakso et al., 2003), amygdala-hippocampal complex (Lawrie, Whalley et al., 2003), and thalamus (Konick and Friedman, 2001).

In schizophrenia, certain affective states have been associated with the onset of psychotic symptoms. There seems to be a stage of heightened awareness, and emotionality combined with a sense of anxiety and impasse has consistently been described as preceding psychosis (Conrad, 1958.; Yung and McGorry, 1996). Moreover, recent evidence indexed an increase in anxiety prior to the onset of hallucinations (Delespaul et al., 2002) and delusions (Freeman et al., 2001). According to Cutting (2003), anxiety is particularly marked at the outset, but is pathologically absent from the chronic stages of schizophrenia. Data from psychophysiology corroborates self-reports regarding the increased anxiety and arousal associated with psychosis.

1.5. Studies on emotion processing in schizophrenia

Some studies have shown that schizophrenic patients are noted to have deficits in the recognition and discrimination of facial emotions (Morrison, Bellack et al., 1988; Mandal, Pandey et al., 1998; Kohler, Bilker et al., 2000; Edwards, Pattison et al., 2001; Habel, Krasenbrink et al., 2006; Holt, Kunkel et al., 2006; Namikia, Hiraob et al., 2007; Turetsky, Kohler et al., 2007). However, there is an ongoing discussion that questions whether these impairments represent a differential deficit for emotion processing or reflect a generalized cognitive deficit (Kerr and Neale, 1993; Leppänen, Niehaus et al., 2006), with some studies in favour of a specific deficit in the processing of a subset of intense negative emotional expressions (anger, sadness and fear) (Kohler, Bilker et al., 2000b; Silver, Shlomo et al., 2002; Bediou, Franck et al., 2005).

In contrast to the large volume of research on facial emotion perception in schizophrenia, studies examining emotional sound processing are scarce. The first known comprehensive study of auditory affect perception in both verbal/semantic and non verbal/semantic modalities showed that patients with auditory hallucination had deficits in the perception of auditory affective stimuli (Rossell and Boundy, 2005).Over the last five years, more articles have been published on emotional prosody perception and have demonstrated that chronic inpatients do less well than normal controls (Edwards, Jackson et al., 2002; Hoekert, Kahn et al., 2007). Only one study has studied the affective recognition of environmental sounds and demonstrated that it was preserved in schizophrenic patients (Tuscher, Silbersweig et al., 2005).

1.6. Aim of the present study

In the present study, we aim to evaluate the emotional processing of unpleasant sounds in schizophrenic patients in early stages of the disease. To the best of our knowledge, this has never been studied before. Our hypothesis is that at the onset of this disease, unpleasant sounds could be very arousing and provoke a strong vestigial response. Perception and cognition of such an emotionally auditory-relevant stimuli (some of them with survival advantage) could lead to abnormally open non-classical auditory pathways. This would allow conduction of auditory information to the amygdala through the subcortical route and, consequently, could be the core of the deregulation of emotional brain in psychiatric disorders, leading to the onset of psychotic symptoms which normally begin with hyperarousal and anxiety. We therefore hypothesized that there is an alteration in the emotional processing of unpleasant sounds in which patients perceive them as much more unpleasant than normal controls.

2. Methods

2.1. Recruitment

This study was performed on schizophrenic outpatients from the Psychiatry Departments of Hospital de Santa Maria and Hospital Júlio de Matos, both in Lisbon. Patients were of both sexes, different ages and diverse socio-economic levels, and were recruited from August to September 2007, when they attended the above institutions for consultations (ambulatory setting).

2.2. Sampling

The study sample consisted of 29 patients diagnosed with schizophrenia according to the 4th Edition of the Diagnostic and Statistical Manual (DSM- IV- TR) (American Psychiatric Association, 2000). Additional entry criteria included: having no prominent organic cognitive disorder or mental retardation; being clinically stable enough to undergo the assessment (stability criteria included no medication changes or hospitalization in the 30 days prior to assessment); willingness to participate in the study and give informed consent. Exclusion criteria were the following**:** illness duration of more than 5 years; history of neurological or developmental disorders, head injury with a loss of consciousness for more than 10 min**;** recent substance abuse or dependence within the last 6 months (except tobacco)**;** axis I diagnosis other than schizophrenia or a medical disorder which might compromise cognitive performance**;** and hearing impairment.

The controls were 29 healthy individuals recruited from the non-professional staff at Lisbon University Medical School and Hospital de Santa Maria, matched in age, and male and female ratio. This group had the same inclusion criteria as the patients, including no

lifetime DSM-IV diagnosis of psychiatric disease, and were excluded if receiving any psychiatric medication.

The study was approved by the Ethics Committees of both hospitals and all participants gave their written informed consent before any procedure (see appendix A).

2.3. Measurements

Assessment took place in a quiet room with the participant and the examiner seated. Subjects were first submitted to a general socio-demographic questionnaire and a semi-structured interview to record clinical information (see appendix B). A Portuguese version of the Mini-Mental State Examination (MMSE) (Folstein, Folstein et al., 1975; Guerreiro, Silva et al., 1994) (see appendix C) was then performed to evaluate the presence of cognitive impairment in all participants. To assess the presence and severity of patients´ symptoms, we used a semi-structured interview of PANNS (Kay, Fizbein et al. 1987, adapted by Leitão) (see appendix D). PANSS is probably the most widely-used rating scale in schizophrenia (Overall and Gorham, 1988), and it allows for simultaneous rating of positive and negative symptoms. It is a 30-item symptom rating scale rated from 1 to 7 (with higher scores indicating more severe symptoms) as well as sub-scales reflecting positive and negative symptoms. Some additional information was obtained from family members and patients' files.

2.3.1 Apparatus

Behavioural Experiment (to test emotional valence on the unpleasantness of sounds):

This experiment was conducted using an Amilo Fujitsu Siemens laptop computer, (Intel® Core Duo® Processor,) with a UA-4FX Edirol® sound card, running MATLAB® 6.1

programme software, which presented sound stimuli, ratings and statistical analysis. The sounds were delivered through a HD 250- II Sennheiser headphones at 70-75 db average of intensity. Subjects were verbally informed about the nature of the experiment, testing apparatus and procedures. Prior to the experiment, subjects underwent three practice trials (heard three examples of the sound stimuli for familarization purposes).

2.3.2. Stimulus selection

All subjects heard the 75 stimulus sounds of the Newcastle Battery of Unpleasant Sounds (NBUS) (see appendix G), a new instrument developed by the Auditory Group of Newcastle Medical School, which consists of 75 sounds. These were compiled from Bailey's sound battery (Bailey, Chrisholm et al., 2002), International Affective Digitized Sound System IADS (Bradley and Lang, 1999) and various internet sources. These reflect a broad range of sounds, including human and animal vocalisations, musical instruments and mechanical processes, and included common sounds with positive and negative valences (e.g. tires screeching, female screaming, baby crying, laughing). It contains no verbal messages. The duration of the stimuli varied between 1.5 seconds and 2 seconds. The intensity level of the stimuli was equalised and the calibrated perceived loudness varied between 70dB and 75dB. Sounds were presented only once and randomly presented for each set of trials. A self-report measure of emotional experience was asked after hearing each sound. Normally, psychologists represent emotions or feelings in n-dimensional space (generally 2- or 3- dimensional) (Chanel, Kronegg et al., 2005). In this experiment, only the valence dimension in which valence represents the way one judges a situation, from unpleasant to pleasant, was assessed. A ten point visual scale from 0 to 9, with 0 being the least unpleasant and 9 being the most unpleasant was used (see appendix F). This self-

assessment was not subject to a time limit so as to allow for a resting period between sounds.

All tests took approximately 40 minutes to administer and were administered by a single investigator in a single session.

Schizophrenic subjects tolerated these long-duration procedures. They understood and performed the experimental testing, and their ratings seemed to be valid and reliable.

2.4. Statistical analysis

Data were expressed in terms of mean ± s.d. values and rounded to the nearest decimal place. Statistical analysis was performed using the SPSS® 15.0 version for Windows® software (Martinez and Ferreira, 2007). Statistical significance was accepted at $p<0.05$. The different tests and the rationale for their use are described in the results section.

3. Results

3.1. Sample characteristics

Fifty-eight participants (29 patients and 29 controls) were assessed. The characteristics of each group are shown in Table 1. As controls were matched in age and sex, there were no significant differences between the groups in respect of these items, or musical training. There were significant differences with respect to race, years of education and Mini Mental State Examination assessment, with the control group being better educated and scoring higher in the cognitive assessment.

Table 1 - Sociodemographic characteristics and symptoms.

Sample Characteristics	**Clinical(N=29)**	**Control(N=29)**	*p*
	Mean (SD) or No. (%)	Mean (SD) or No. (%)	
Demographic			
Age (Years)	28.7 (6.7) Range 19-43	28.7 (6.7) Range 19-43	1.000(*)
Sex (M/F), no. (%)	20 (69.0) / 9 (31.0)	20 (69.0) / 9 (31.0)	1.000(**)
Race (White/Black), no. (%)	21 (72.4) / 8 (27.0)	29 (100.0) / 0.0	**0.004(**)**
Education (Years)	10.4 (3.4) Range 6-16	14.3 (2.6) Range 6-16	**0.000(*)**
Musical Training (Yes/No), no.(%)	18 (62.1) / 11 (37.9)	21 (72.4) / 8 (27.6)	0.576(**)
Clinical			
Age of onset (Years)	26.8 (6.8) Range 18-41		
Illness duration (Years)	2.3 (1.5) Range 0-5		
Subtype, no (%)			
Paranoid	26 (89.7)		
Disorganized	1 (3.4)		
Undifferentiated	1 (3.4)		
Residual	1 (3.4)		
Family history of disease (Yes/No), no (%)	21 (72.4) / 8 (27.6)		
Number of hospitalizations	1.3 (0.9) Range 0-3		
MMSE	28.6 (1.5) Range 25-30	29.6 (0.6) Range 28-30	**0.002(*)**
PANSS			
Positive subscale	10.1 (3.7) Range 7-17		
Negative subscale	13.2 (2.9) Range 8-19		
General subscale	26.3 (4.7) Range 18-37		
Total	49.6 (8.9) Range 33-66		

Abbreviations: MMSE= Mini-Mental State Examination; Sex (M=male; F=female);
(*) result of the Mann-Whitney Test; (**) result of the Chi-Square Tests

3.2. Clinical variables

Most patients were diagnosed with paranoid type of schizophrenia (n=26, 89%). One patient was diagnosed with disorganized type, one with catatonic type and only one with residual type. Concerning medication, all patients used antipsychotic medication (typical for one patient, atypical for twenty-five and both medications for three patients). It was not possible to assess mean antipsychotic doses because patients used different types of antipsychotic drugs. Some patients were also medicated with: benzodiazepines (n=11), anticholinergics (n=9) and antidepressants (n=5).

Table 2 –Patients' medication status

	Clinical(N=29)	
	n	**%**
Antipsychotics		
Typical	1	3.4
Atypical	25	86.2
Both	3	10.3
Benzodiazepines		
No	18	62.1
Yes	11	37.9
Anticholinergics		
No	20	69.0
Yes	9	31.0
Antidepressants		
No	24	82.8
Yes	5	17.2

The severity of patients' symptoms was assessed using PANSS (see Table 1). The PANSS total mean score amounted to 49.58 ± 8.8. The mean score was 10.10 (s.d.3.6) on the positive subscale and 13.17 (s.d.2.8) on the negative subscale. The general subscale had a mean of 26.31 (s.d.4.6).The PANSS positive subscale contributed less to overall score than the negative, a finding that is consistent with their outpatient status. This fact made it possible to perform the experiment task reliably.

Table 3 - Male and female patients' severity of PANSS

Measure	Male(N=20)		Female(N=9)		*p*
	Mean (SD)	Range	Mean (SD)	Range	
PANSS					
Positive subscale items					
Delusions	2.0 (1.2)	1-4	1.4 (0.9)	1-3	0.220
Conceptual disorganization	1.4 (0.5)	1-2	1.1 (0.3)	1-2	0.191
Hallucinatory behaviour	1.9 (1.3)	1-5	1.0 (0.0)	1-1	**0.048**
Excitement	1.2 (0.4)	1-2	1.1 (0.3)	1-2	0.782
Grandiosity	1.5 (0.9)	1-3	1.0 (0.0)	1-1	0.105
Suspiciousness/persecution	2.0 (1.1)	1-4	1.7 (0.9)	1-3	0.535
Hostility	1.1 (0.3)	1-2	1.0 (0.0)	1-1	0.334
Positive subscale	10.9 (4.0)	7-17	8.3 (1.9)	7-12	0.255
Negative subscale items					
Blunted affect	2.1 (0.5)	1-3	2.1 (0.3)	2-3	0.764
Emotional withdrawal	2.3 (0.7)	1-4	2.1 (0.6)	1-3	0.662
Poor rapport	1.6 (0.7)	1-3	1.6 (0.5)	1-2	0.812
Passive/apathetic social withdrawal	2.6 (0.7)	2-4	2.3 (1.0)	1-4	0.573
Difficulty in abstract thinking	2.1 (0.9)	1-4	2.2 (1.1)	1-4	0.692
Lack of spontaneity and flow of conversation	1.4 (0.5)	1-2	1.8 (0.7)	1-3	0.133
Sterotyped thinking	1.2 (0.4)	1-2	1.3 (0.5)	1-2	0.446
Negative subscale	13.1 (2.8)	10-18	13.4 (3.2)	8-19	0.583
General subscale items					
Somatic concern	1.5 (0.8)	1-3	1.8 (0.8)	1-3	0.337
Anxiety	2.0 (0.8)	1-3	2.3 (1.6)	1-6	0.881
Guilt feelings	1.7 (0.7)	1-3	1.8 (1.0)	1-3	0.836
Tension	1.9 (0.7)	1-3	1.8 (1.0)	1-4	0.610
Mannerisms and posturing	1.4 (0.6)	1-3	1.6 (0.7)	1-3	0.582
Depression	2.7 (1.0)	1-4	2.4 (1.3)	1-5	0.418
Motor Retardation	1.3 (0.6)	1-3	1.6 (1.3)	1-5	0.815
Uncooperativeness	1.1 (0.2)	1-2	1.0 (0.0)	1-1	0.502
Unusual Thought content	1.2 (0.5)	1-3	1.3 (0.7)	1-3	0.616
Disorientation	1.1 (0.2)	1-2	1.0 (0.0)	1-1	0.502
Poor attention	1.4 (0.5)	1-2	1.2 (0.4)	1-2	0.360
Lack of judgment and insight	2.4 (0.6)	1-3	1.3 (0.5)	1-2	**0.001**
Disturbance of volition	1.3 (0.4)	1-2	1.3 (0.5)	1-2	0.648
Poor impulse control	1.1 (0.3)	1-2	1.1 (0.3)	1-2	0.929
Preoccupation	2.0 (0.7)	1-3	1.3 (0.5)	1-2	**0.025**
Active social avoidance	2.9 (0.9)	1-4	2.8 (1.1)	1-4	0.786
General subscale	26.6 (3.6)	21-32	25.7 (6.7)	18-37	0.477
Total subscale	50.6 (8.4)	39-66	47.4 (10.0)	33-58	0.408

(*) result of the Mann-Whitney Test;

There were significant differences between the severity of the male and female symptoms measured by PANSS, with men showing severe symptoms in items such as: hallucinatory behaviour, lack of judgment and insight, and preoccupation ($p<0.05$).

3.3. Analysis of the Unpleasantness of Sounds

3.3.1. Reliability of the Instrument

We measured the reliability of The Newcastle Battery of Unpleasant Sounds (75 sounds). For both groups, Cronbach's Alpha was above 0.6, which demonstrated a good internal consistency reliability of the test (0.916 for clinical group; 0.951 for control group) (Pestana and Gageiro, 2005).

3.3.2. Preliminary analysis

All 75 sounds were classified between 0 and 9 (ten point scale).

First, we analysed the mean unpleasantness rating and standard deviation of the 58 ratings of each 75 sounds split by group (clinical and control) as shown in Table 4.

The sound set used contains a large variation in perceived unpleasantness across a broad range of sounds. It can be seen that female screaming-2 obtained the highest mean unpleasantness rating of 7.3 in the clinical group, while blackboard chalk-1 1 was the highest in the control group, scoring 7.8. Baby laugh had the least mean unpleasantness rating of 0.80 in both groups (1.5 for clinical and 1.2 for control). It can also be seen that the standard deviations of the ratings of each sound vary from 1.1 to 2.8.

Table 4 - Mean unpleasantness rating of the 58 ratings of each sound, split by group, displayed in order of mean unpleasantness from the most unpleasant to the least unpleasant

Sound Name	Clinical		Sound Name	Control	
	Mean	Standard Deviation		Mean	Standard Deviation
Femalescream_2	7.3	1.8	Blackboard_chalk_1	7.8	1.3
Fork_glass_3	7.2	1.7	Knife_bottle_1	7.8	1.5
Angle_grind_2	7.2	2.1	Fork_glass_1	7.7	1.4
Femalescream	7.1	2.0	Fork_glass_3	7.6	1.7
Fork_glass_1	7.1	1.8	Femalescream	7.5	1.5
Ruler_bottle_2	7.0	1.9	Blackboard_chalk_2	7.3	1.2
Blackboard_chalk_1	7.0	1.9	Ruler_bottle_1	7.3	1.7
Electric_drill_2	6.9	2.0	Femalescream_2	7.2	1.7
Ruler_bottle_1	6.9	2.2	Ruler_bottle_2	7.2	2.0
Fork_bottle_3	6.9	1.7	Fork_bottle_4	7.1	1.4
Tire_skids	6.8	1.8	Fork_bottle_1	7.0	2.1
Electric_drill	6.8	2.3	Angle_grind_2	6.9	1.9
Angle_grind1	6.7	1.7	Blackboard_nails_1	6.9	1.3
Blackboard_chalk_2	6.6	2.0	Fork_bottle_3	6.9	1.8
Spade_drag_2	6.6	1.7	Electric_drill_2	6.8	1.6
Fork_bottle_1	6.5	2.0	Electric_drill	6.6	2.0
Blackboard_nails_2	6.5	1.8	Brake_double	6.6	1.6
Lion2	6.5	2.2	Fork_glass_4	6.5	2.1
Knife_bottle_1	6.4	2.6	Angle_grind1	6.4	1.5
Blackboard_nails_1	6.4	2.0	Blackboard_nails_2	6.4	1.5
Cougar	6.2	1.8	Tire_skids	6.4	1.9
Wasp_1	6.2	2.7	Lion2	6.3	1.7
Record_scratch_1	6.2	2.4	Spade_drag_1	6.3	1.4
Fork_glass_4	6.2	2.4	Hippo	6.2	1.3
Doggrowl	6.2	2.3	Wasp_1	6.1	1.9
Anteater	6.0	2.3	Record_scratch_1	6.0	1.8
Fork_bottle_4	6.0	2.7	Spade_drag_2	5.9	1.8
Gorilla	6.0	1.7	Gorilla	5.8	1.7
Leopard1	5.9	2.3	Anteater	5.8	1.4
Bear2	5.8	1.7	Mixer_glass_1	5.7	1.6
Macaca	5.8	2.3	Guitar_1	5.7	1.7
Junglebird2	5.7	2.1	Doggrowl	5.7	1.8
Brake_double	5.7	2.3	Buzzer	5.6	1.7
Domesticcat	5.7	1.6	Panther	5.6	1.7
Catpurr2	5.7	2.1	Camel	5.6	1.5
Film_projector	5.6	2.1	Leopard1	5.6	1.8

Buzzer	5.6	2.5	Clarinet_squeak	5.6	2.3
Camel	5.6	1.9	Bear2	5.6	1.6
Glassbreaking	5.6	2.5	Cougar	5.5	1.9
Spade_drag_1	5.5	2.5	Domesticcat	5.5	1.5
Pig_	5.5	2.1	Glassbreaking	5.5	1.5
Clarinet_squeak	5.5	2.6	Junglebird2	5.3	1.7
Hippo	5.4	2.2	Cat_screaming	5.3	1.8
Cat_screaming	5.3	1.9	Bull frog	5.3	1.6
Bull frog	5.3	2.2	Film_projector	5.3	1.6
Baby cry	5.3	2.8	Violin	5.2	1.7
Clarinet_honk	5.1	2.5	Pig_	5.1	1.5
Violin	5.1	1.9	Catpurr2	5.1	2.2
Spade_drop_1	5.1	2.4	Clarinet_honk	5.0	1.6
Elephant	5.0	2.4	Elephant	5.0	1.8
Thunder1	5.0	2.7	Spade_drop_1	4.9	1.7
Mixer_glass_1	4.9	2.4	Guitar_2	4.9	1.6
Panther	4.8	2.6	Thunder1	4.8	2.0
Guitar_1	4.8	2.2	Firealarm	4.8	1.9
Guitar_2	4.6	2.7	Puffer	4.7	1.7
Zeb	4.6	2.5	Howlin_wolf	4.5	1.7
Multiple_babies	4.6	2.3	Baby cry	4.4	2.1
Puffer	4.6	2.3	Macaca	4.4	2.0
Falcon	4.6	2.0	Phone_ringing	4.3	1.9
Firealarm	4.5	1.9	Falcon	4.2	2.0
Howlin_wolf	4.2	2.7	Thunder2_	4.1	2.1
Lamb	4.0	1.9	Multiple_babies	3.9	1.3
Phone_ringing	3.8	2.4	Reving_Engine	3.8	1.6
Thunder2_	3.6	3.0	Zeb	3.8	1.6
Reving_Engine	3.6	2.5	Dolphinclicks	3.8	1.4
Dolphinclicks	3.4	2.1	Lioncub	3.3	1.7
Frog1	3.3	2.3	Lamb	3.1	1.2
Lioncub	3.2	2.4	Eagle2	2.9	1.7
Eagle2	3.1	2.0	Frog1	2.7	1.3
Applause	2.6	2.2	Applause	2.5	1.4
Bubblingwater	2.5	2.3	Bubblingwater	2.0	1.6
Smallwaterfall	2.1	2.4	Running water_short	1.7	1.3
Running water_short	1.9	2.4	Smallwaterfall	1.6	1.4
Waterflow	1.7	1.8	Waterflow	1.5	1.2
Baby laugh	1.5	1.9	Baby laugh	1.2	1.1

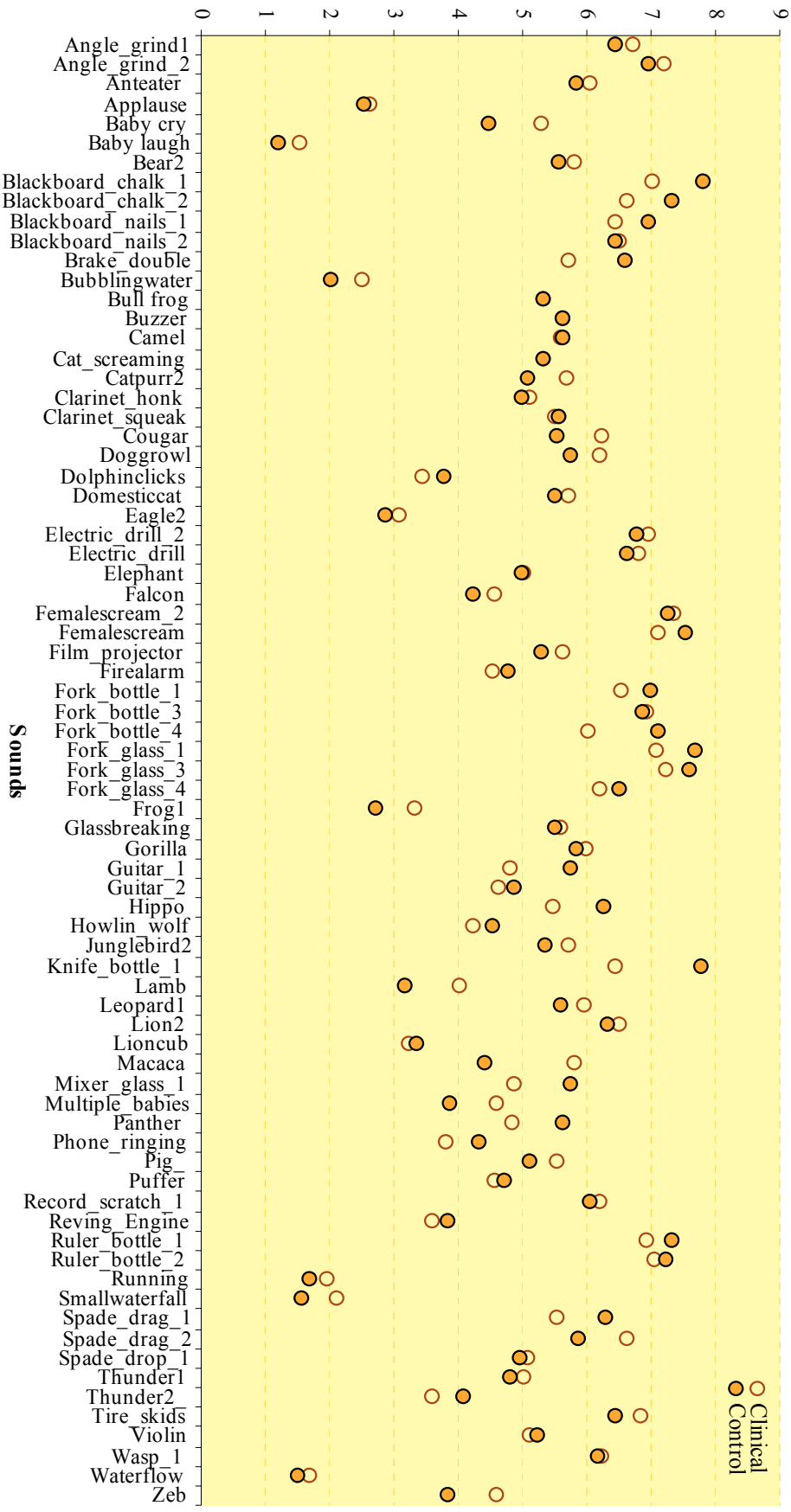


Figure 2 - Mean unpleasantness rating of the 58 ratings of each sound, split by group, displayed in alphabetical

The Mann-Whitney test was then used to compare this mean rating between these two groups. Only one sound (macaca) had a statistically significant difference for $p<0.05$.

Table 5 – Sounds with a statistical difference in mean between groups

Sound Name	Group	Mean	Standard Deviation	p
Guitar_1	Clinical	4.8	2.2	0.086(**)
	Control	5.7	1.7	
Knife_bottle_1	Clinical	6.4	2.6	0.061(**)
	Control	7.8	1.5	
Lamb	Clinical	4.0	1.9	0.075(**)
	Control	3.1	1.2	
Macaca	Clinical	5.8	2.3	0.027(*)
	Control	4.4	2.0	

(*)$p<0.05$; (**)$p<0.1$

Table 6 - Sounds with a statistical difference in mean between years of illness duration

Sound Name	Illness duration	n	Mean	Standard Deviation	p
Doggrowl	0	3	6.0	4.4	0.047(*)
	1	9	5.0	1.8	
	2	5	7.6	1.3	
	3	4	6.0	1.4	
	4	5	5.4	2.1	
	5	3	9.0	0.0	
Firealarm	0	3	3.3	2.5	0.014(*)
	1	9	4.9	0.9	
	2	5	3.8	2.4	
	3	4	6.5	1.3	
	4	5	2.6	1.1	
	5	3	6.3	0.6	
Macaca	0	3	8.3	0.6	0.024(*)
	1	9	4.4	0.9	
	2	5	5.0	2.1	
	3	4	4.8	2.8	
	4	5	6.8	2.9	
	5	3	8.3	1.2	
Thunder1	0	3	7.0	1.0	0.043(*)
	1	9	5.0	1.3	
	2	5	6.2	2.4	
	3	4	6.5	3.0	
	4	5	1.6	2.1	
	5	3	4.7	3.8	

(*)$p<0.05$ result of Kruskal Wallis test

Four sounds had a significant difference in mean unpleasantness rating by years of illness duration. In two cases, patients with longer illness duration had higher ratings (see table 6).

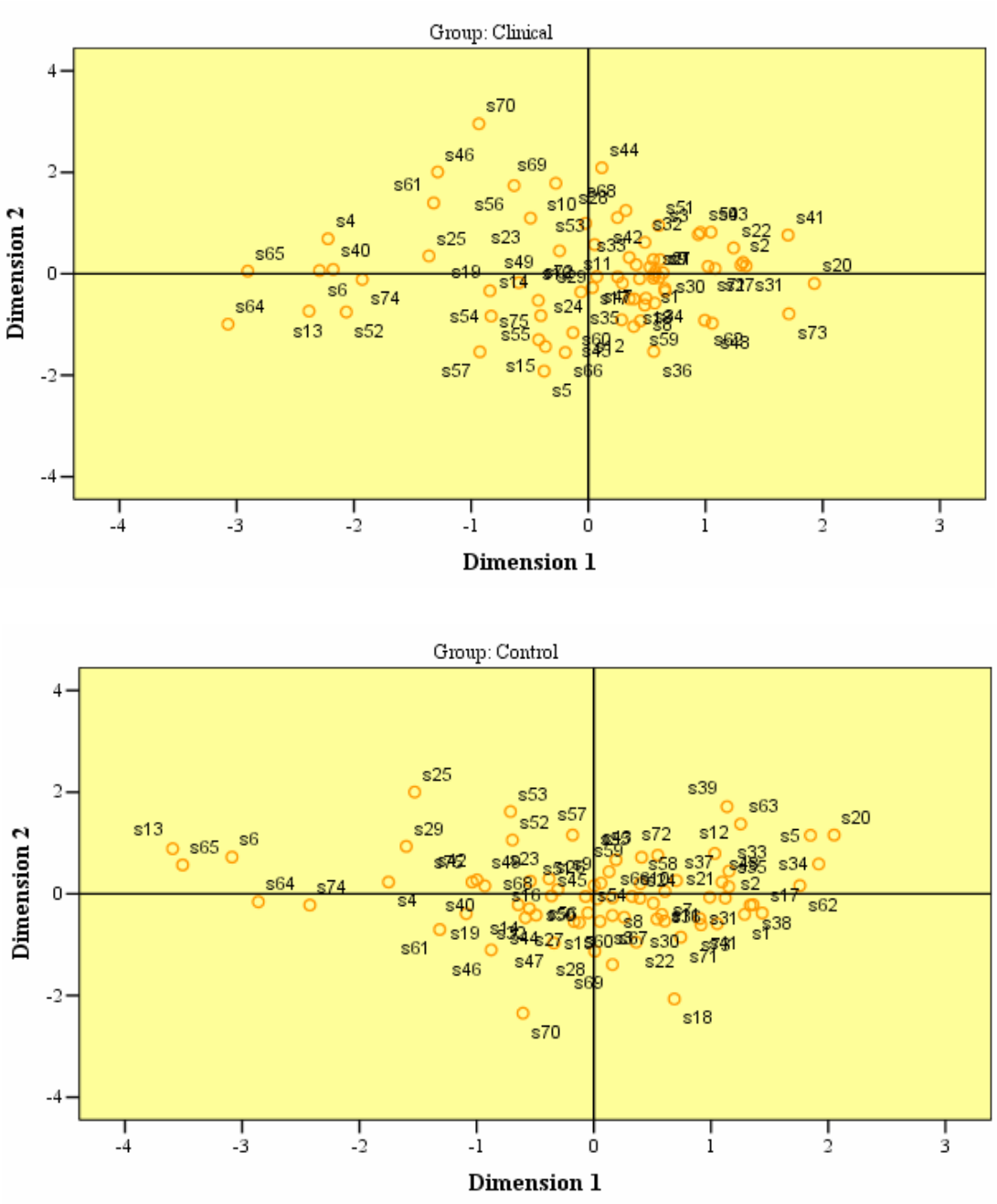
We also performed a Multidimensional Scale (MDS) analysis of the unpleasantness ratings of the 75 sounds for each group. This was done by producing a 75x75 correlation matrix which calculated all possible correlations of sound rating profiles. These correlations were converted into a measure of distance to produce a graph which displayed each sound as a point in two-dimensional space, where the two dimensions were unknown. This analysis allowed us to identify any clusters of sounds which would indicate that the sounds were perceived similarly. The distance between two sounds reflected the degree of similarity in the perceived unpleasantness of the sounds, with sounds appearing close together being perceived as similarly unpleasant and those farther apart being perceived as dissimilarly unpleasant.

Figure 3 displays the resulting two-dimensional plots: the numbers correspond to the position of the sound in alphabetical order (see appendix F).

The graphs in both groups revealed that the experimental sound set used reflected a broad range of unpleasantness, as desired. The patterns were different for both groups, but both seemed to have clusters of sounds, which mean that sounds were perceived very similarly. In the clinical group, there seem to be some sound clusters: for example, sound 2 (angle-grind-2), sound 27 (electric-drill) and sound 31 (female scream). The stress value from the analysis was 0.24, and the two dimensions represented 76.3% of the variance in unpleasantness ratings of the sounds. There were clusters in the control group too, for

example, sound 11 (blackboard-nails-2) and sound 30 Femalescream-2. The stress value was 0.22 and the level of variance was 83.1%.

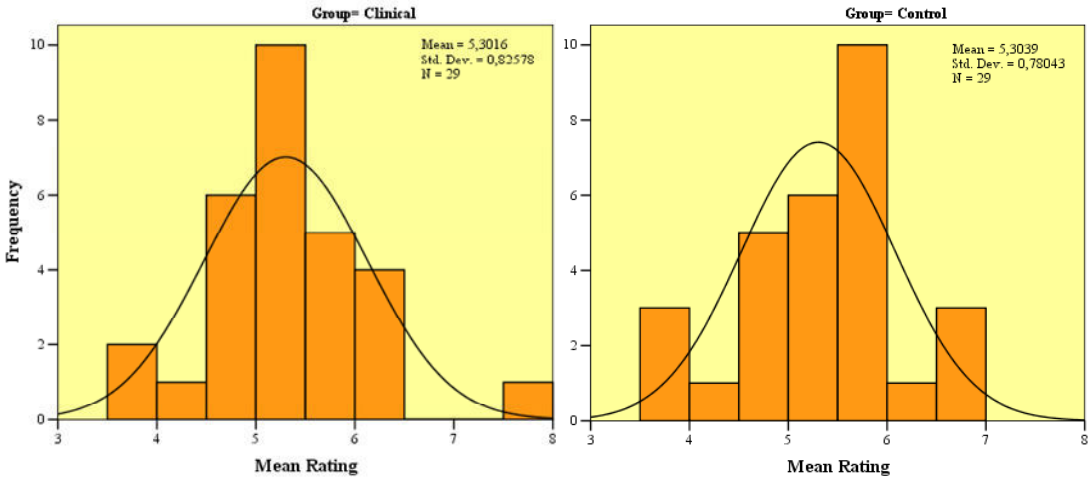
Figure 3 - A two-dimensional MDS plot of the unpleasantness ratings of 75 sounds for each group



3.3.3. Secondary analysis

In a second phase, we made a mean unpleasantness rating of the 75 sounds of each participant in the study, which we then split by group. In figure 4 we can see the normal distribution of the variable.

Figure 4 – Mean unpleasantness rating of the 75 sounds of each participant by group



After using the Shapiro Wilk test, which confirmed the normal distribution of this variable, the Student's t-test was used to compare groups and verify our hypothesis that schizophrenic patients would perceive our battery of sounds as more unpleasant than controls.

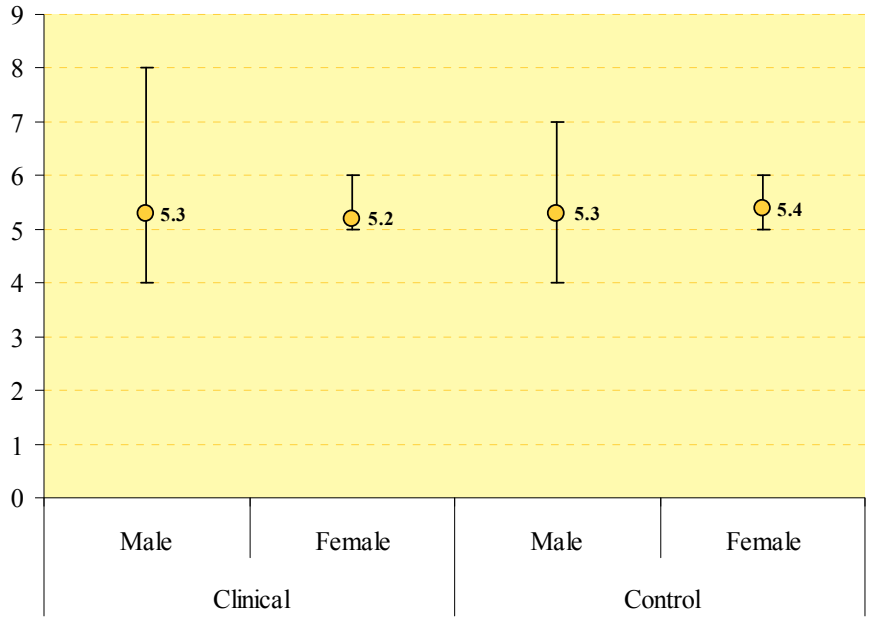
Table 7 – Mean unpleasantness rating by group

	Group	**n**	**Mean**	**Standard Deviation**	**p**
Mean Rating	Clinical	29	5.3	0.8	0.991
	Control	29	5.3	0.8	

In this study, with these data, there were no statistical differences between patients and controls as regards mean ratings of unpleasantness of sounds (p>0.05). Patients did not rate sounds as more unpleasant than controls.

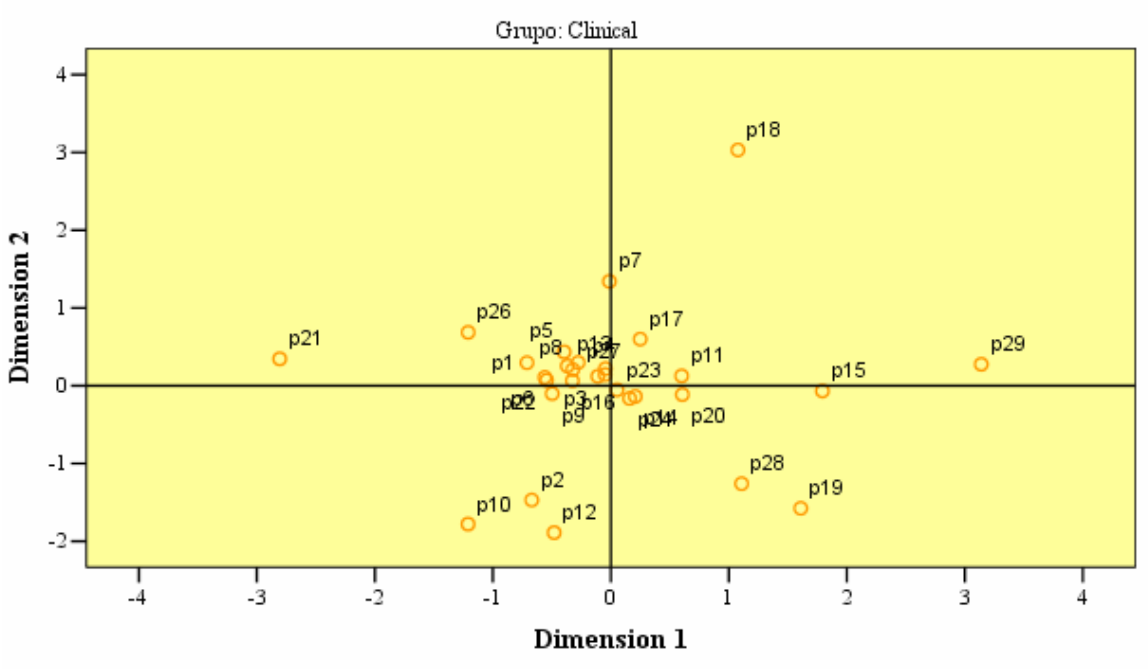
We also used the Student's t-test to compare mean ratings with sex variables in both groups, and no significant difference was found either. In the clinical group: male: 5.3 (s.d. 0.9); female: 5.2 (s.d. 0.5); p=0.697; In the control group: male: 5.3 (s.d. 0.9); female 5.4 (s.d. 0.4); p=0.778.

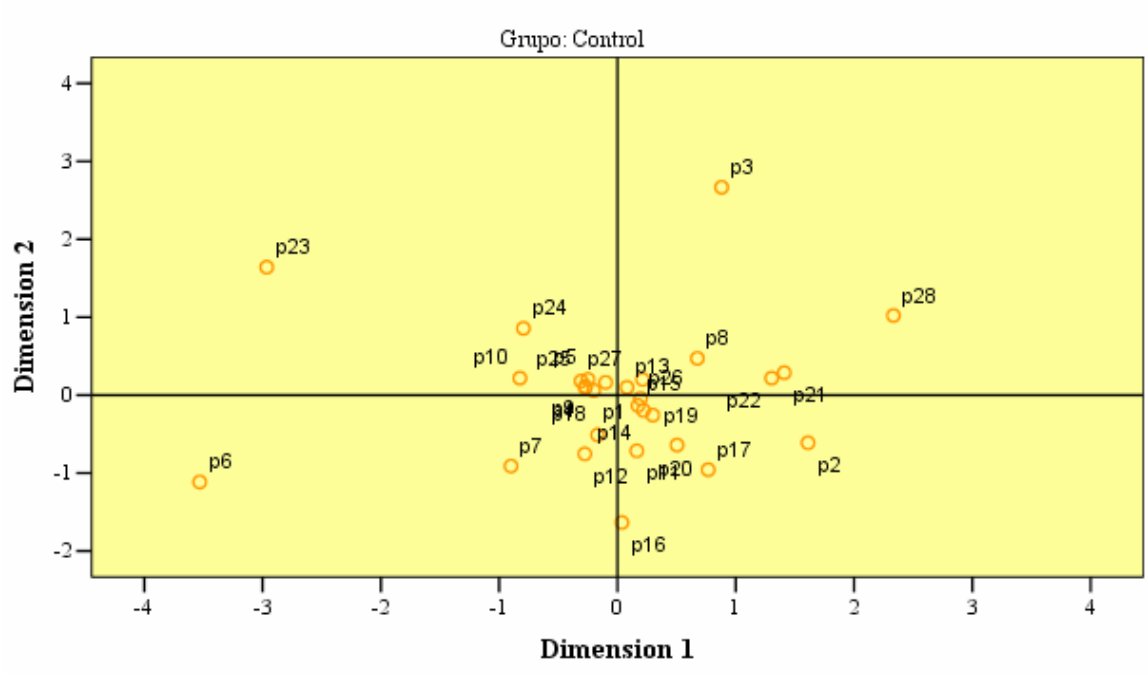
Figure 5 – Mean unpleasantness rating by group and sex



Although there were no significant differences in mean unpleasantness rating, we performed an MDS analysis of the mean unpleasantness ratings of the 29 participants in each group to look for differences in group profile patterns. This was achieved by producing a 29x29 correlation matrix. These correlations were then converted into a distance measure in order to produce a graph showing each participant's unpleasantness rating as a point in a two-dimensional space. The distance between two participants reflected the degree of similarity in their perceived mean unpleasantness ratings.

Figure 6- A two-dimensional MDS plot of the unpleasantness ratings of the 29 participants in each group





For the clinical group, the stress value from the analysis was 0.20 and the level of variance was 87.3%, while for the control group, the stress value was 0.16 and the level of variance 92.5%.

3.4. Association between clinical characteristics and mean unpleasantness rating

Correlations (Spearman's *p*) between sex and measures of unpleasantness rating (i.e. mean) were generally low and non-significant (*p* values >0.05). In addition, no significant correlations were found between clinical characteristics (i.e. years of diagnosis, PANSS subscales) and unpleasantness rating (*p* values >0.05).

Table 9 – Correlations between mean rating and some clinical characteristics

		Years of diagnosis	Illness duration	Positive subscale	Negative subscale	General subscale
Mean Rating	Correlation Coefficient	0.283	0.218	0.162	-0.138	0.145
	p	0.137	0.255	0.400	0.476	0.453

An analysis of the family history of disease status was performed with the Mann-Whitney test. No statistical difference was found either.

3.5. Cluster Analysis

In order to study the clinical group in more detail and to search for subgroups, we performed a K-means cluster analysis to find clusters based on their mean rating.

In clusters, the degree of association is strong between members of the same cluster and weak between members of different clusters. We decided on two clusters as there were 29 subjects in our sample.

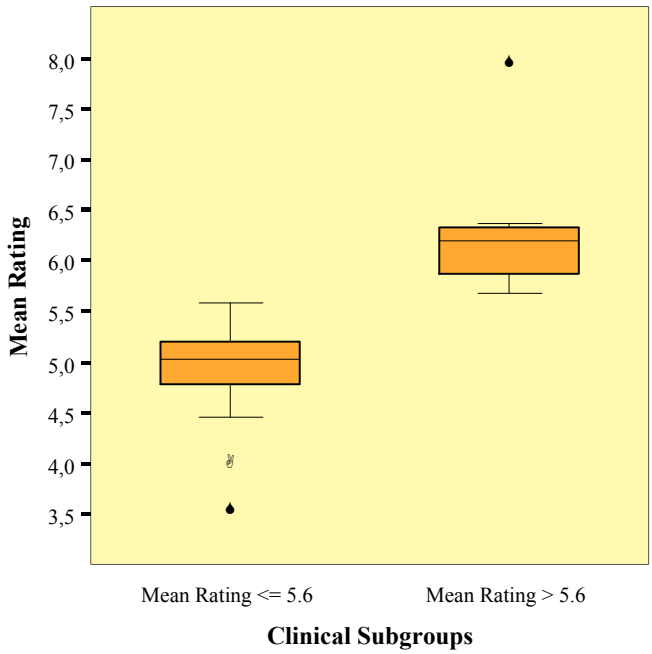
Table 10 – Cluster Analysis

Measure	Cluster	
	1	**2**
Number of cases	21	8
Mean rating	4.9	6.3
Median	5.0	6.1
Variance	0.2	0.4
Standard Deviation	0.4	0.4
Minimum	3.5	5.7
Maximum	5.6	7.9
Range	2.0	2.2

The analysis indicated a 5.6 point cut-off as the ideal threshold for patients' mean ratings. We called Clinical Subgroup 1 cluster 1 (mean rating <= 5.6) and Clinical Subgroup 2 cluster 2 (mean rating > 5.6).

We then used the Mann-Whitney test to confirm whether these two subgroups were really statistically different, and to accept this cluster analysis (p=0.000).

Figure 4 - Clinical Subgroups



After that, we searched for statistical differences between these two clinical subgroups for sociodemographic and clinical characteristics, which we did not find.

Table 11- Sociodemographic and clinical characteristics of Clinical Subgroups

Sample Characteristics (N=29)	**Clinical Subgroup 1 (N=21) Mean rating <=5.6**	**Clinical Subgroup 2 (N=8) Mean rating >5.6**	***p***
	Mean (SD) or No. (%)	Mean (SD) or No. (%)	
Demographic			
Age (years)	27.6 (6.4) Range 19-42	31.4 (7.0) Range 23-43	0.101(*)
Sex (M/F), no. (%)	14 (66.7) / 7 (33.3)	6 (75.0) / 2 (25.0)	1.000(**)
Race (White/Black), no. (%)	17 (81.0) / 4 (19.0)	4 (50.0) / 4 (50.0)	0.164(**)
Education (years)	10.7 (3.8) Range 6-16	9.8 (2.1) Range 6-12	0.757(*)
Musical Training (yes/no), no (%)	14 (66.7) / 7 (33.3)	4 (50.0) / 4 (50.0)	0.433(**)
Clinical			
Age of onset (years)	26.1 (7.0) Range 18-41	28.4 (6.5) Range 22-40	0.281(*)
Illness duration (years)	2.0 (1.4) Range 0-4	3.0 (1.9) Range 0-5	0.162(*)
Subtype, no (%)			
Paranoid	19 (90.5)	7 (87.5)	0.335(**)
Disorganized	0 (0.0)	1 (12.5)	
Undifferentiated	1 (4.8)	0 (0.0)	
Residual	1 (4.8)	0 (0.0)	
Family history of disease (yes/no), no (%)	16 (76.2) / 5 (23.8)	5 (62.5) / 3 (37.5)	0.646(**)
Number of hospitalizations	1.2 (0.8) Range 0-3	1.6 (0.9) Range 0-3	0.159(*)
MMSE	28.8 (1.3) Range 25-30	28.0 (2.0) Range 25-30	0.463(*)
PANSS			
Positive subscale	10.1 (3.6) Range 7-17	10.0 (4.1) Range 7-17	0.858(*)
Negative subscale	13.6 (3.0) Range 8-19	12.1 (2.3) Range 10-17	0.199(*)
General subscale	25.9 (4.5) Range 18-32	27.4 (5.2) Range 20-37	0.606(*)
Total	49.6 (8.9) Range 33-65	49.5 (9.3) Range 40-66	0.864(*)

MMSE= Mini-Mental State Examination; Sex (M=male; F=female);
(*) result of the Mann-Whitney Test; (**) result of the Chi-Square Tests

We also searched for differences in medication status, but there were none either.

4. Discussion

The main goal of this study was to evaluate emotional processing of unpleasant sounds in schizophrenic outpatients in early stages of the disease (less than five years of illness duration). To our knowledge, this has never been studied before. We developed and applied a new instrument called the Newcastle Battery of Unpleasant Sounds (NBUS). Our hypothesis was that these patients could have an altered emotional perception of unpleasant sounds, perceiving them as more unpleasant than healthy controls. We also hypothesized the existence of an ancient route, responsible for the conduction of emotionally auditory relevant stimuli to the amygdala, a direct thalamo-amygdala pathway.

4.1. Sample characteristics

Usually, men and women are affected equally, but the age of onset is earlier in men (Sadock and Sadock, 2005). Our sample was outpatients in early stages of the disease and the ratio of male to female was 2:1. With respect to the Mini Mental State Examination (a screening test for cognitive impairment) schizophrenic patients had a lower and significantly different mean score from controls (clinical group: 28.5; control group: 29.6; $p<0.05$). However, this result was not indicative of significant global cognitive impairment (score >24). The Mini Mental State Examination (MMSE) has been used as a broad test of global cognitive function in schizophrenia (Harvey, White et al., 1995) but is sometimes less sensitive and underestimates cognitive impairments in these patients (Palha, Branco et al., 2006). There is much debate about cognitive decline in schizophrenia, and whether it is progressive or static. Some studies suggest that these deficits are lifelong and pre-date the onset of schizophrenia (Russell, Munro et al., 1997). It has also been suggested that after a

period of initial deterioration early in the illness, cognitive deficits become static (Hyde, Nawroz et al., 1994).

4.2. Emotional processing of unpleasant sounds

In this study, we did not find any significant difference between clinical and control groups in mean ratings of sound unpleasantness. Patients did not perceive unpleasant sounds as more unpleasant than controls. These findings are in agreement with another study conducted on schizophrenics, in which it was demonstrated that emotional processing of environmental sounds measured by valence and arousal rating scales was preserved (Tuscher, Silbersweig et al., 2005). Regarding correlations between clinical severity measures (disease duration, PANSS total and sub scores) and mean unpleasantness rating, we found no statistical difference. This could suggest that the emotional processing of unpleasant sounds is rather stable during the first five years of illness. Nevertheless, we must reiterate that these patients were outpatients, and thus not in an acute state of psychotic symptom exacerbation.

The sounds presented varied widely in perceived unpleasantness. Pleasantness-unpleasantness depends not only on the loudness level or frequency component but on the accuracy in sound identification. Semantic associations may have had an effect upon unpleasantness ratings, as well as certain acoustic features which automatically caused an unpleasant perception (Shimai, Fukuda et al., 1993).

Some studies on facial emotion identification in schizophrenia have reported progressive impairments (Edwards, Jackson et al., 2002).Taken together this data raises the question as to why emotion processing of unpleasant sounds is perceived while other types of emotion processing are not. Is it because audition plays a role in the processing of environmental

cues with direct survival significance (e.g., growls, shouts, cries)(Verona, Patrick et al., 2004)? The amygdala has an evolutionary history in terms of the emotional processing needed for survival, and perhaps unpleasant sounds stimulate it directly through a second auditory pathway. Future studies will be needed to identify this pathway.

4.3. Sex differences in emotional sound processing

In this study, we found no sex differences in emotional processing of unpleasant sounds in either the clinical group or the control group. This could, however, have been due to the small size of the sample.

In contrast, one Japanese study on pleasantness-unpleasantness of environmental sounds did show gender differences: women rated the pleasant sounds as being more pleasant than the men did, and men rated the unpleasant sounds as not so unpleasant as the women's ratings of the same sounds (Shimai, Fukuda et al., 1993). Furthermore, in previous research in healthy subjects, a clear sex difference was observed in the ability to recognise facial emotions, especially negative ones, with women outperforming men (McClure, 2000). In schizophrenic patients, some studies have found sex differences in emotional processing for facial emotions, which could explain why women with schizophrenia are less impaired in social life than men (Seeman and Lang, 1990; Castle, Wessely et al., 1993; Scholten, Aleman et al., 2005).

4.4. Emotional experience, a subjective experience

As we have already mentioned, schizophrenic subjects tolerated the study procedures. They understood and performed the experimental testing, and their ratings seemed to be valid and reliable. Although some authors argue the opposite (Steinberg, 1986; Kallstrand,

Montnemery et al., 2002), others assume that these patients can accurately complete a self report measure of their affective experience, and that they have the same mental structure with regard to semantic knowledge of emotional phenomena as healthy people (Aleman A. and Kahn R., 2005). A recent study reported that the structure of affective representations is similar in schizophrenia patients and healthy controls. Nevertheless, there have been studies where emotional responses can vary within and between subjects, affected by factors such as the presentation context, personal experience relating to the emotional content, and also the subject's mood (Lang, Bradley et al., 1998).

4.5. Limitations

This study has some limitations. First, although diagnoses were established by an experienced psychiatrists, they could have also been confirmed on the basis of a Structured Clinical Interview for DSM-IV Disorders (SCID) (First, Spitzer et al., 1996). On assessment, the use of a neuropsychological test battery could have been more informative of the cognitive status of patients, while physiological measures such as skin conductance response (SCR) and heart rate (HR), as well as electromyography measures (EMG): facial muscle activity of corrugator and zygomatic, might have provided more details on emotional expression.

Concerning medication, we were unable to estimate the mean dose, as the patients had different medication status. This made it difficult to make a detailed assessment of the potential effect of the type of antipsychotic treatment (atypical v. typical) on task performance.

The relatively small sample size in this study limits the general applicability of our findings, which should be confirmed in future studies.

4.6. Conclusions

Notwithstanding these limitations, the current study demonstrated that schizophrenic patients in early stages of the disease have a preserved emotional perception of unpleasant sounds. This study raises several questions such as why emotional processing of unpleasant sounds is perceived in schizophrenics and facial emotion recognition is impaired. Is it because of the importance of audition for survival? Our study also indicated that there were no sex differences, although our sample was too small. Future longitudinal studies with larger samples and cognitive measures examining emotional sound processing stability during the course of the disease will be needed. More studies on psychoacoustics to determine which features cause the unpleasant perception of certain sounds would also be of great interest. The Newcastle Battery of Unpleasant Sounds used in this study demonstrated a very good internal consistency. In the future it could be used in neuroimaging experiments to determine the neural substrates activated by exposure to unpleasant auditory signals. Perhaps a second auditory pathway might become apparent. Future research in this area is important for the larger study of emotion and cognition.

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APPENDICES

Appendix A: Written Consents (one for each hospital)

INFORMAÇÃO PARA OS DOENTES DO SERVIÇO DE PSIQUIATRIA DO HOSPITAL DE SANTA MARIA

INTRODUÇÃO

No âmbito de um projecto de investigação (dissertação de mestrado em Neurociências) pela Faculdade de Medicina da Universidade de Lisboa, fazemos-lhe o seguinte convite para participar:

OBJECTIVO E DURAÇÃO DO ESTUDO

A investigação que faremos tem como objectivo estudar a percepção emocional dos sons.
O estudo tem a duração de três meses (Agosto, Setembro e Outubro de 2007) e a sua colaboração será necessária apenas uma vez.

PROCEDIMENTOS DE ESTUDO E INSTRUMENTOS

A sua participação no projecto é totalmente voluntária.
Pode decidir não participar no projecto ou desistir em qualquer momento. Independentemente da decisão que tomar, não sofrerá qualquer prejuízo.

Ao aceitar fazer parte deste projecto será submetido a:
Após a consulta com o seu médico psiquiatra assistente, pedimos-lhe que:

- Participe numa entrevista médica para colheita de dados pessoais, história familiar
- Coopere na aplicação das escalas

Escalas a serem aplicadas:

- Mini Mental State – para avaliar o estado cognitivo
- PANSS – Escala que avalia os sintomas positivos e negativos
- Bateria de Sons de Newcastle - para avaliação emocional dos sons. Os sons serão emitidos através de auscultadores a partir de um computador portátil. Após a audição individual dos 75 sons, dará a sua avaliação do grau de prazer ou desprazer dos mesmos.

RISCOS E INCÓMODOS POR PARTICIPAR

Ao aceitar participar neste estudo a sua saúde não é colocada em risco.

A sua participação será solicitada apenas num momento:

O QUE ACONTECERÁ AOS DADOS E À INFORMAÇÃO COLHIDA

Toda as informações que serão colhidas sobre os seus dados pessoais serão mantidas confidenciais e tratadas em anonimato. Após a conclusão do estudo serão destruídos os dados.

FORMULÁRIO DE CONSENTIMENTO INFORMADO

- Declaro que li e compreendi a informação
- Todas as dúvidas adicionais me foram esclarecidas por um dos membros do projecto.
- Estou informado de que poderei desistir a qualquer momento ou ser excluído do estudo.
- Aceito participar no projecto de investigação científica, conhecendo os meus direitos e deveres, bem como os riscos e benefícios da minha participação.

Assinatura: Data:

Assinatura do investigador: Data:

A preencher pelos serviços:
Identificação do Doente (ID):

INFORMAÇÃO PARA OS DOENTES DO HOSPITAL JÚLIO DE MATOS

INTRODUÇÃO

No âmbito de um projecto de investigação (dissertação de mestrado em Neurociências) pela Faculdade de Medicina da Universidade de Lisboa, fazemos-lhe o seguinte convite para participar:

OBJECTIVO E DURAÇÃO DO ESTUDO

A investigação que faremos tem como objectivo estudar a percepção emocional dos sons.
O estudo tem a duração de três meses (Agosto, Setembro e Outubro de 2007) e a sua colaboração será necessária apenas uma vez.

PROCEDIMENTOS DE ESTUDO E INSTRUMENTOS

A sua participação no projecto é totalmente voluntária.
Pode decidir não participar no projecto ou desistir em qualquer momento. Independentemente da decisão que tomar, não sofrerá qualquer prejuízo.

Ao aceitar fazer parte deste projecto será submetido a:

Após a consulta com o seu médico psiquiatra assistente, pedimos-lhe que:

- Participe numa entrevista médica para colheita de dados pessoais, história familiar
- Coopere na aplicação das escalas

Escalas a serem aplicadas:

- Mini Mental State – para avaliar o estado cognitivo
- PANSS – Escala que avalia os sintomas positivos e negativos da esquizofrenia
- Bateria de Sons de Newcastle - para avaliação emocional dos sons. Os sons serão emitidos através de auscultadores a partir de um computador portátil. Após a audição individual dos 75 sons, dará a sua avaliação do grau de prazer ou desprazer dos mesmos.

RISCOS E INCÓMODOS POR PARTICIPAR

Ao aceitar participar neste estudo a sua saúde não é colocada em risco.

A sua participação será solicitada apenas num momento:

O QUE ACONTECERÁ AOS DADOS E À INFORMAÇÃO COLHIDA

Todas as informações que serão colhidas sobre os seus dados pessoais serão mantidas confidenciais e tratadas em anonimato. Após a conclusão do estudo serão destruídos os dados.

FORMULÁRIO DE CONSENTIMENTO INFORMADO

- Declaro que li e compreendi a informação
- Todas as dúvidas adicionais me foram esclarecidas por um dos membros do projecto.
- Estou informado de que poderei desistir a qualquer momento ou ser excluído do estudo.
- Aceito participar no projecto de investigação científica, conhecendo os meus direitos e deveres, bem como os riscos e benefícios da minha participação.

Assinatura: Data:

Assinatura do investigador: Data:

A preencher pelos serviços:
Identificação do Doente:

Appendix B: Sociodemographic and Clinic Questionnaire

CADERNO DE RECOLHA DE DADOS

"Analysis of the unpleasantness of sounds by schizophrenic patients"

ID: _____

Grupo: Controlos _ Pacientes __

Sexo: Mas. ___ Fem.___ **Idade** ____ anos

Raça: Branca ___ Negra ___

Estado Civil: Solteiro ___ Casado/Junto ___ Divorciado/Separado ___

Escolaridade: 6º ano __ 9 º ano __ 12º ano __ Universidade _

Profissão: _____

Lateralidade: Esquerda __ Dextro __ Ambidextro __

Treino Musical Não _ Sim __

Anos de evolução dos sintomas _____

Anos de diagnóstico _____

História familiar da doença Não _ Sim __ Quem _____

Hospitalizações: _____ (número)

Medicação e dose

Medicação 1:_____ Dose 1:_____

Medicação 2:_____ Dose 2:_____

Medicação 3:_____ Dose 3:_____

Medicação 4:_____ Dose 4:_____

Medicação 5:_____ Dose 5:_____

Appendix C: Mini-Mental State Examination (MMSE)

Portuguese version adapted by Guerreiro et al.,1994

MINI-MENTAL STATE - MMS

NOME: _____
IDADE:_____Anos DATA: _____ de _____ de _____ _____

1. ORIENTAÇÃO (1 ponto por cada resposta correcta).

Em que ano estamos? _____
Em que mês estamos? _____
Em que dia do mês estamos? _____
Em que dia da semana estamos? _____
Em que estação do ano estamos? _____
Em que país estamos? _____
Em que distrito vive? _____
Em que terra vive? _____
Em que casa estamos _____
Em que andar estamos _____ Nota:

2. RETENÇÃO (contar 1 ponto por cada palavra correctamente repetida).
"Vou dizer três palavras; queria que as repetisse, mas só depois de eu as dizer todas; procure ficar a sabê-las de cór".
Pêra _____
Gato _____
Bola _____ Nota:

3. ATENÇÃO E CÁLCULO (1 ponto por cada resposta correcta. Se der uma errada mas depois continuar a subtrair bem, consideram-se as seguintes como correctas. Parar ao fim de 5 respostas.)
"Agora peço-lhe que me diga quantos são 30 menos 3 e depois ao número encontrado volta a tirar 3 e repete assim até eu lhe dizer para parar".
27 __ 24 __ 21 __ 18 __ 15 __ Nota:

4. EVOCAÇÃO (1 ponto por cada resposta correcta.)
"Veja se consegue dizer as três palavras que pedi há pouco para decorar".
Pêra _____
Gato _____
Bola _____ Nota:

5. LINGUAGEM (1 ponto por cada resposta correcta).
a. "Como se chama isto? Mostrar os objectos:
Relógio _____
Lápis _____ Nota:

b. "Repita a frase que eu vou dizer: O RATO ROEU A ROLHA" Nota:

c. "Quando eu lhe der esta folha de papel, pegue nela com a mão direita, dobre-a ao meio e ponha sobre a mesa", (ou "sobre a cama", se for o caso); dar a folha segurando com as duas mãos.
Pega com a mão direita _____
Dobra ao meio _____
Coloca onde deve _____ Nota:

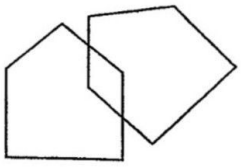
d. "Leia o que está neste cartão e faça o que lá diz". Mostrar um cartão com a frase bem legível, "FECHE OS OLHOS"; sendo analfabeto ler-se a frase.
Fechou os olhos Nota:

e. "Escreva uma frase inteira aqui". Deve ter sujeito e verbo e fazer sentido; os erros gramaticais não prejudicam a pontuação.
Nota:

Folstein, Folstein e McHugh, 1975, segundo adaptação portuguesa de Manuela Guerreiro e colabs., 1993. Laboratório de Estudos de Linguagem do Centro de Estudos Egas Moniz, Hosp. Sta. Maria

6. **HABILIDADE CONSTRUTIVA** (1 ponto pela cópia correcta.)
Deve copiar um desenho. Dois pentágonos parcialmente sobrepostos; cada um deve ficar com 5 lados, dois dos quais intersectados. Não valorizar, tremor ou rotação.

DESENHO



CÓPIA

(Máximo 30 pontos) TOTAL:

Pontos de Corte
(População Portuguesa)

Considera-se com Defeito Cognitivo:

- Analfabetos ≤ 15
- 1 a 11 anos de escolaridade ≤ 22
- Com escolaridade superior a 11 anos ≤ 27

FECHE OS OLHOS

Appendix D: Positive and Negative Syndrome Scale (PANSS)

SCI-PANSS

Stanley R. Kay, Ph.D.
Lewis A. Opler, M.D., Ph.D.
Abraham Fiszbein, M.D.

Traduçao de:
DR. OLIVIA ROBUSTO-LAITÃO
DR. MANUEL DELGADO

Entrevista Clínica Estruturada para a Escala dos Síndromas Positivos e Negativos

SCI-PANSS

L. A. Opler, M.D., Ph.D. S. R. Kay, Ph.D. J. P. Lindenmayer, M.D. A. Fiszbein, M.D.

Nome do paciente, ou identificação: _____

Entrevistador: _____ Data: _____

Dados sobre "Ausência de espontaneidade e curso da conversa" (N6) 'Relação pobre,' (N3) e "Desorganização Conceptual" (P2)

Olá, eu sou ... vamos passar os próximos 30 a 40 minutos a falar sobre si, e sobre os motivos que o (a) levaram a vir cá. Talvez possa começar por me contar qualquer coisa sobre si próprio e sobre o seu passado?

(Instruções para o entrevistador: Conceda, pelo menos, 5 minutos para estabelecer uma relação não dirigida no contexto da entrevista, antes de prosseguir para as questões específicas da lista que se segue)

Dados sobre "Ansiedade" (G2)

Sentiu-se preocupado, ou nervoso na semana passada? _____

SE NÃO: Diria que é geralmente calmo e relaxado? _____

SE SIM: O que é que o tem trazido nervoso (preocupado, inquieto, tenso)? _____

Qual é a intensidade do nervosismo (preocupação, etc.) que tem sentido? _____

Tem-se sentido por vezes a tremer, ou com o coração acelerado? _____

Entra em pânico? _____

Sente que o seu sono, a alimentação, ou a participação em actividades foram afectados? _____

Dados sobre "Delírios (em geral)" (PI) e "Conteúdo Invulgar do Pensamento' (G9)

As coisas têm-lhe corrido bem? _____

Há alguma coisa que o tenha incomodado ultimamente? _____

Pode-me contar um pouco sobre o que pensa da vida e da sua finalidade? _____

Segue uma filosofia em particular? _____

Algumas pessoas contam-me que acreditam no Diabo; o que é que pensa disso? _____

Consegue ler o pensamento das outras pessoas? _____

SE SIM: Como é que isso acontece? _____

Os outros conseguem ler o seu pensamento? _____

SE SIM: Como é que eles conseguem fazer isso? _____

Existe algum motivo para que alguém queira ler o seu pensamento? _____

Quem controla a sua mente? _____

Dados sobre "Desconfiança/Perseguição," (P6) "Isolamento Social Passivo/Apático," (N4) "Evicção Social Activa," (GI6) e "Mau Controlo dos Impulsos" (GI4)

Como é que tem passado o tempo nestes dias? _____

Prefere estar sozinho? _____

Junta-se aos outros para fazer coisas? _____

SE NÃO: Porque não? ... Tem medo das pessoas, ou não gosta delas? _____

SE SIM: Pode explicar? _____

SE SIM: Fale-me sobre isso. _____

Tem muitos amigos? _____

SE NÃO: Só alguns? _____

SE NÃO: Nenhuns? .... Porquê? _____

SE SIM: Porquê só alguns amigos? _____

SE SIM: Amigos íntimos? _____

SE NÃO: Porque não? _____

Sente que pode confiar na maioria das pessoas? _____

SE NÃO: Porque não? _____

Há algumas pessoas em particular em quem não confia? _____

SE SIM: Pode-me dizer quem são? _____

Porque é que não confia nas pessoas? (ou nomeadamente numa pessoa)? _____

SE "NÃO SEI", OU "NÃO SEI O QUE DIZER: Tem uma boa razão para não confiar...? _____

Há alguma coisa que .... lhe tenham feito a si? _____

Talvez lhe venham a fazer agora? _____

SE SIM: Pode explicar-me? _____

Dá-se bem com os outros? _____

SE NÃO: Qual é o problema? _____

Tem um feitio irritável? _____

Envolve-se em lutas? _____

SE SIM: Como é que essas lutas começam? _____

Fale-me dessas lutas. _____

Com que frequência acontecem ? _____

Perde às vezes o controlo de si próprio? _____

Gosta da maioria das pessoas? _____

SE NÃO: Porque não? _____

Existem algumas pessoas que não gostem de si? _____

SE SIM: Por que razão? _____

Os outros falam de si nas suas costas? _____

SE SIM: O que dizem eles de si? _____

Porquê? _____

Alguém anda a espiá-lo, ou a conspirar contra si? _____

Sente-se, por vezes, em perigo? _____

SE SIM: Diria que a sua vida corre perigo? _____

Anda alguém a pensar fazer-lhe mal, ou talvez mesmo a pensar em matá-lo? _____

Foi à polícia pedir ajuda? _____

Trata às vezes dos assuntos por sua conta, ou levanta queixa contra quem o possa atacar? _____

SE SIM: O que é que fez? _____

Dados sobre "Comportamento Alucinatório" (P3) e delírios associados

Tem, uma vez por outra sensações estranhas, ou pouco usuais? _____

As pessoas às vezes contam-me que conseguem ouvir ruídos ou vozes dentro da cabeça delas que os outros não ouvem. Também consegue? _____

SE NÃO: Recebe, por vezes, comunicações pessoais da rádio ou da TV? _____

SE NÃO: De Deus, ou do Diabo?: _____

SE NÃO: O que é que ouve? _____

Ouve-as tão bem e tão alto como a minha voz? _____

Com que frequência ouve essas vozes (barulhos, mensagens, etc.)? _____

Isso acontece numa altura particular do dia, ou durante todo o tempo? _____

SE OUVE VOZES: Reconhece de quem são as vozes? _____

O que dizem as vozes? _____

As vozes são boas, ou más? _____

Agradáveis, ou desagradáveis? _____

As vozes interrompem o seu pensamento, ou os seus afazeres? _____

Elas por vezes dão-lhe ordens, ou instruções? _____

SE SIM: Por exemplo? _____

Costuma obedecer a essas ordens (instruções)? _____

O que faz com essas vozes (ou ruídos): donde vêm elas, de facto? _____

Porque é que tem essas sensações? _____

São sensações normais? _____

Às vezes as coisas vulgares parecem-lhe ter um ar estranho ou distorcido? _____

Tem por vezes "visões", ou vê coisas que os outros não conseguem ver? _____

SE SIM: Por exemplo? _____

Essas visões parecem muito reais, ou ao vivo? _____

Com que frequência tem essas experiências? _____

Sente por vezes cheiros que são invulgares, ou que os outros não sentem? _____

SE SIM: Por favor explique. _____

Tem sensações estranhas ou pouco usuais, vindas de dentro do seu corpo? _____

SE SIM: Fale-me disso. _____

Dados de "Âmbito Somático" (GI)

Como se tem sentido em termos de saúde? _____

SE NÃO RESPONDEU "BEM": O quê que o tem incomodado? _____

SE RESPONDEU "BEM": Acha que está de perfeita saúde? _____

SE RESPONDEU "NÃO": O que o tem importunado? _____

Tem algum problema médico, ou doença? _____

Alguma parte do seu corpo o tem incomodado? _____

SE NÃO: Como está a sua cabeça? O seu coração? Estômago? O resto do seu organismo? _____

SE SIM: Pode explicar? _____

Houve mudança da forma ou do tamanho da sua cabeça, ou do seu corpo ? _____

SE SIM: Por favor explique. _____

O que originou estas mudanças? _____

Dados sobre "Depressão" (G6)

Como esteve a sua disposição na semana passada: em geral bem, em geral mal? _____

SE "EM GERAL BEM": Houve, na semana passada, alturas em que se tenha sentido triste, ou infeliz? _____ SE SIM, PASSE À PERGUNTA SEGUINTE:

SE "EM GERAL MAL": Há algo em particular que o entristeça? _____

Quantas vezes se sente triste? _____

Qual tem sido a intensidade dessa tristeza ? _____

Tem chorado ultimamente? _____

O seu sono tem sido de alguma forma afectado pelo seu estado de humor? _____

O seu apetite foi afectado por isso? _____

Tem participado menos em actividades por causa do seu humor? _____

Tem tido por vezes ideias de fazer mal a si próprio? _____

SE SIM: Algumas ideias em acabar com a sua vida? _____

SE SIM: Tentou suicidar-se? _____

Dados sobre "Sentimentos de culpa" (G3) e Grandiosidade (PS)

Se tivesse que se comparar a uma pessoa dita normal, como é que se acharia: um pouco melhor, talvez um pouco pior, ou semelhante? _____

SE PIOR: Pior em que aspectos? _____

Como se sente, exactamente, em relação a si próprio? _____

SE MELHOR: Melhor em que aspectos? _____

SE SEMELHANTE: Acha-se especial nalguns aspectos? _____

SE SIM: Em que aspectos? _____

Considerar-se-ia a si próprio dotado? _____

Tem talentos ou capacidades que a maioria das pessoas não têm? _____

SE SIM: Por favor explique. _____

Tem alguns poderes especiais? _____

SE SIM: Quais são? _____

De onde vêm esses poderes? _____

Tem percepções extrasensoriais (PES), ou consegue ler a mente de outras pessoas? _____

É muito saudável? _____

SE SIM: Por favor explique. _____

Acha que pode ser considerado muito esperto? _____

SE SIM: Porque é que acha isso? _____

Descrever-se-ia a si próprio como famoso? _____

Algumas pessoas reconhecê-lo-iam da TV, da rádio, ou dos jornais? _____

SE SIM: Pode-me falar disso? _____

É uma pessoa religiosa? _____

SE SIM: Está próximo de Deus? _____

SE SIM: Deus incumbiu-o de algum papel, ou fim especial,? _____

Pode acontecer que seja um dos mensageiros, ou anjos de Deus? _____

SE SIM: Como mensageiro (anjo) de Deus, que poderes especiais tem? _____

Considera-se, talvez, a si próprio como sendo Deus? _____

Tem alguma missão especial na vida? _____

SE SIM: Qual é a sua missão? _____

Quem o designou para essa missão? _____

Alguma vez fez algo errado - algo sobre o que se sinta mal, ou culpado? _____

SE SIM: Exactamente até que ponto isso o incomoda agora ? _____

Acha que merece ser castigado por isso? _____

SE SIM: Que tipo de castigo acha que merece? _____

Já tem pensado em se castigar a si próprio? _____

SE SIM: Já alguma vez agiu de acordo com esses pensamentos de se auto-punir? _____

Dados sobre "Desorientação" (GlO)

Pode-me dizer a data de hoje (i.e., o dia, mês, e ano)? _____

Qual é o nome do sítio onde estamos agora? _____

(Se estiver hospitalizado) Em que enfermaria está? _____

Qual é a morada do local onde está agora? _____

Se alguém precisar de lhe telefonar, para que número deve essa pessoa ligar? _____

Qual é o nome do médico que o está a tratar? _____

(Se estiver hospitalizado) Pode-me dizer que pessoas há mais na equipa, e o que fazem? _____

Sabe quem é actual Presidente da República? _____

Quem é o nosso Primeiro Ministro? _____

Quem é o Presidente da Câmara desta cidade? _____

Dados sobre "Dificuldade com o Pensamento Abstracto" (N5)

Vou agora dizer umas quantas palavras, e gostaria que me dissesse em que medida elas são importantes. Vamos começar, por exemplo, com as palavras "maçã" e "banana." O que lhe fazem lembrar – o que é que têm em comum?

SE RESPONDER "SÃO AMBAS UM FRUTO": Bem. E agora destas...?
(Seleccione outros três items da lista "Semelhanças", do Apêndice A. com níveis variados de dificuldade)

SE É DADA UMA RESPOSTA QUE É CONCRETA, TANGENCIAL, OU IDIOSSINCRÁTICA, COMO P. EX.: "AMBAS TÊM CASCA," "SÃO AMBAS PARA COMER," "SÃO PEQUENAS" OU "OS MACACOS GOSTAM DELAS": Está bem, mas ambas são fruta. Agora o que se passa com ... e ... : o que parecem estas?
(Escolha outros três items da lista "Semelhanças", do Apêndice A com vários níveis de dificuldade)

APÊNDICE A

Items para semelhanças na avaliação de "Dificuldades com o pensamento abstracto"

1. O que têm de comum uma bola e uma laranja?
2. Maçã e banana ?
3. Lápis e caneta?
4. Um tostão e dez tostões?

5. Mesa e cadeira?
6. Tigre e elefante?
7. Chapéu e camisola?
8. Autocarro e combóio?

9. Braço e perna?
10. Rosa e tulipa?
11. Tio and primo?
12. O Sol e a Lua?

13. Pintura e poema?
14. Topo da montanha e vale?

Nota ao Apêndice A: As semelhanças são em regra avaliadas, seleccionando quatro items com diferentes níveis de dificuldade (i.e., seleccionando um item de cada quarteto do conjunto). Ao usar a PANSS longitudinalmente, os items devem ser sistematicamente alterados, com sucessivas entrevistas, de modo a fornecer selecções diferentes dos vários níveis de dificuldade, minimizando assim a repetição.

Notas relativas às respostas sobre semelhanças:

_____

_____

_____

15. Ar e água?
16. Paz e prosperidade?

Faça um círculo em redor das semelhanças escolhidas.

Provavelmente já ouviu a expressão: "Quem não tem cão, caça com gato." O que quer isto de facto dizer? Há um dizer muito antigo: "A capa não faz o livro." Qual é o verdadeiro significado deste provérbio?

(Escolha mais outros dois provérbios da lista do Apêndice B, com vários níveis de dificuldade.)

APÊNDICE B

Items para a INTERPRETAÇÃO DE PROVÉRBIOS na avaliação de "Dificuldade com o Pensamento abstracto"

O que quer dizer:

1. "Seco que nem um carapau"
2. "Quem não tem cão, caça com gato"
3. "Mais vale sê-lo, do que parecê-lo"
4. "Quem corre por gosto não cansa"

5. "Quem vê caras não vê corações"
6. "Quem tudo quer, tudo perde"
7. "Nem tudo o que luz é ouro"
8. "Mais vale prevenir do que remediar.

9. "Depois da tempestade vem a bonança"
10. "A galinha da minha vizinha é sempre melhor do que a minha"
11. "Mais vale um pássaro na mão do que dois a voar"
12. "Uma andorinha não faz a Primavera"

13. "Candeia que vai à frente alumia duas vezes"
14. "Água mole em pedra dura tanto dá até que fura"
15. "Em tempo de guerra não se limpam armas"
16. "Quem tem telhados de vidro não atira pedras ao do vizinho"

Nota ao Apêndice B: A interpretação dos provérbios é geralmente avaliada pela selecção de quatro items a níveis diferentes de dificuldade (p.ex., um item seleccionado de cada quarteto do conjunto completo). Ao usar a PANSS longitudinalmente, os items devem ser sistematicamente alterados nas entrevistas sucessivas, de modo a fornecer diferentes selecções dos vários níveis de dificuldade, minimizando assim a repetição.

Notas às respostas aos provérbios:

Faça um círculo em volta dos provérbios escolhidos..

Dados sobre "Falta de Senso Crítico e de Insight" (G12)

Há quanto tempo está internado ?

Porque veio para o hospital (clínica, etc.)?

Precisava de estar internado ?

SE NÃO: Tinha algum problema que necessitava tratamento?

SE SIM: Acha que tinha um problema psiquiátrico ou mental?

SE SIM: Porquê?...que acha que tinha um problema psiquiátrico ou mental?

SE SIM: Em quê que isso consiste? Pode-me falar disso? _____

SE SIM: Em sua opinião precisaria de tomar medicamentos? _____

SE NÃO:

(Se está medicado:) Porque está então a tomar medicamentos? _____

(Se não está medicado:) Porque está ainda internado? _____

SE SIM: Porquê?... Os medicamentos ajudam-no? _____

Nesta altura tem alguns problemas psiquiátricos ou mentais? _____

SE NÃO: Porque razão está ainda internado? _____

SE SIM: Explique, por favor. _____

Até que ponto é que esses problemas são graves? _____

(Se está hospitalizado:)

Está pronto para ter alta? _____

Pensa que vai continuar a tomar medicamentos depois de ter alta ? _____

Quais são os seus planos para o futuro? _____

Quais são os seus objectivos mais significativos? _____

Bom, isto é tudo o que tinha para lhe perguntar. Tem alguma pergunta que gostasse de me fazer?
Muito obrigado pela sua colaboração.

PANSS

1) Subescala positiva

P1	Delírios	1.....2.....3.....4.....5.....6.....7
P2	Desorganização conceptual	1.....2.....3.....4.....5.....6.....7
P3	Comportamento alucinatório	1.....2.....3.....4.....5.....6.....7
P4	Excitação	1.....2.....3.....4.....5.....6.....7
P5	Grandiosidade	1.....2.....3.....4.....5.....6.....7
P6	Desconfiança / Perseguição	1.....2.....3.....4.....5.....6.....7
P7	Hostilidade	1.....2.....3.....4.....5.....6.....7

Subtotal ☐☐

2) Subescala negativa

N1	Embotamento afectivo	1.....2.....3.....4.....5.....6.....7
N2	Isolamento afectivo	1.....2.....3.....4.....5.....6.....7
N3	Contacto pobre	1.....2.....3.....4.....5.....6.....7
N4	Isolamento social passivo/apático	1.....2.....3.....4.....5.....6.....7
N5	Dificuldades com o pensamento abstracto	1.....2.....3.....4.....5.....6.....7
N6	Ausência de espontaneidade e de fluxo na conversa	1.....2.....3.....4.....5.....6.....7
N7	Pensamento estereotipado	1.....2.....3.....4.....5.....6.....7

Subtotal ☐☐

3) Subescala de psicopatologia geral

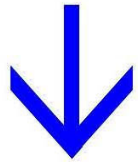
G1	Implicações psicossomáticas	1.....2.....3.....4.....5.....6.....7
G2	Ansiedade	1.....2.....3.....4.....5.....6.....7
G3	Sentimentos de culpa	1.....2.....3.....4.....5.....6.....7
G4	Tensão	1.....2.....3.....4.....5.....6.....7
G5	Maneirismos e postura	1.....2.....3.....4.....5.....6.....7
G6	Depressão	1.....2.....3.....4.....5.....6.....7
G7	Lentificação motora	1.....2.....3.....4.....5.....6.....7
G8	Não cooperação	1.....2.....3.....4.....5.....6.....7
G9	Conteúdo invulgar do pensamento	1.....2.....3.....4.....5.....6.....7
G10	Desorientação	1.....2.....3.....4.....5.....6.....7
G11	Atenção reduzida	1.....2.....3.....4.....5.....6.....7
G12	Ausência de juízo e de "insight"	1.....2.....3.....4.....5.....6.....7
G13	Perturbação da vontade	1.....2.....3.....4.....5.....6.....7
G14	Controlo deficientes dos impulsos	1.....2.....3.....4.....5.....6.....7
G15	Preocupação	1.....2.....3.....4.....5.....6.....7
G16	Evicção social activa	1.....2.....3.....4.....5.....6.....7

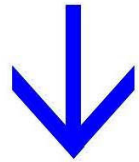
Subtotal ☐☐☐

Score total ☐☐☐

Appendix E: Visual Scale

0 1 2 3 4 5 6 7 8 9





Menos Desagradável

Mais Desagradável

Appendix F: Sound list of Newcastle Battery of Unpleasant Sounds

		0= least unpleasant	1	2	3	4	5	6	7	8	9= most unpleasant			0= least unpleasant	1	2	3	4	5	6	7	8	9= most unpleasant
1	Angle_grind1	0	1	2	3	4	5	6	7	8	9	39	Fork_glass_4	0	1	2	3	4	5	6	7	8	9
2	Angle_grind_2	0	1	2	3	4	5	6	7	8	9	40	Frog1	0	1	2	3	4	5	6	7	8	9
3	Anteater	0	1	2	3	4	5	6	7	8	9	41	Glassbreaking	0	1	2	3	4	5	6	7	8	9
4	Applause	0	1	2	3	4	5	6	7	8	9	42	Gorilla	0	1	2	3	4	5	6	7	8	9
5	Baby cry	0	1	2	3	4	5	6	7	8	9	43	Guitar_1	0	1	2	3	4	5	6	7	8	9
6	Baby laugh	0	1	2	3	4	5	6	7	8	9	44	Guitar_2	0	1	2	3	4	5	6	7	8	9
7	Bear2	0	1	2	3	4	5	6	7	8	9	45	Hippo	0	1	2	3	4	5	6	7	8	9
8	Blackboard_chalk_1	0	1	2	3	4	5	6	7	8	9	46	Howlin_wolf	0	1	2	3	4	5	6	7	8	9
9	Blackboard_chalk_2	0	1	2	3	4	5	6	7	8	9	47	Junglebird2	0	1	2	3	4	5	6	7	8	9
10	Blackboard_nails_1	0	1	2	3	4	5	6	7	8	9	48	Knife_bottle_1	0	1	2	3	4	5	6	7	8	9
11	Blackboard_nails_2	0	1	2	3	4	5	6	7	8	9	49	Lamb	0	1	2	3	4	5	6	7	8	9
12	Brake_double	0	1	2	3	4	5	6	7	8	9	50	Leopard1	0	1	2	3	4	5	6	7	8	9
13	Bubblingwater	0	1	2	3	4	5	6	7	8	9	51	Lion2	0	1	2	3	4	5	6	7	8	9
14	Bull frog	0	1	2	3	4	5	6	7	8	9	52	Lioncub	0	1	2	3	4	5	6	7	8	9
15	Buzzer	0	1	2	3	4	5	6	7	8	9	53	Macaca	0	1	2	3	4	5	6	7	8	9
16	Camel	0	1	2	3	4	5	6	7	8	9	54	Mixer_glass_1	0	1	2	3	4	5	6	7	8	9
17	Cat_screaming	0	1	2	3	4	5	6	7	8	9	55	Multiple_babies	0	1	2	3	4	5	6	7	8	9
18	Catpurr2	0	1	2	3	4	5	6	7	8	9	56	Panther	0	1	2	3	4	5	6	7	8	9
19	Clarinet_honk	0	1	2	3	4	5	6	7	8	9	57	Phone_ringing	0	1	2	3	4	5	6	7	8	9
20	Clarinet_squeak	0	1	2	3	4	5	6	7	8	9	58	Pig_	0	1	2	3	4	5	6	7	8	9
21	Cougar	0	1	2	3	4	5	6	7	8	9	59	Puffer	0	1	2	3	4	5	6	7	8	9
22	Doggrowl	0	1	2	3	4	5	6	7	8	9	60	Record_scratch_1	0	1	2	3	4	5	6	7	8	9
23	Dolphinclicks	0	1	2	3	4	5	6	7	8	9	61	Reving_Engine	0	1	2	3	4	5	6	7	8	9
24	Domesticcat	0	1	2	3	4	5	6	7	8	9	62	Ruler_bottle_1	0	1	2	3	4	5	6	7	8	9
25	Eagle2	0	1	2	3	4	5	6	7	8	9	63	Ruler_bottle_2	0	1	2	3	4	5	6	7	8	9
26	Electric_drill_2	0	1	2	3	4	5	6	7	8	9	64	Running water_short	0	1	2	3	4	5	6	7	8	9
27	Electric_drill	0	1	2	3	4	5	6	7	8	9	65	Smallwaterfall	0	1	2	3	4	5	6	7	8	9
28	Elephant	0	1	2	3	4	5	6	7	8	9	66	Spade_drag_1	0	1	2	3	4	5	6	7	8	9
29	Falcon	0	1	2	3	4	5	6	7	8	9	67	Spade_drag_2	0	1	2	3	4	5	6	7	8	9
30	Femalescream_2	0	1	2	3	4	5	6	7	8	9	68	Spade_drop_1	0	1	2	3	4	5	6	7	8	9
31	Femalescream	0	1	2	3	4	5	6	7	8	9	69	Thunder1	0	1	2	3	4	5	6	7	8	9
32	Film_projector	0	1	2	3	4	5	6	7	8	9	70	Thunder2_	0	1	2	3	4	5	6	7	8	9
33	Firealarm	0	1	2	3	4	5	6	7	8	9	71	Tire_skids	0	1	2	3	4	5	6	7	8	9
34	Fork_bottle_1	0	1	2	3	4	5	6	7	8	9	72	Violin	0	1	2	3	4	5	6	7	8	9
35	Fork_bottle_3	0	1	2	3	4	5	6	7	8	9	73	Wasp_1	0	1	2	3	4	5	6	7	8	9
36	Fork_bottle_4	0	1	2	3	4	5	6	7	8	9	74	Waterflow	0	1	2	3	4	5	6	7	8	9
37	Fork_glass_1	0	1	2	3	4	5	6	7	8	9	75	Zeb	0	1	2	3	4	5	6	7	8	9
38	Fork_glass_3	0	1	2	3	4	5	6	7	8	9												

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Universidade de Lisboa
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Dissertação orientada pelo Senhor Professor Doutor Timothy Griffiths

e pelo Senhor Professor Joaquim Alexandre Ribeiro

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CITMA
CENTRO DE CIÊNCIA E TECNOLOGIA DA MADEIRA

“Men ought to know that from the brain, and from the brain only, arise our pleasures, joys, laughter and jests, as well as our sorrows, pains, griefs and fears.
Through it, in particular, we think, see, hear and distinguish the ugly from the beautiful, the bad from the good, and the pleasant from the unpleasant”

On the sacred disease

Hippocrates - 400 B.C.

Table of contents

Resumo

No presente trabalho estudámos o processamento emocional de sons desagradáveis em doentes esquizofrénicos, em fases iniciais da doença.

O estudo decorreu em doentes pertencentes à consulta externa dos Serviços de Psiquiatria do Hospital de Santa Maria e Hospital Júlio de Matos e a amostra consistiu em 29 doentes e 29 controlos emparelhados para o sexo e idade.

As avaliações realizadas incluíram uma escala de Avaliação Breve do Estado Mental (MMSE), uma escala de gravidade dos sintomas positivos e negativos da esquizofrenia (PANSS) e uma bateria de sons desagradáveis desenvolvida para este estudo, intitulada de Newcastle Battery of Unpleasant Sounds (NBUS).

Os resultados mostraram que os doentes esquizofrénicos têm uma percepção emocional preservada dos sons desagradáveis, na fase inicial da doença. Não se observaram correlações significativas entre medidas de gravidade clínica (duração da doença e sub-escalas da PANSS) e os valores da avaliação dos referidos sons.

Observou-se ainda que a bateria de sons apresentada revelou grande variabilidade nos valores obtidos na avaliação. Associações semânticas, assim como certas características acústicas dos sons poderão ter influenciado a percepção e avaliação emocional dos mesmos.

Palavras-chave: esquizofrenia, sons desagradáveis, processamento emocional

Abstract

In the present study, we evaluated the emotional processing of unpleasant sounds in schizophrenic patients in early stages of the disease.

This study was performed on schizophrenic outpatients from the Psychiatry Departments of Hospital Santa Maria and Hospital Júlio de Matos. The sample group comprised 29 schizophrenic patients and 29 matched healthy controls, equal in sex and age.

Evaluations included the Mini Mental State Examination, the Positive and Negative Syndrome Scale (PANSS) and the Newcastle Battery of Unpleasant Sounds, which we developed to study this issue.

Results showed that schizophrenic patients in early stages of the disease have a preserved emotional perception of unpleasant sounds. No correlation was found between clinical severity measures (disease duration, PANSS total and sub scores) and mean unpleasantness rating, which suggests that the emotional processing of unpleasant sounds is rather stable during the first five years of illness.

We observed that the sound set presented varied widely in perceived unpleasantness. Semantic associations as well as certain acoustic features may have had an effect upon unpleasantness ratings of sounds.

Keywords: Schizophrenia, unpleasant sounds, emotional processing

1. Introduction

1.1. About unpleasant sounds

Unpleasant sounds, referred to by Aristotle as "hard sounds", have been bothering scientists for at least 2,300 years. These sounds exist in everyday life and can sometimes induce such psychological aversion, as well as the intense involuntary physiological response reaction known as "a shiver down the spine", that even thinking about them can be unpleasant. Nevertheless, little is actually known about this phenomenon. It has been suggested that this strong visceral/somatic response, often described as a "tingling sensation" running down the spine or along the sides of the body, like a synastesia (somatic sensation), harks back to our early fish-like ancestors. These had lateral-line organs consisting of horizontal rows of hair cells on either side of the body, which were thought to be used for detecting vibrations in the water, which might help with schooling, as well as for detecting obstacles and predators (Ramachandran, 1996). The same author also suggested that this lateral line system could have become "internalized", becoming the cochlea in the higher vertebrates and still present in vestigial form in humans. Other authors have suggested that the visceral reaction to these sounds mimics some "naturally occurring, innately aversive event" (Green, 1975) or is a reaction to sounds similar to the vocalizations of some predators (Halpern, Blake et al., 1986). Audition, especially the ability to quickly identify environmentally salient information, including danger and reward, and to react rapidly, has always been critical for survival (Darwin, 1872/1965).

Neuroimaging studies have shown that the amygdala is involved in evaluating and/or responding to a sensory input of aversive stimuli, not only for auditory, but for other

sensory modalities (visual, olfactory, and gustatory) (Zald and Pardo, 2002). Some inconsistency in amygdala responses has been found in previous studies of unpleasant sounds , and contributing factors might have been the use of a mildly unpleasant sound or an extremely rapid habituation of the amygdala (Bordi, LeDoux et al., 1993). Other structures are also triggered in reaction to aversive stimulus, such as the limbic/paralimbic areas (Zald and Pardo, 2002).

In normal subjects, unpleasant sounds provoke autonomic responses and musculoskeletal tension (Davis, 1997).

1.2. Neural substrates triggered by auditory emotionally salient stimuli

It has been suggested that emotionally-charged stimuli produce preferential rapid routing of the impulse which bypasses the cortical route via the amygdale. Studies in the rat showed that thalamic sensory nuclei relay afferent signals to subcortical as well as cortical areas (LeDoux, Ruggiero et al., 1985; LeDoux, Farb et al., 1990). Auditory information from the posterior thalamus reaches the lateral nucleus of the amygdala (LA) by means of two pathways: a direct thalamo-amygdala projection (classical auditory pathway, “low route”) and a polysynaptic thalamo-cortico-amygdala projection (non–classical auditory pathway, “high route”). The medial division of the medial geniculate body (MGm), the suprageniculate nucleus (SG) and the posterior intralaminar nucleus (PIN) are the thalamic areas that receive input from both the inferior collicullus and the spinal cord and project it to the lateral nucleus of the amygdale (LeDoux, 2000). Many of these mechanisms have been best studied in auditory fear conditioning conditions. Recent research in this field has suggested that the thalamo-cortico-amygdala is the principal CS pathway route when the

brain is intact, contrary to several lines of evidence in favour of the direct thalamo-amygdala pathway (Boatman and Kim, 2006).

In humans, these pathways have been studied in tinnitus patients, in whom there seems to be a cross-modal interaction between the auditory and the somatosensory system. Normally, this interaction occurs in young children and decreases with age, and is rare in individuals above the age of 20 years who do not have tinnitus (Moller, 2003). One main difference between these two auditory pathways is that neurons in the classical pathway only respond to sound, while neurons in the non-classical pathway respond to sound and other sensory modalities, such as touch and light. It has been suggested that non-classical auditory pathways may be abnormally active in some tinnitus patients, which would allow the conduction of auditory information to the amygdala through the subcortical route. This may explain the affective symptoms that often accompany severe tinnitus, such as depression and phonophobia.

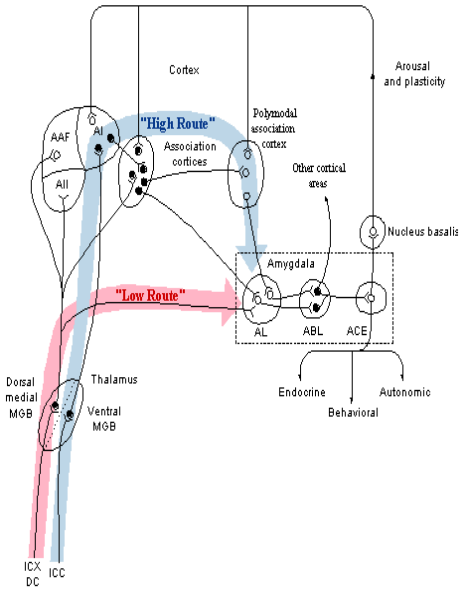


Figure 1: Connections from the auditory system to the amygdala, through the high route and the low route. AL: lateral nucleus of the amygdala, ABL: basal nucleus of the amygdala, ACL: central nucleus of the amygdala (Moller, 2003).

This mechanism is not well understood but there are indications that neural plasticity expression is involved. The non-classical auditory pathways might be activated through the expression of neural plasticity by which "dormant" synapses could be "unmasked" , thereby opening connections that are normally blocked by non-conducting (masked) synapses (Moller, 2003).

1.3. About emotion

Our motivational organization of emotions has a simpler, biphasic structure. Circuits are activated by unconditioned appetitive and aversive stimuli. Pleasant emotions are associated with an appetitive system, whereas unpleasant emotions are driven by a defensive system. These neural circuits were laid down early in our evolutionary history, in the primitive cortex, sub cortex and mid brain areas, and mediate behaviour which is fundamental to the survival of individuals and species. They mediate a broad range of physiological and behavioural events: changes in the facial musculature, skin conductance, heart rate and cortical event-related potentials recorded from the scalp surface. All are valuable measures of emotional expression.

An emotion begins with appraisal of an emotional stimulus, and signals evoked by that stimulus are carried from sensory areas to a number of emotion-triggering sites in the brain, including the amygdala and orbitofrontal cortex: the amygdala is more engaged in triggering emotions when the emotional stimulus is present; the orbitofrontal cortex is more important when it is recalled from memory. To create an emotional state, activity must propagate to the execution sites, which include the hypothalamus, the basal forebrain and nuclei in the brainstem tegmentum (Lang, Bradley et al., 1998; Lang, Davis et al., 2000; Phillips, Drevets et al., 2003). However, studies on emotion are far from exhaustive.

Damasio distinguishes emotions from feelings. Emotions are changes in body and brain states triggered by a dedicated brain system which responds to the content of one's perceptions, whether actual or recalled. Body responses range from changes in heart rate or smooth muscle contraction to changes which are perceptible to an external observer (such as those of posture or facial expression). The signals generated by these body responses produce brain changes that are perceptible mostly to the individual and provide the essential ingredients for what is ultimately perceived as a feeling. Emotions are what an outside observer can see; feelings are what the individual subjectively experiences (Damasio, 1994; Damasio, 1998; Lang, Bradley et al., 1998; Damasio, 1999; Bechara and Naqvi, 2004).

1.4. Emotional disturbances in schizophrenia

Since its original description, emotional dysfunction has been regarded as a hallmark of the disease (Bleuler, 1911). Bleuler considered that affective symptoms belong to the primary symptoms of schizophrenia and even raised the question as to whether emotional disturbances are a cause or an effect. In the past, researchers and clinicians have seen emotional disturbance more as a reaction to the illness. Nevertheless, some authors argue that the dysfunction of emotional brain systems may be very important in understanding this disorder. Recent theoretical proposals incorporate the growing body of evidence that emotional disturbances and dysfunction of the corresponding brain circuits may be at the core of schizophrenia, more specifically, the role of amygdala abnormalities in dysregulating the emotional brain as well as the medial prefrontal and orbitofrontal cortex, anterior cingulate, and insula (LeDoux, 1995; Aleman A. and Kahn R., 2005). Furthermore, MRI studies in schizophrenic patients have demonstrated volume reductions of the

amygdala (Joyal, Laakso et al., 2003), amygdala-hippocampal complex (Lawrie, Whalley et al., 2003), and thalamus (Konick and Friedman, 2001).

In schizophrenia, certain affective states have been associated with the onset of psychotic symptoms. There seems to be a stage of heightened awareness, and emotionality combined with a sense of anxiety and impasse has consistently been described as preceding psychosis (Conrad, 1958.; Yung and McGorry, 1996). Moreover, recent evidence indexed an increase in anxiety prior to the onset of hallucinations (Delespaul et al., 2002) and delusions (Freeman et al., 2001). According to Cutting (2003), anxiety is particularly marked at the outset, but is pathologically absent from the chronic stages of schizophrenia. Data from psychophysiology corroborates self-reports regarding the increased anxiety and arousal associated with psychosis.

1.5. Studies on emotion processing in schizophrenia

Some studies have shown that schizophrenic patients are noted to have deficits in the recognition and discrimination of facial emotions (Morrison, Bellack et al., 1988; Mandal, Pandey et al., 1998; Kohler, Bilker et al., 2000; Edwards, Pattison et al., 2001; Habel, Krasenbrink et al., 2006; Holt, Kunkel et al., 2006; Namikia, Hiraob et al., 2007; Turetsky, Kohler et al., 2007). However, there is an ongoing discussion that questions whether these impairments represent a differential deficit for emotion processing or reflect a generalized cognitive deficit (Kerr and Neale, 1993; Leppänen, Niehaus et al., 2006), with some studies in favour of a specific deficit in the processing of a subset of intense negative emotional expressions (anger, sadness and fear) (Kohler, Bilker et al., 2000b; Silver, Shlomo et al., 2002; Bediou, Franck et al., 2005).

In contrast to the large volume of research on facial emotion perception in schizophrenia, studies examining emotional sound processing are scarce. The first known comprehensive study of auditory affect perception in both verbal/semantic and non verbal/semantic modalities showed that patients with auditory hallucination had deficits in the perception of auditory affective stimuli (Rossell and Boundy, 2005).Over the last five years, more articles have been published on emotional prosody perception and have demonstrated that chronic inpatients do less well than normal controls (Edwards, Jackson et al., 2002; Hoekert, Kahn et al., 2007). Only one study has studied the affective recognition of environmental sounds and demonstrated that it was preserved in schizophrenic patients (Tuscher, Silbersweig et al., 2005).

1.6. Aim of the present study

In the present study, we aim to evaluate the emotional processing of unpleasant sounds in schizophrenic patients in early stages of the disease. To the best of our knowledge, this has never been studied before. Our hypothesis is that at the onset of this disease, unpleasant sounds could be very arousing and provoke a strong vestigial response. Perception and cognition of such an emotionally auditory-relevant stimuli (some of them with survival advantage) could lead to abnormally open non-classical auditory pathways. This would allow conduction of auditory information to the amygdala through the subcortical route and, consequently, could be the core of the deregulation of emotional brain in psychiatric disorders, leading to the onset of psychotic symptoms which normally begin with hyperarousal and anxiety. We therefore hypothesized that there is an alteration in the emotional processing of unpleasant sounds in which patients perceive them as much more unpleasant than normal controls.

2. Methods

2.1. Recruitment

This study was performed on schizophrenic outpatients from the Psychiatry Departments of Hospital de Santa Maria and Hospital Júlio de Matos, both in Lisbon. Patients were of both sexes, different ages and diverse socio-economic levels, and were recruited from August to September 2007, when they attended the above institutions for consultations (ambulatory setting).

2.2. Sampling

The study sample consisted of 29 patients diagnosed with schizophrenia according to the 4th Edition of the Diagnostic and Statistical Manual (DSM- IV- TR) (American Psychiatric Association, 2000). Additional entry criteria included: having no prominent organic cognitive disorder or mental retardation; being clinically stable enough to undergo the assessment (stability criteria included no medication changes or hospitalization in the 30 days prior to assessment); willingness to participate in the study and give informed consent. Exclusion criteria were the following**:** illness duration of more than 5 years; history of neurological or developmental disorders, head injury with a loss of consciousness for more than 10 min**;** recent substance abuse or dependence within the last 6 months (except tobacco)**;** axis I diagnosis other than schizophrenia or a medical disorder which might compromise cognitive performance**;** and hearing impairment.

The controls were 29 healthy individuals recruited from the non-professional staff at Lisbon University Medical School and Hospital de Santa Maria, matched in age, and male and female ratio. This group had the same inclusion criteria as the patients, including no

lifetime DSM-IV diagnosis of psychiatric disease, and were excluded if receiving any psychiatric medication.

The study was approved by the Ethics Committees of both hospitals and all participants gave their written informed consent before any procedure (see appendix A).

2.3. Measurements

Assessment took place in a quiet room with the participant and the examiner seated. Subjects were first submitted to a general socio-demographic questionnaire and a semi-structured interview to record clinical information (see appendix B). A Portuguese version of the Mini-Mental State Examination (MMSE) (Folstein, Folstein et al., 1975; Guerreiro, Silva et al., 1994) (see appendix C) was then performed to evaluate the presence of cognitive impairment in all participants. To assess the presence and severity of patients´ symptoms, we used a semi-structured interview of PANNS (Kay, Fizbein et al. 1987, adapted by Leitão) (see appendix D). PANSS is probably the most widely-used rating scale in schizophrenia (Overall and Gorham, 1988), and it allows for simultaneous rating of positive and negative symptoms. It is a 30-item symptom rating scale rated from 1 to 7 (with higher scores indicating more severe symptoms) as well as sub-scales reflecting positive and negative symptoms. Some additional information was obtained from family members and patients' files.

2.3.1 Apparatus

Behavioural Experiment (to test emotional valence on the unpleasantness of sounds):

This experiment was conducted using an Amilo Fujitsu Siemens laptop computer, (Intel® Core Duo® Processor,) with a UA-4FX Edirol® sound card, running MATLAB® 6.1

programme software, which presented sound stimuli, ratings and statistical analysis. The sounds were delivered through a HD 250- II Sennheiser headphones at 70-75 db average of intensity. Subjects were verbally informed about the nature of the experiment, testing apparatus and procedures. Prior to the experiment, subjects underwent three practice trials (heard three examples of the sound stimuli for familarization purposes).

2.3.2. Stimulus selection

All subjects heard the 75 stimulus sounds of the Newcastle Battery of Unpleasant Sounds (NBUS) (see appendix G), a new instrument developed by the Auditory Group of Newcastle Medical School, which consists of 75 sounds. These were compiled from Bailey's sound battery (Bailey, Chrisholm et al., 2002), International Affective Digitized Sound System IADS (Bradley and Lang, 1999) and various internet sources. These reflect a broad range of sounds, including human and animal vocalisations, musical instruments and mechanical processes, and included common sounds with positive and negative valences (e.g. tires screeching, female screaming, baby crying, laughing). It contains no verbal messages. The duration of the stimuli varied between 1.5 seconds and 2 seconds. The intensity level of the stimuli was equalised and the calibrated perceived loudness varied between 70dB and 75dB. Sounds were presented only once and randomly presented for each set of trials. A self-report measure of emotional experience was asked after hearing each sound. Normally, psychologists represent emotions or feelings in n-dimensional space (generally 2- or 3- dimensional) (Chanel, Kronegg et al., 2005). In this experiment, only the valence dimension in which valence represents the way one judges a situation, from unpleasant to pleasant, was assessed. A ten point visual scale from 0 to 9, with 0 being the least unpleasant and 9 being the most unpleasant was used (see appendix F). This self-

assessment was not subject to a time limit so as to allow for a resting period between sounds.

All tests took approximately 40 minutes to administer and were administered by a single investigator in a single session.

Schizophrenic subjects tolerated these long-duration procedures. They understood and performed the experimental testing, and their ratings seemed to be valid and reliable.

2.4. Statistical analysis

Data were expressed in terms of mean ± s.d. values and rounded to the nearest decimal place. Statistical analysis was performed using the SPSS® 15.0 version for Windows® software (Martinez and Ferreira, 2007). Statistical significance was accepted at $p<0.05$. The different tests and the rationale for their use are described in the results section.

3. Results

3.1. Sample characteristics

Fifty-eight participants (29 patients and 29 controls) were assessed. The characteristics of each group are shown in Table 1. As controls were matched in age and sex, there were no significant differences between the groups in respect of these items, or musical training. There were significant differences with respect to race, years of education and Mini Mental State Examination assessment, with the control group being better educated and scoring higher in the cognitive assessment.

Table 1 - Sociodemographic characteristics and symptoms.

Sample Characteristics	**Clinical(N=29)**	**Control(N=29)**	*p*
	Mean (SD) or No. (%)	Mean (SD) or No. (%)	
Demographic			
Age (Years)	28.7 (6.7) Range 19-43	28.7 (6.7) Range 19-43	1.000(*)
Sex (M/F), no. (%)	20 (69.0) / 9 (31.0)	20 (69.0) / 9 (31.0)	1.000(**)
Race (White/Black), no. (%)	21 (72.4) / 8 (27.0)	29 (100.0) / 0.0	**0.004(**)**
Education (Years)	10.4 (3.4) Range 6-16	14.3 (2.6) Range 6-16	**0.000(*)**
Musical Training (Yes/No), no.(%)	18 (62.1) / 11 (37.9)	21 (72.4) / 8 (27.6)	0.576(**)
Clinical			
Age of onset (Years)	26.8 (6.8) Range 18-41		
Illness duration (Years)	2.3 (1.5) Range 0-5		
Subtype, no (%)			
Paranoid	26 (89.7)		
Disorganized	1 (3.4)		
Undifferentiated	1 (3.4)		
Residual	1 (3.4)		
Family history of disease (Yes/No), no (%)	21 (72.4) / 8 (27.6)		
Number of hospitalizations	1.3 (0.9) Range 0-3		
MMSE	28.6 (1.5) Range 25-30	29.6 (0.6) Range 28-30	**0.002(*)**
PANSS			
Positive subscale	10.1 (3.7) Range 7-17		
Negative subscale	13.2 (2.9) Range 8-19		
General subscale	26.3 (4.7) Range 18-37		
Total	49.6 (8.9) Range 33-66		

Abbreviations: MMSE= Mini-Mental State Examination; Sex (M=male; F=female);
(*) result of the Mann-Whitney Test; (**) result of the Chi-Square Tests

3.2. Clinical variables

Most patients were diagnosed with paranoid type of schizophrenia (n=26, 89%). One patient was diagnosed with disorganized type, one with catatonic type and only one with residual type. Concerning medication, all patients used antipsychotic medication (typical for one patient, atypical for twenty-five and both medications for three patients). It was not possible to assess mean antipsychotic doses because patients used different types of antipsychotic drugs. Some patients were also medicated with: benzodiazepines (n=11), anticholinergics (n=9) and antidepressants (n=5).

Table 2 –Patients' medication status

	Clinical(N=29)	
	n	**%**
Antipsychotics		
Typical	1	3.4
Atypical	25	86.2
Both	3	10.3
Benzodiazepines		
No	18	62.1
Yes	11	37.9
Anticholinergics		
No	20	69.0
Yes	9	31.0
Antidepressants		
No	24	82.8
Yes	5	17.2

The severity of patients' symptoms was assessed using PANSS (see Table 1). The PANSS total mean score amounted to 49.58 ± 8.8. The mean score was 10.10 (s.d.3.6) on the positive subscale and 13.17 (s.d.2.8) on the negative subscale. The general subscale had a mean of 26.31 (s.d.4.6).The PANSS positive subscale contributed less to overall score than the negative, a finding that is consistent with their outpatient status. This fact made it possible to perform the experiment task reliably.

Table 3 - Male and female patients' severity of PANSS

Measure	Male(N=20)		Female(N=9)		*p*
	Mean (SD)	Range	Mean (SD)	Range	
PANSS					
Positive subscale items					
Delusions	2.0 (1.2)	1-4	1.4 (0.9)	1-3	0.220
Conceptual disorganization	1.4 (0.5)	1-2	1.1 (0.3)	1-2	0.191
Hallucinatory behaviour	1.9 (1.3)	1-5	1.0 (0.0)	1-1	**0.048**
Excitement	1.2 (0.4)	1-2	1.1 (0.3)	1-2	0.782
Grandiosity	1.5 (0.9)	1-3	1.0 (0.0)	1-1	0.105
Suspiciousness/persecution	2.0 (1.1)	1-4	1.7 (0.9)	1-3	0.535
Hostility	1.1 (0.3)	1-2	1.0 (0.0)	1-1	0.334
Positive subscale	10.9 (4.0)	7-17	8.3 (1.9)	7-12	0.255
Negative subscale items					
Blunted affect	2.1 (0.5)	1-3	2.1 (0.3)	2-3	0.764
Emotional withdrawal	2.3 (0.7)	1-4	2.1 (0.6)	1-3	0.662
Poor rapport	1.6 (0.7)	1-3	1.6 (0.5)	1-2	0.812
Passive/apathetic social withdrawal	2.6 (0.7)	2-4	2.3 (1.0)	1-4	0.573
Difficulty in abstract thinking	2.1 (0.9)	1-4	2.2 (1.1)	1-4	0.692
Lack of spontaneity and flow of conversation	1.4 (0.5)	1-2	1.8 (0.7)	1-3	0.133
Sterotyped thinking	1.2 (0.4)	1-2	1.3 (0.5)	1-2	0.446
Negative subscale	13.1 (2.8)	10-18	13.4 (3.2)	8-19	0.583
General subscale items					
Somatic concern	1.5 (0.8)	1-3	1.8 (0.8)	1-3	0.337
Anxiety	2.0 (0.8)	1-3	2.3 (1.6)	1-6	0.881
Guilt feelings	1.7 (0.7)	1-3	1.8 (1.0)	1-3	0.836
Tension	1.9 (0.7)	1-3	1.8 (1.0)	1-4	0.610
Mannerisms and posturing	1.4 (0.6)	1-3	1.6 (0.7)	1-3	0.582
Depression	2.7 (1.0)	1-4	2.4 (1.3)	1-5	0.418
Motor Retardation	1.3 (0.6)	1-3	1.6 (1.3)	1-5	0.815
Uncooperativeness	1.1 (0.2)	1-2	1.0 (0.0)	1-1	0.502
Unusual Thought content	1.2 (0.5)	1-3	1.3 (0.7)	1-3	0.616
Disorientation	1.1 (0.2)	1-2	1.0 (0.0)	1-1	0.502
Poor attention	1.4 (0.5)	1-2	1.2 (0.4)	1-2	0.360
Lack of judgment and insight	2.4 (0.6)	1-3	1.3 (0.5)	1-2	**0.001**
Disturbance of volition	1.3 (0.4)	1-2	1.3 (0.5)	1-2	0.648
Poor impulse control	1.1 (0.3)	1-2	1.1 (0.3)	1-2	0.929
Preoccupation	2.0 (0.7)	1-3	1.3 (0.5)	1-2	**0.025**
Active social avoidance	2.9 (0.9)	1-4	2.8 (1.1)	1-4	0.786
General subscale	26.6 (3.6)	21-32	25.7 (6.7)	18-37	0.477
Total subscale	50.6 (8.4)	39-66	47.4 (10.0)	33-58	0.408

(*) result of the Mann-Whitney Test;

There were significant differences between the severity of the male and female symptoms measured by PANSS, with men showing severe symptoms in items such as: hallucinatory behaviour, lack of judgment and insight, and preoccupation ($p<0.05$).

3.3. Analysis of the Unpleasantness of Sounds

3.3.1. Reliability of the Instrument

We measured the reliability of The Newcastle Battery of Unpleasant Sounds (75 sounds). For both groups, Cronbach's Alpha was above 0.6, which demonstrated a good internal consistency reliability of the test (0.916 for clinical group; 0.951 for control group) (Pestana and Gageiro, 2005).

3.3.2. Preliminary analysis

All 75 sounds were classified between 0 and 9 (ten point scale).

First, we analysed the mean unpleasantness rating and standard deviation of the 58 ratings of each 75 sounds split by group (clinical and control) as shown in Table 4.

The sound set used contains a large variation in perceived unpleasantness across a broad range of sounds. It can be seen that female screaming-2 obtained the highest mean unpleasantness rating of 7.3 in the clinical group, while blackboard chalk-1 1 was the highest in the control group, scoring 7.8. Baby laugh had the least mean unpleasantness rating of 0.80 in both groups (1.5 for clinical and 1.2 for control). It can also be seen that the standard deviations of the ratings of each sound vary from 1.1 to 2.8.

Table 4 - Mean unpleasantness rating of the 58 ratings of each sound, split by group, displayed in order of mean unpleasantness from the most unpleasant to the least unpleasant

Sound Name	Clinical		Sound Name	Control	
	Mean	Standard Deviation		Mean	Standard Deviation
Femalescream_2	7.3	1.8	Blackboard_chalk_1	7.8	1.3
Fork_glass_3	7.2	1.7	Knife_bottle_1	7.8	1.5
Angle_grind_2	7.2	2.1	Fork_glass_1	7.7	1.4
Femalescream	7.1	2.0	Fork_glass_3	7.6	1.7
Fork_glass_1	7.1	1.8	Femalescream	7.5	1.5
Ruler_bottle_2	7.0	1.9	Blackboard_chalk_2	7.3	1.2
Blackboard_chalk_1	7.0	1.9	Ruler_bottle_1	7.3	1.7
Electric_drill_2	6.9	2.0	Femalescream_2	7.2	1.7
Ruler_bottle_1	6.9	2.2	Ruler_bottle_2	7.2	2.0
Fork_bottle_3	6.9	1.7	Fork_bottle_4	7.1	1.4
Tire_skids	6.8	1.8	Fork_bottle_1	7.0	2.1
Electric_drill	6.8	2.3	Angle_grind_2	6.9	1.9
Angle_grind1	6.7	1.7	Blackboard_nails_1	6.9	1.3
Blackboard_chalk_2	6.6	2.0	Fork_bottle_3	6.9	1.8
Spade_drag_2	6.6	1.7	Electric_drill_2	6.8	1.6
Fork_bottle_1	6.5	2.0	Electric_drill	6.6	2.0
Blackboard_nails_2	6.5	1.8	Brake_double	6.6	1.6
Lion2	6.5	2.2	Fork_glass_4	6.5	2.1
Knife_bottle_1	6.4	2.6	Angle_grind1	6.4	1.5
Blackboard_nails_1	6.4	2.0	Blackboard_nails_2	6.4	1.5
Cougar	6.2	1.8	Tire_skids	6.4	1.9
Wasp_1	6.2	2.7	Lion2	6.3	1.7
Record_scratch_1	6.2	2.4	Spade_drag_1	6.3	1.4
Fork_glass_4	6.2	2.4	Hippo	6.2	1.3
Doggrowl	6.2	2.3	Wasp_1	6.1	1.9
Anteater	6.0	2.3	Record_scratch_1	6.0	1.8
Fork_bottle_4	6.0	2.7	Spade_drag_2	5.9	1.8
Gorilla	6.0	1.7	Gorilla	5.8	1.7
Leopard1	5.9	2.3	Anteater	5.8	1.4
Bear2	5.8	1.7	Mixer_glass_1	5.7	1.6
Macaca	5.8	2.3	Guitar_1	5.7	1.7
Junglebird2	5.7	2.1	Doggrowl	5.7	1.8
Brake_double	5.7	2.3	Buzzer	5.6	1.7
Domesticcat	5.7	1.6	Panther	5.6	1.7
Catpurr2	5.7	2.1	Camel	5.6	1.5
Film_projector	5.6	2.1	Leopard1	5.6	1.8

Buzzer	5.6	2.5	Clarinet_squeak	5.6	2.3
Camel	5.6	1.9	Bear2	5.6	1.6
Glassbreaking	5.6	2.5	Cougar	5.5	1.9
Spade_drag_1	5.5	2.5	Domesticcat	5.5	1.5
Pig_	5.5	2.1	Glassbreaking	5.5	1.5
Clarinet_squeak	5.5	2.6	Junglebird2	5.3	1.7
Hippo	5.4	2.2	Cat_screaming	5.3	1.8
Cat_screaming	5.3	1.9	Bull frog	5.3	1.6
Bull frog	5.3	2.2	Film_projector	5.3	1.6
Baby cry	5.3	2.8	Violin	5.2	1.7
Clarinet_honk	5.1	2.5	Pig_	5.1	1.5
Violin	5.1	1.9	Catpurr2	5.1	2.2
Spade_drop_1	5.1	2.4	Clarinet_honk	5.0	1.6
Elephant	5.0	2.4	Elephant	5.0	1.8
Thunder1	5.0	2.7	Spade_drop_1	4.9	1.7
Mixer_glass_1	4.9	2.4	Guitar_2	4.9	1.6
Panther	4.8	2.6	Thunder1	4.8	2.0
Guitar_1	4.8	2.2	Firealarm	4.8	1.9
Guitar_2	4.6	2.7	Puffer	4.7	1.7
Zeb	4.6	2.5	Howlin_wolf	4.5	1.7
Multiple_babies	4.6	2.3	Baby cry	4.4	2.1
Puffer	4.6	2.3	Macaca	4.4	2.0
Falcon	4.6	2.0	Phone_ringing	4.3	1.9
Firealarm	4.5	1.9	Falcon	4.2	2.0
Howlin_wolf	4.2	2.7	Thunder2_	4.1	2.1
Lamb	4.0	1.9	Multiple_babies	3.9	1.3
Phone_ringing	3.8	2.4	Reving_Engine	3.8	1.6
Thunder2_	3.6	3.0	Zeb	3.8	1.6
Reving_Engine	3.6	2.5	Dolphinclicks	3.8	1.4
Dolphinclicks	3.4	2.1	Lioncub	3.3	1.7
Frog1	3.3	2.3	Lamb	3.1	1.2
Lioncub	3.2	2.4	Eagle2	2.9	1.7
Eagle2	3.1	2.0	Frog1	2.7	1.3
Applause	2.6	2.2	Applause	2.5	1.4
Bubblingwater	2.5	2.3	Bubblingwater	2.0	1.6
Smallwaterfall	2.1	2.4	Running water_short	1.7	1.3
Running water_short	1.9	2.4	Smallwaterfall	1.6	1.4
Waterflow	1.7	1.8	Waterflow	1.5	1.2
Baby laugh	1.5	1.9	Baby laugh	1.2	1.1

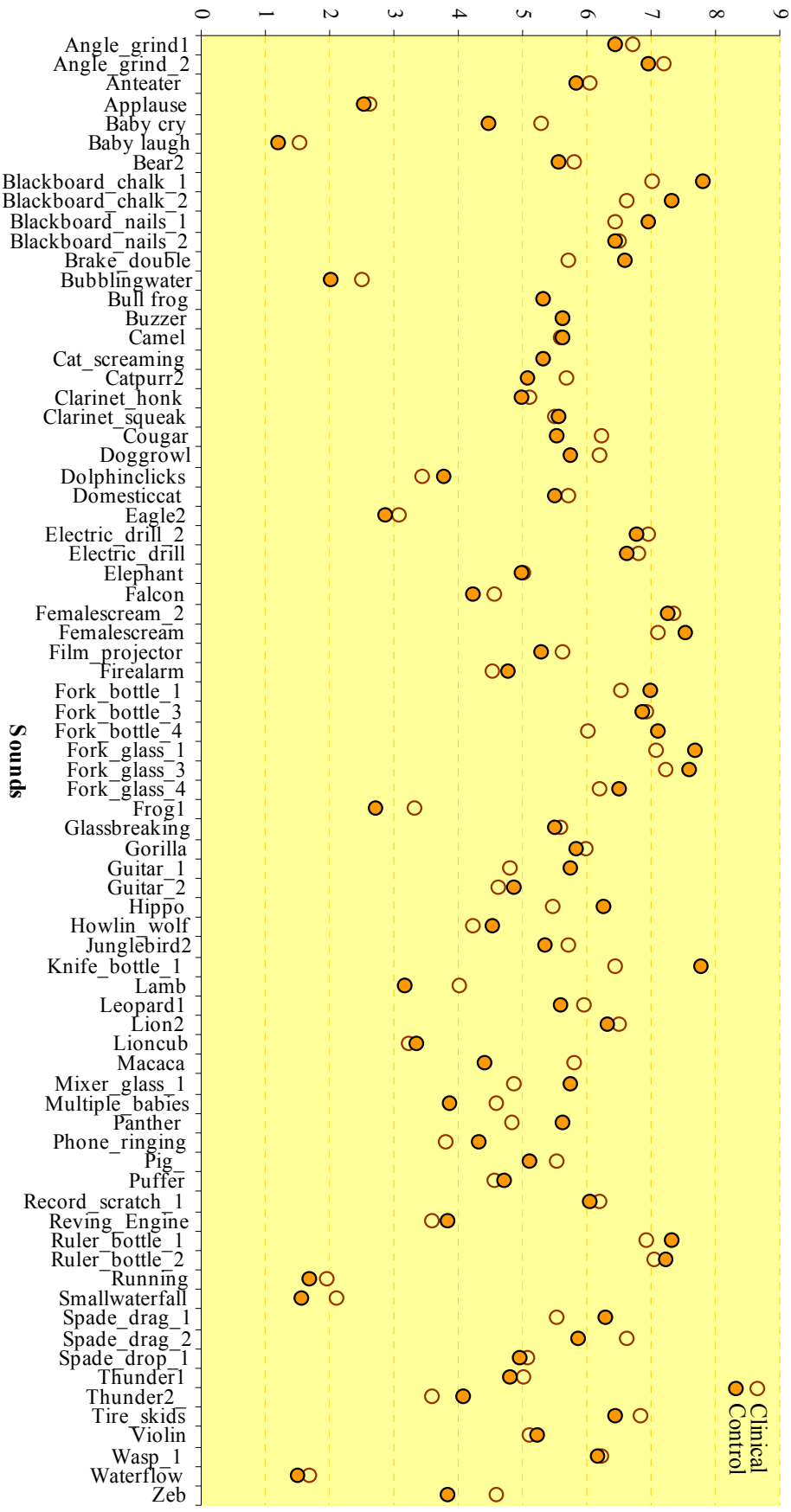


Figure 2 - Mean unpleasantness rating of the 58 ratings of each sound, split by group, displayed in alphabetical

The Mann-Whitney test was then used to compare this mean rating between these two groups. Only one sound (macaca) had a statistically significant difference for $p<0.05$.

Table 5 – Sounds with a statistical difference in mean between groups

Sound Name	Group	Mean	Standard Deviation	p
Guitar_1	Clinical	4.8	2.2	0.086(**)
	Control	5.7	1.7	
Knife_bottle_1	Clinical	6.4	2.6	0.061(**)
	Control	7.8	1.5	
Lamb	Clinical	4.0	1.9	0.075(**)
	Control	3.1	1.2	
Macaca	Clinical	5.8	2.3	0.027(*)
	Control	4.4	2.0	

(*)$p<0.05$; (**)$p<0.1$

Table 6 - Sounds with a statistical difference in mean between years of illness duration

Sound Name	Illness duration	n	Mean	Standard Deviation	p
Doggrowl	0	3	6.0	4.4	0.047(*)
	1	9	5.0	1.8	
	2	5	7.6	1.3	
	3	4	6.0	1.4	
	4	5	5.4	2.1	
	5	3	9.0	0.0	
Firealarm	0	3	3.3	2.5	0.014(*)
	1	9	4.9	0.9	
	2	5	3.8	2.4	
	3	4	6.5	1.3	
	4	5	2.6	1.1	
	5	3	6.3	0.6	
Macaca	0	3	8.3	0.6	0.024(*)
	1	9	4.4	0.9	
	2	5	5.0	2.1	
	3	4	4.8	2.8	
	4	5	6.8	2.9	
	5	3	8.3	1.2	
Thunder1	0	3	7.0	1.0	0.043(*)
	1	9	5.0	1.3	
	2	5	6.2	2.4	
	3	4	6.5	3.0	
	4	5	1.6	2.1	
	5	3	4.7	3.8	

(*)$p<0.05$ result of Kruskal Wallis test

Four sounds had a significant difference in mean unpleasantness rating by years of illness duration. In two cases, patients with longer illness duration had higher ratings (see table 6).

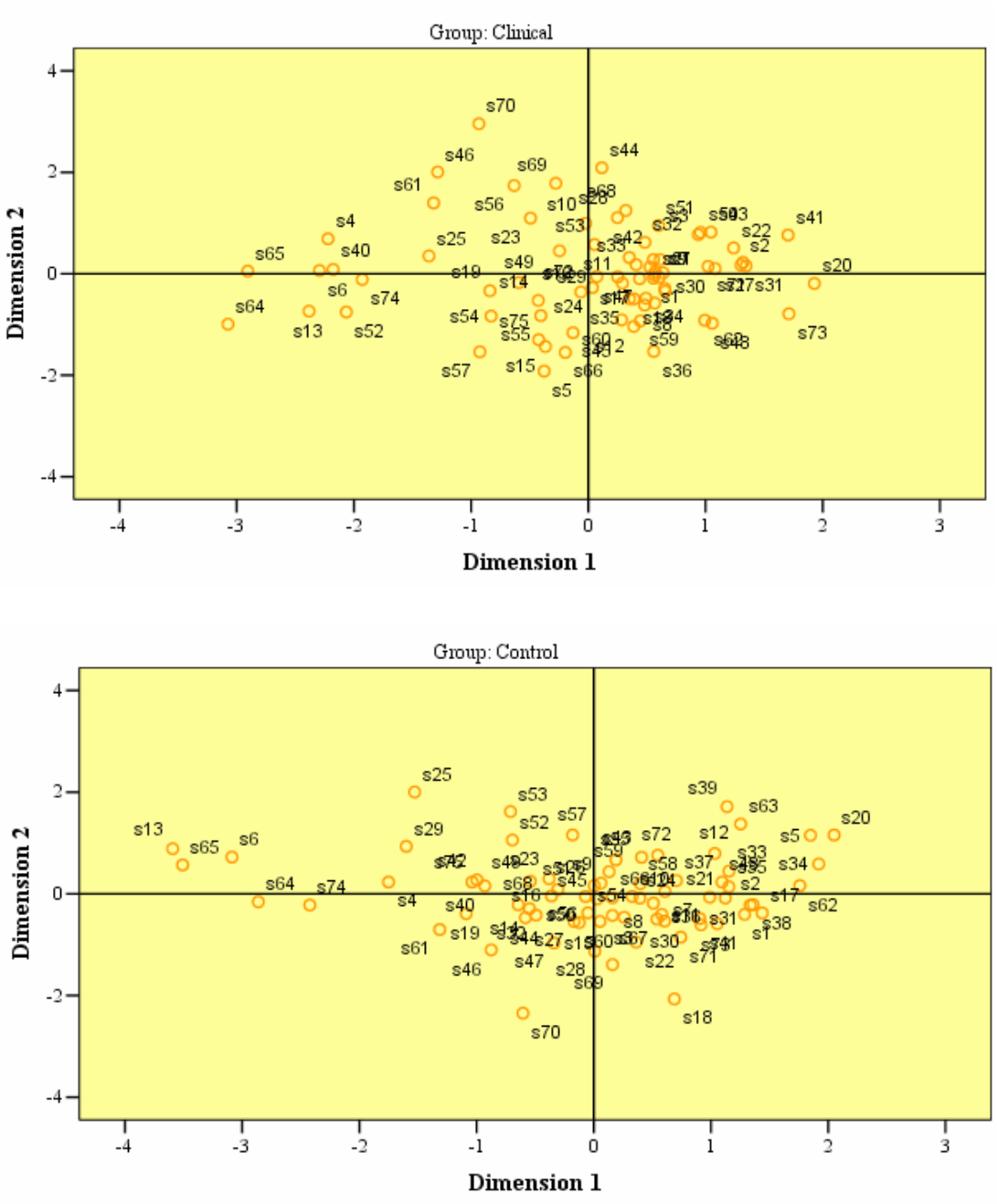
We also performed a Multidimensional Scale (MDS) analysis of the unpleasantness ratings of the 75 sounds for each group. This was done by producing a 75x75 correlation matrix which calculated all possible correlations of sound rating profiles. These correlations were converted into a measure of distance to produce a graph which displayed each sound as a point in two-dimensional space, where the two dimensions were unknown. This analysis allowed us to identify any clusters of sounds which would indicate that the sounds were perceived similarly. The distance between two sounds reflected the degree of similarity in the perceived unpleasantness of the sounds, with sounds appearing close together being perceived as similarly unpleasant and those farther apart being perceived as dissimilarly unpleasant.

Figure 3 displays the resulting two-dimensional plots: the numbers correspond to the position of the sound in alphabetical order (see appendix F).

The graphs in both groups revealed that the experimental sound set used reflected a broad range of unpleasantness, as desired. The patterns were different for both groups, but both seemed to have clusters of sounds, which mean that sounds were perceived very similarly. In the clinical group, there seem to be some sound clusters: for example, sound 2 (angle-grind-2), sound 27 (electric-drill) and sound 31 (female scream). The stress value from the analysis was 0.24, and the two dimensions represented 76.3% of the variance in unpleasantness ratings of the sounds. There were clusters in the control group too, for

example, sound 11 (blackboard-nails-2) and sound 30 Femalescream-2. The stress value was 0.22 and the level of variance was 83.1%.

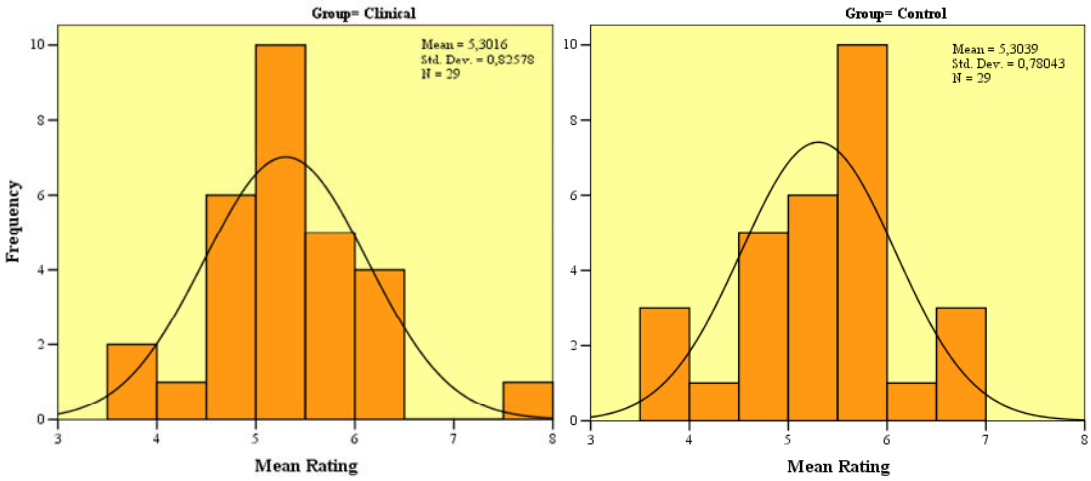
Figure 3 - A two-dimensional MDS plot of the unpleasantness ratings of 75 sounds for each group



3.3.3. Secondary analysis

In a second phase, we made a mean unpleasantness rating of the 75 sounds of each participant in the study, which we then split by group. In figure 4 we can see the normal distribution of the variable.

Figure 4 – Mean unpleasantness rating of the 75 sounds of each participant by group



After using the Shapiro Wilk test, which confirmed the normal distribution of this variable, the Student's t-test was used to compare groups and verify our hypothesis that schizophrenic patients would perceive our battery of sounds as more unpleasant than controls.

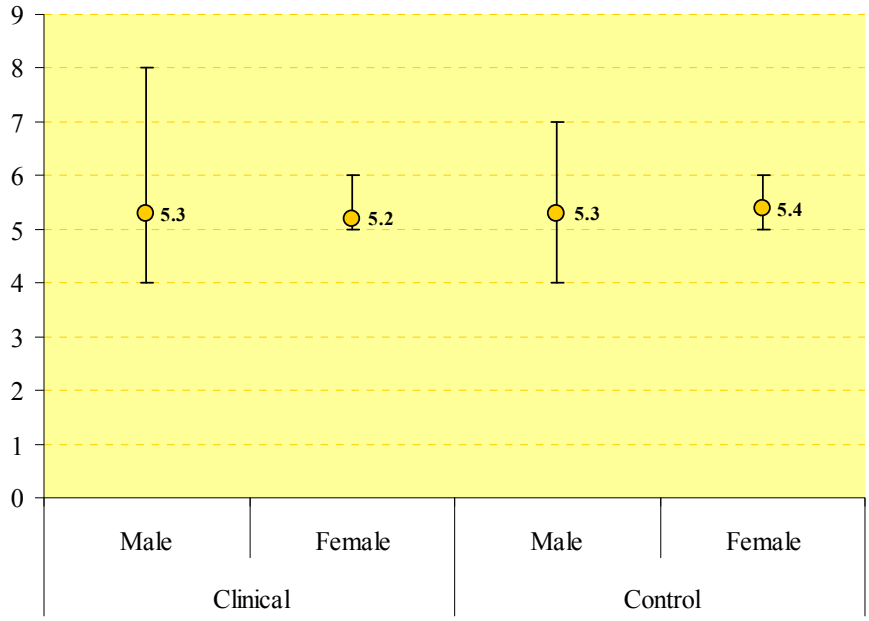
Table 7 – Mean unpleasantness rating by group

	Group	n	Mean	Standard Deviation	p
Mean Rating	Clinical	29	5.3	0.8	0.991
	Control	29	5.3	0.8	

In this study, with these data, there were no statistical differences between patients and controls as regards mean ratings of unpleasantness of sounds (p>0.05). Patients did not rate sounds as more unpleasant than controls.

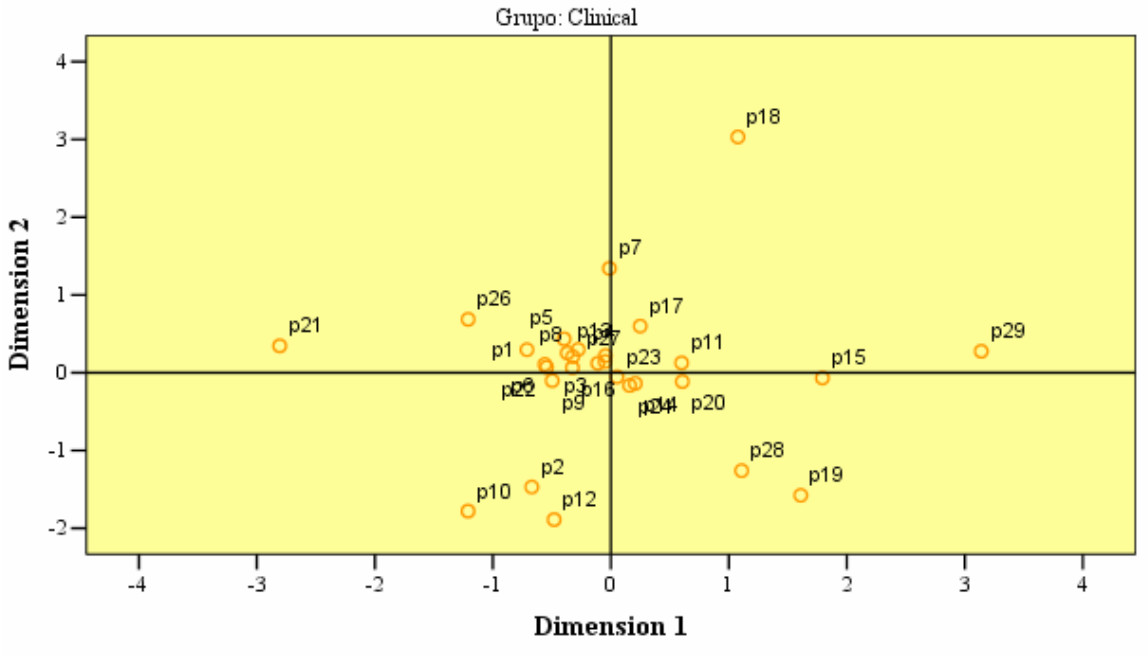
We also used the Student's t-test to compare mean ratings with sex variables in both groups, and no significant difference was found either. In the clinical group: male: 5.3 (s.d. 0.9); female: 5.2 (s.d. 0.5); p=0.697; In the control group: male: 5.3 (s.d. 0.9); female 5.4 (s.d. 0.4); p=0.778.

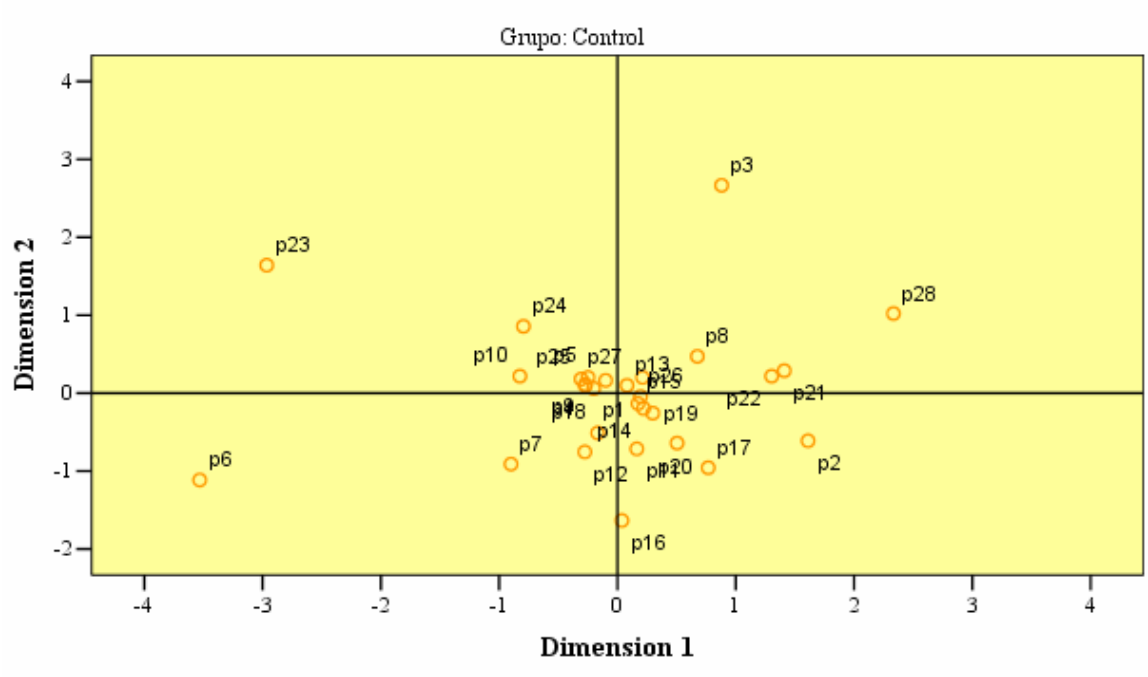
Figure 5 – Mean unpleasantness rating by group and sex



Although there were no significant differences in mean unpleasantness rating, we performed an MDS analysis of the mean unpleasantness ratings of the 29 participants in each group to look for differences in group profile patterns. This was achieved by producing a 29x29 correlation matrix. These correlations were then converted into a distance measure in order to produce a graph showing each participant's unpleasantness rating as a point in a two-dimensional space. The distance between two participants reflected the degree of similarity in their perceived mean unpleasantness ratings.

Figure 6- A two-dimensional MDS plot of the unpleasantness ratings of the 29 participants in each group





For the clinical group, the stress value from the analysis was 0.20 and the level of variance was 87.3%, while for the control group, the stress value was 0.16 and the level of variance 92.5%.

3.4. Association between clinical characteristics and mean unpleasantness rating

Correlations (Spearman's *p*) between sex and measures of unpleasantness rating (i.e. mean) were generally low and non-significant (*p* values >0.05). In addition, no significant correlations were found between clinical characteristics (i.e. years of diagnosis, PANSS subscales) and unpleasantness rating (*p* values >0.05).

Table 9 – Correlations between mean rating and some clinical characteristics

		Years of diagnosis	Illness duration	Positive subscale	Negative subscale	General subscale
Mean Rating	Correlation Coefficient	0.283	0.218	0.162	-0.138	0.145
	p	0.137	0.255	0.400	0.476	0.453

An analysis of the family history of disease status was performed with the Mann-Whitney test. No statistical difference was found either.

3.5. Cluster Analysis

In order to study the clinical group in more detail and to search for subgroups, we performed a K-means cluster analysis to find clusters based on their mean rating.

In clusters, the degree of association is strong between members of the same cluster and weak between members of different clusters. We decided on two clusters as there were 29 subjects in our sample.

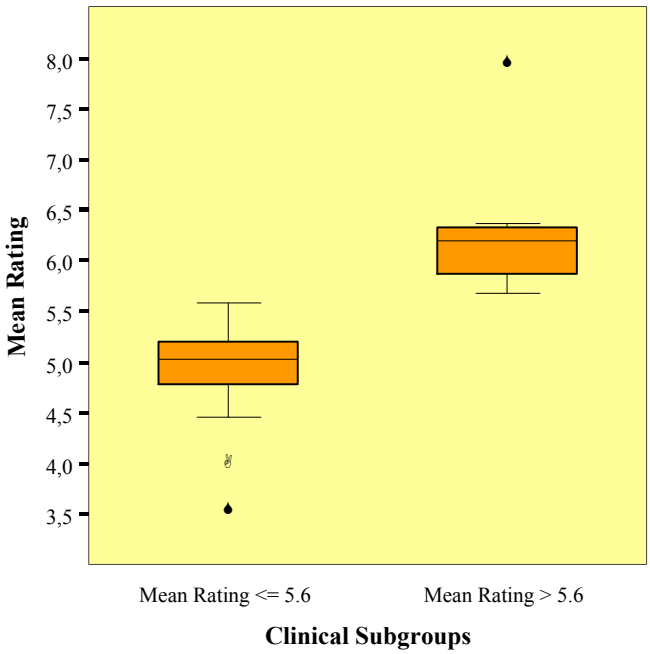
Table 10 – Cluster Analysis

Measure	Cluster	
	1	**2**
Number of cases	21	8
Mean rating	4.9	6.3
Median	5.0	6.1
Variance	0.2	0.4
Standard Deviation	0.4	0.4
Minimum	3.5	5.7
Maximum	5.6	7.9
Range	2.0	2.2

The analysis indicated a 5.6 point cut-off as the ideal threshold for patients' mean ratings. We called Clinical Subgroup 1 cluster 1 (mean rating <= 5.6) and Clinical Subgroup 2 cluster 2 (mean rating > 5.6).

We then used the Mann-Whitney test to confirm whether these two subgroups were really statistically different, and to accept this cluster analysis (p=0.000).

Figure 4 - Clinical Subgroups



After that, we searched for statistical differences between these two clinical subgroups for sociodemographic and clinical characteristics, which we did not find.

Table 11- Sociodemographic and clinical characteristics of Clinical Subgroups

Sample Characteristics (N=29)	**Clinical Subgroup 1 (N=21) Mean rating <=5.6**	**Clinical Subgroup 2 (N=8) Mean rating >5.6**	***p***
	Mean (SD) or No. (%)	Mean (SD) or No. (%)	
Demographic			
Age (years)	27.6 (6.4) Range 19-42	31.4 (7.0) Range 23-43	0.101(*)
Sex (M/F), no. (%)	14 (66.7) / 7 (33.3)	6 (75.0) / 2 (25.0)	1.000(**)
Race (White/Black), no. (%)	17 (81.0) / 4 (19.0)	4 (50.0) / 4 (50.0)	0.164(**)
Education (years)	10.7 (3.8) Range 6-16	9.8 (2.1) Range 6-12	0.757(*)
Musical Training (yes/no), no (%)	14 (66.7) / 7 (33.3)	4 (50.0) / 4 (50.0)	0.433(**)
Clinical			
Age of onset (years)	26.1 (7.0) Range 18-41	28.4 (6.5) Range 22-40	0.281(*)
Illness duration (years)	2.0 (1.4) Range 0-4	3.0 (1.9) Range 0-5	0.162(*)
Subtype, no (%)			
Paranoid	19 (90.5)	7 (87.5)	0.335(**)
Disorganized	0 (0.0)	1 (12.5)	
Undifferentiated	1 (4.8)	0 (0.0)	
Residual	1 (4.8)	0 (0.0)	
Family history of disease (yes/no), no (%)	16 (76.2) / 5 (23.8)	5 (62.5) / 3 (37.5)	0.646(**)
Number of hospitalizations	1.2 (0.8) Range 0-3	1.6 (0.9) Range 0-3	0.159(*)
MMSE	28.8 (1.3) Range 25-30	28.0 (2.0) Range 25-30	0.463(*)
PANSS			
Positive subscale	10.1 (3.6) Range 7-17	10.0 (4.1) Range 7-17	0.858(*)
Negative subscale	13.6 (3.0) Range 8-19	12.1 (2.3) Range 10-17	0.199(*)
General subscale	25.9 (4.5) Range 18-32	27.4 (5.2) Range 20-37	0.606(*)
Total	49.6 (8.9) Range 33-65	49.5 (9.3) Range 40-66	0.864(*)

MMSE= Mini-Mental State Examination; Sex (M=male; F=female);
(*) result of the Mann-Whitney Test; (**) result of the Chi-Square Tests

We also searched for differences in medication status, but there were none either.

4. Discussion

The main goal of this study was to evaluate emotional processing of unpleasant sounds in schizophrenic outpatients in early stages of the disease (less than five years of illness duration). To our knowledge, this has never been studied before. We developed and applied a new instrument called the Newcastle Battery of Unpleasant Sounds (NBUS). Our hypothesis was that these patients could have an altered emotional perception of unpleasant sounds, perceiving them as more unpleasant than healthy controls. We also hypothesized the existence of an ancient route, responsible for the conduction of emotionally auditory relevant stimuli to the amygdala, a direct thalamo-amygdala pathway.

4.1. Sample characteristics

Usually, men and women are affected equally, but the age of onset is earlier in men (Sadock and Sadock, 2005). Our sample was outpatients in early stages of the disease and the ratio of male to female was 2:1. With respect to the Mini Mental State Examination (a screening test for cognitive impairment) schizophrenic patients had a lower and significantly different mean score from controls (clinical group: 28.5; control group: 29.6; $p<0.05$). However, this result was not indicative of significant global cognitive impairment (score >24). The Mini Mental State Examination (MMSE) has been used as a broad test of global cognitive function in schizophrenia (Harvey, White et al., 1995) but is sometimes less sensitive and underestimates cognitive impairments in these patients (Palha, Branco et al., 2006). There is much debate about cognitive decline in schizophrenia, and whether it is progressive or static. Some studies suggest that these deficits are lifelong and pre-date the onset of schizophrenia (Russell, Munro et al., 1997). It has also been suggested that after a

period of initial deterioration early in the illness, cognitive deficits become static (Hyde, Nawroz et al., 1994).

4.2. Emotional processing of unpleasant sounds

In this study, we did not find any significant difference between clinical and control groups in mean ratings of sound unpleasantness. Patients did not perceive unpleasant sounds as more unpleasant than controls. These findings are in agreement with another study conducted on schizophrenics, in which it was demonstrated that emotional processing of environmental sounds measured by valence and arousal rating scales was preserved (Tuscher, Silbersweig et al., 2005). Regarding correlations between clinical severity measures (disease duration, PANSS total and sub scores) and mean unpleasantness rating, we found no statistical difference. This could suggest that the emotional processing of unpleasant sounds is rather stable during the first five years of illness. Nevertheless, we must reiterate that these patients were outpatients, and thus not in an acute state of psychotic symptom exacerbation.

The sounds presented varied widely in perceived unpleasantness. Pleasantness-unpleasantness depends not only on the loudness level or frequency component but on the accuracy in sound identification. Semantic associations may have had an effect upon unpleasantness ratings, as well as certain acoustic features which automatically caused an unpleasant perception (Shimai, Fukuda et al., 1993).

Some studies on facial emotion identification in schizophrenia have reported progressive impairments (Edwards, Jackson et al., 2002).Taken together this data raises the question as to why emotion processing of unpleasant sounds is perceived while other types of emotion processing are not. Is it because audition plays a role in the processing of environmental

cues with direct survival significance (e.g., growls, shouts, cries)(Verona, Patrick et al., 2004)? The amygdala has an evolutionary history in terms of the emotional processing needed for survival, and perhaps unpleasant sounds stimulate it directly through a second auditory pathway. Future studies will be needed to identify this pathway.

4.3. Sex differences in emotional sound processing

In this study, we found no sex differences in emotional processing of unpleasant sounds in either the clinical group or the control group. This could, however, have been due to the small size of the sample.

In contrast, one Japanese study on pleasantness-unpleasantness of environmental sounds did show gender differences: women rated the pleasant sounds as being more pleasant than the men did, and men rated the unpleasant sounds as not so unpleasant as the women's ratings of the same sounds (Shimai, Fukuda et al., 1993). Furthermore, in previous research in healthy subjects, a clear sex difference was observed in the ability to recognise facial emotions, especially negative ones, with women outperforming men (McClure, 2000). In schizophrenic patients, some studies have found sex differences in emotional processing for facial emotions, which could explain why women with schizophrenia are less impaired in social life than men (Seeman and Lang, 1990; Castle, Wessely et al., 1993; Scholten, Aleman et al., 2005).

4.4. Emotional experience, a subjective experience

As we have already mentioned, schizophrenic subjects tolerated the study procedures. They understood and performed the experimental testing, and their ratings seemed to be valid and reliable. Although some authors argue the opposite (Steinberg, 1986; Kallstrand,

Montnemery et al., 2002), others assume that these patients can accurately complete a self report measure of their affective experience, and that they have the same mental structure with regard to semantic knowledge of emotional phenomena as healthy people (Aleman A. and Kahn R., 2005). A recent study reported that the structure of affective representations is similar in schizophrenia patients and healthy controls. Nevertheless, there have been studies where emotional responses can vary within and between subjects, affected by factors such as the presentation context, personal experience relating to the emotional content, and also the subject's mood (Lang, Bradley et al., 1998).

4.5. Limitations

This study has some limitations. First, although diagnoses were established by an experienced psychiatrists, they could have also been confirmed on the basis of a Structured Clinical Interview for DSM-IV Disorders (SCID) (First, Spitzer et al., 1996). On assessment, the use of a neuropsychological test battery could have been more informative of the cognitive status of patients, while physiological measures such as skin conductance response (SCR) and heart rate (HR), as well as electromyography measures (EMG): facial muscle activity of corrugator and zygomatic, might have provided more details on emotional expression.

Concerning medication, we were unable to estimate the mean dose, as the patients had different medication status. This made it difficult to make a detailed assessment of the potential effect of the type of antipsychotic treatment (atypical v. typical) on task performance.

The relatively small sample size in this study limits the general applicability of our findings, which should be confirmed in future studies.

4.6. Conclusions

Notwithstanding these limitations, the current study demonstrated that schizophrenic patients in early stages of the disease have a preserved emotional perception of unpleasant sounds. This study raises several questions such as why emotional processing of unpleasant sounds is perceived in schizophrenics and facial emotion recognition is impaired. Is it because of the importance of audition for survival? Our study also indicated that there were no sex differences, although our sample was too small. Future longitudinal studies with larger samples and cognitive measures examining emotional sound processing stability during the course of the disease will be needed. More studies on psychoacoustics to determine which features cause the unpleasant perception of certain sounds would also be of great interest. The Newcastle Battery of Unpleasant Sounds used in this study demonstrated a very good internal consistency. In the future it could be used in neuroimaging experiments to determine the neural substrates activated by exposure to unpleasant auditory signals. Perhaps a second auditory pathway might become apparent. Future research in this area is important for the larger study of emotion and cognition.

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APPENDICES

Appendix A: Written Consents (one for each hospital)

INFORMAÇÃO PARA OS DOENTES DO SERVIÇO DE PSIQUIATRIA DO HOSPITAL DE SANTA MARIA

INTRODUÇÃO

No âmbito de um projecto de investigação (dissertação de mestrado em Neurociências) pela Faculdade de Medicina da Universidade de Lisboa, fazemos-lhe o seguinte convite para participar:

OBJECTIVO E DURAÇÃO DO ESTUDO

A investigação que faremos tem como objectivo estudar a percepção emocional dos sons.
O estudo tem a duração de três meses (Agosto, Setembro e Outubro de 2007) e a sua colaboração será necessária apenas uma vez.

PROCEDIMENTOS DE ESTUDO E INSTRUMENTOS

A sua participação no projecto é totalmente voluntária.
Pode decidir não participar no projecto ou desistir em qualquer momento. Independentemente da decisão que tomar, não sofrerá qualquer prejuízo.

Ao aceitar fazer parte deste projecto será submetido a:
Após a consulta com o seu médico psiquiatra assistente, pedimos-lhe que:

- Participe numa entrevista médica para colheita de dados pessoais, história familiar
- Coopere na aplicação das escalas

Escalas a serem aplicadas:

- Mini Mental State – para avaliar o estado cognitivo
- PANSS – Escala que avalia os sintomas positivos e negativos
- Bateria de Sons de Newcastle - para avaliação emocional dos sons. Os sons serão emitidos através de auscultadores a partir de um computador portátil. Após a audição individual dos 75 sons, dará a sua avaliação do grau de prazer ou desprazer dos mesmos.

RISCOS E INCÓMODOS POR PARTICIPAR

Ao aceitar participar neste estudo a sua saúde não é colocada em risco.

A sua participação será solicitada apenas num momento:

O QUE ACONTECERÁ AOS DADOS E À INFORMAÇÃO COLHIDA

Toda as informações que serão colhidas sobre os seus dados pessoais serão mantidas confidenciais e tratadas em anonimato. Após a conclusão do estudo serão destruídos os dados.

FORMULÁRIO DE CONSENTIMENTO INFORMADO

- Declaro que li e compreendi a informação
- Todas as dúvidas adicionais me foram esclarecidas por um dos membros do projecto.
- Estou informado de que poderei desistir a qualquer momento ou ser excluído do estudo.
- Aceito participar no projecto de investigação científica, conhecendo os meus direitos e deveres, bem como os riscos e benefícios da minha participação.

Assinatura: Data:

Assinatura do investigador: Data:

A preencher pelos serviços:
Identificação do Doente (ID):

INFORMAÇÃO PARA OS DOENTES DO HOSPITAL JÚLIO DE MATOS

INTRODUÇÃO

No âmbito de um projecto de investigação (dissertação de mestrado em Neurociências) pela Faculdade de Medicina da Universidade de Lisboa, fazemos-lhe o seguinte convite para participar:

OBJECTIVO E DURAÇÃO DO ESTUDO

A investigação que faremos tem como objectivo estudar a percepção emocional dos sons.
O estudo tem a duração de três meses (Agosto, Setembro e Outubro de 2007) e a sua colaboração será necessária apenas uma vez.

PROCEDIMENTOS DE ESTUDO E INSTRUMENTOS

A sua participação no projecto é totalmente voluntária.
Pode decidir não participar no projecto ou desistir em qualquer momento. Independentemente da decisão que tomar, não sofrerá qualquer prejuízo.

Ao aceitar fazer parte deste projecto será submetido a:
Após a consulta com o seu médico psiquiatra assistente, pedimos-lhe que:

- Participe numa entrevista médica para colheita de dados pessoais, história familiar
- Coopere na aplicação das escalas

Escalas a serem aplicadas:

- Mini Mental State – para avaliar o estado cognitivo
- PANSS – Escala que avalia os sintomas positivos e negativos da esquizofrenia
- Bateria de Sons de Newcastle - para avaliação emocional dos sons. Os sons serão emitidos através de auscultadores a partir de um computador portátil. Após a audição individual dos 75 sons, dará a sua avaliação do grau de prazer ou desprazer dos mesmos.

RISCOS E INCÓMODOS POR PARTICIPAR

Ao aceitar participar neste estudo a sua saúde não é colocada em risco.
A sua participação será solicitada apenas num momento:

O QUE ACONTECERÁ AOS DADOS E À INFORMAÇÃO COLHIDA

Todas as informações que serão colhidas sobre os seus dados pessoais serão mantidas confidenciais e tratadas em anonimato. Após a conclusão do estudo serão destruídos os dados.

FORMULÁRIO DE CONSENTIMENTO INFORMADO

- Declaro que li e compreendi a informação
- Todas as dúvidas adicionais me foram esclarecidas por um dos membros do projecto.
- Estou informado de que poderei desistir a qualquer momento ou ser excluído do estudo.
- Aceito participar no projecto de investigação científica, conhecendo os meus direitos e deveres, bem como os riscos e benefícios da minha participação.

Assinatura: Data:

Assinatura do investigador: Data:

A preencher pelos serviços:
Identificação do Doente:

Appendix B: Sociodemographic and Clinic Questionnaire

CADERNO DE RECOLHA DE DADOS

"Analysis of the unpleasantness of sounds by schizophrenic patients"

ID: _____

Grupo: Controlos _ Pacientes __

Sexo: Mas. ___ Fem.___ **Idade** ____ anos

Raça: Branca ___ Negra ___

Estado Civil: Solteiro ___ Casado/Junto ___ Divorciado/Separado ___

Escolaridade: 6º ano __ 9 º ano __ 12º ano __ Universidade _

Profissão: _____

Lateralidade: Esquerda __ Dextro __ Ambidextro __

Treino Musical Não _ Sim __

Anos de evolução dos sintomas _____

Anos de diagnóstico _____

História familiar da doença Não _ Sim __ Quem _____

Hospitalizações: _____ (número)

Medicação e dose

Medicação 1:_____ Dose 1:_____

Medicação 2:_____ Dose 2:_____

Medicação 3:_____ Dose 3:_____

Medicação 4:_____ Dose 4:_____

Medicação 5:_____ Dose 5:_____

Appendix C: Mini-Mental State Examination (MMSE)

Portuguese version adapted by Guerreiro et al.,1994

MINI-MENTAL STATE - MMS

NOME: _____
IDADE:_____Anos DATA: _____ de _____ de _____ _____

1. ORIENTAÇÃO (1 ponto por cada resposta correcta).

Em que ano estamos? _____
Em que mês estamos? _____
Em que dia do mês estamos? _____
Em que dia da semana estamos? _____
Em que estação do ano estamos? _____
Em que país estamos? _____
Em que distrito vive? _____
Em que terra vive? _____
Em que casa estamos _____
Em que andar estamos _____ Nota:

2. RETENÇÃO (contar 1 ponto por cada palavra correctamente repetida).
"Vou dizer três palavras; queria que as repetisse, mas só depois de eu as dizer todas; procure ficar a sabê-las de cór".
Pêra _____
Gato _____
Bola _____ Nota:

3. ATENÇÃO E CÁLCULO (1 ponto por cada resposta correcta. Se der uma errada mas depois continuar a subtrair bem, consideram-se as seguintes como correctas. Parar ao fim de 5 respostas.)
"Agora peço-lhe que me diga quantos são 30 menos 3 e depois ao número encontrado volta a tirar 3 e repete assim até eu lhe dizer para parar".
27 __ 24 __ 21 __ 18 __ 15 __ Nota:

4. EVOCAÇÃO (1 ponto por cada resposta correcta.)
"Veja se consegue dizer as três palavras que pedi há pouco para decorar".
Pêra _____
Gato _____
Bola _____ Nota:

5. LINGUAGEM (1 ponto por cada resposta correcta).
a. "Como se chama isto? Mostrar os objectos:
Relógio _____
Lápis _____ Nota:

b. "Repita a frase que eu vou dizer: O RATO ROEU A ROLHA" Nota:

c. "Quando eu lhe der esta folha de papel, pegue nela com a mão direita, dobre-a ao meio e ponha sobre a mesa", (ou "sobre a cama", se for o caso); dar a folha segurando com as duas mãos.
Pega com a mão direita _____
Dobra ao meio _____
Coloca onde deve _____ Nota:

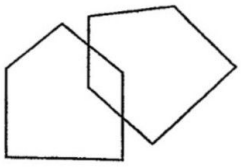
d. "Leia o que está neste cartão e faça o que lá diz". Mostrar um cartão com a frase bem legível, "FECHE OS OLHOS"; sendo analfabeto ler-se a frase.
Fechou os olhos Nota:

e. "Escreva uma frase inteira aqui". Deve ter sujeito e verbo e fazer sentido; os erros gramaticais não prejudicam a pontuação.
Nota:

Folstein, Folstein e McHugh, 1975, segundo adaptação portuguesa de Manuela Guerreiro e colabs., 1993. Laboratório de Estudos de Linguagem do Centro de Estudos Egas Moniz, Hosp. Sta. Maria

6. **HABILIDADE CONSTRUTIVA** (1 ponto pela cópia correcta.)
Deve copiar um desenho. Dois pentágonos parcialmente sobrepostos; cada um deve ficar com 5 lados, dois dos quais intersectados. Não valorizar, tremor ou rotação.

DESENHO



CÓPIA

(Máximo 30 pontos) TOTAL:

Pontos de Corte
(População Portuguesa)

Considera-se com Defeito Cognitivo:

- Analfabetos ≤ 15
- 1 a 11 anos de escolaridade ≤ 22
- Com escolaridade superior a 11 anos ≤ 27

FECHE OS OLHOS

Appendix D: Positive and Negative Syndrome Scale (PANSS)

SCI-PANSS

Stanley R. Kay, Ph.D.
Lewis A. Opler, M.D., Ph.D.
Abraham Fiszbein, M.D.

Traduçao de:
DR. OLIVIA ROBUSTO-LAITÃO
DR. MANUEL DELGADO

Entrevista Clínica Estruturada para a Escala dos Síndromas Positivos e Negativos

SCI-PANSS

L. A. Opler, M.D., Ph.D. S. R. Kay, Ph.D. J. P. Lindenmayer, M.D. A. Fiszbein, M.D.

Nome do paciente, ou identificação: _____

Entrevistador: _____ Data: _____

Dados sobre "Ausência de espontaneidade e curso da conversa" (N6) 'Relação pobre,' (N3) e "Desorganização Conceptual" (P2)

Olá, eu sou ... vamos passar os próximos 30 a 40 minutos a falar sobre si, e sobre os motivos que o (a) levaram a vir cá. Talvez possa começar por me contar qualquer coisa sobre si próprio e sobre o seu passado?

(Instruções para o entrevistador: Conceda, pelo menos, 5 minutos para estabelecer uma relação não dirigida no contexto da entrevista, antes de prosseguir para as questões específicas da lista que se segue)

Dados sobre "Ansiedade" (G2)

Sentiu-se preocupado, ou nervoso na semana passada? _____

SE NÃO: Diria que é geralmente calmo e relaxado? _____

SE SIM: O que é que o tem trazido nervoso (preocupado, inquieto, tenso)? _____

Qual é a intensidade do nervosismo (preocupação, etc.) que tem sentido? _____

Tem-se sentido por vezes a tremer, ou com o coração acelerado? _____

Entra em pânico? _____

Sente que o seu sono, a alimentação, ou a participação em actividades foram afectados? _____

Dados sobre "Delírios (em geral)" (PI) e "Conteúdo Invulgar do Pensamento' (G9)

As coisas têm-lhe corrido bem? _____

Há alguma coisa que o tenha incomodado ultimamente? _____

Pode-me contar um pouco sobre o que pensa da vida e da sua finalidade? _____

Segue uma filosofia em particular? _____

Algumas pessoas contam-me que acreditam no Diabo; o que é que pensa disso? _____

Consegue ler o pensamento das outras pessoas? _____

SE SIM: Como é que isso acontece? _____

Os outros conseguem ler o seu pensamento? _____

SE SIM: Como é que eles conseguem fazer isso? _____

Existe algum motivo para que alguém queira ler o seu pensamento? _____

Quem controla a sua mente? _____

Dados sobre "Desconfiança/Perseguição," (P6) "Isolamento Social Passivo/Apático," (N4) "Evicção Social Activa," (GI6) e "Mau Controlo dos Impulsos" (GI4)

Como é que tem passado o tempo nestes dias? _____

Prefere estar sozinho? _____

Junta-se aos outros para fazer coisas? _____

SE NÃO: Porque não? ... Tem medo das pessoas, ou não gosta delas? _____

SE SIM: Pode explicar? _____

SE SIM: Fale-me sobre isso. _____

Tem muitos amigos? _____

SE NÃO: Só alguns? _____

SE NÃO: Nenhuns? .... Porquê? _____

SE SIM: Porquê só alguns amigos? _____

SE SIM: Amigos íntimos? _____

SE NÃO: Porque não? _____

Sente que pode confiar na maioria das pessoas? _____

SE NÃO: Porque não? _____

Há algumas pessoas em particular em quem não confia? _____

SE SIM: Pode-me dizer quem são? _____

Porque é que não confia nas pessoas? (ou nomeadamente numa pessoa)? _____

SE "NÃO SEI", OU "NÃO SEI O QUE DIZER: Tem uma boa razão para não confiar...? _____

Há alguma coisa que .... lhe tenham feito a si? _____

Talvez lhe venham a fazer agora? _____

SE SIM: Pode explicar-me? _____

Dá-se bem com os outros? _____

SE NÃO: Qual é o problema? _____

Tem um feitio irritável? _____

Envolve-se em lutas? _____

SE SIM: Como é que essas lutas começam? _____

Fale-me dessas lutas. _____

Com que frequência acontecem ? _____

Perde às vezes o controlo de si próprio? _____

Gosta da maioria das pessoas? _____

SE NÃO: Porque não? _____

Existem algumas pessoas que não gostem de si? _____

SE SIM: Por que razão? _____

Os outros falam de si nas suas costas? _____

SE SIM: O que dizem eles de si? _____

Porquê? _____

Alguém anda a espiá-lo, ou a conspirar contra si? _____

Sente-se, por vezes, em perigo? _____

SE SIM: Diria que a sua vida corre perigo? _____

Anda alguém a pensar fazer-lhe mal, ou talvez mesmo a pensar em matá-lo? _____

Foi à polícia pedir ajuda? _____

Trata às vezes dos assuntos por sua conta, ou levanta queixa contra quem o possa atacar? _____

SE SIM: O que é que fez? _____

Dados sobre "Comportamento Alucinatório" (P3) e delírios associados

Tem, uma vez por outra sensações estranhas, ou pouco usuais? _____

As pessoas às vezes contam-me que conseguem ouvir ruídos ou vozes dentro da cabeça delas que os outros não ouvem. Também consegue? _____

SE NÃO: Recebe, por vezes, comunicações pessoais da rádio ou da TV? _____

SE NÃO: De Deus, ou do Diabo?: _____

SE NÃO: O que é que ouve? _____

Ouve-as tão bem e tão alto como a minha voz? _____

Com que frequência ouve essas vozes (barulhos, mensagens, etc.)? _____

Isso acontece numa altura particular do dia, ou durante todo o tempo? _____

SE OUVE VOZES: Reconhece de quem são as vozes? _____

O que dizem as vozes? _____

As vozes são boas, ou más? _____

Agradáveis, ou desagradáveis? _____

As vozes interrompem o seu pensamento, ou os seus afazeres? _____

Elas por vezes dão-lhe ordens, ou instruções? _____

SE SIM: Por exemplo? _____

Costuma obedecer a essas ordens (instruções)? _____

O que faz com essas vozes (ou ruídos): donde vêm elas, de facto? _____

Porque é que tem essas sensações? _____

São sensações normais? _____

Às vezes as coisas vulgares parecem-lhe ter um ar estranho ou distorcido? _____

Tem por vezes "visões", ou vê coisas que os outros não conseguem ver? _____

SE SIM: Por exemplo? _____

Essas visões parecem muito reais, ou ao vivo? _____

Com que frequência tem essas experiências? _____

Sente por vezes cheiros que são invulgares, ou que os outros não sentem? _____

SE SIM: Por favor explique. _____

Tem sensações estranhas ou pouco usuais, vindas de dentro do seu corpo? _____

SE SIM: Fale-me disso. _____

Dados de "Âmbito Somático" (GI)

Como se tem sentido em termos de saúde? _____

SE NÃO RESPONDEU "BEM": O quê que o tem incomodado? _____

SE RESPONDEU "BEM": Acha que está de perfeita saúde? _____

SE RESPONDEU "NÃO": O que o tem importunado? _____

Tem algum problema médico, ou doença? _____

Alguma parte do seu corpo o tem incomodado? _____

SE NÃO: Como está a sua cabeça? O seu coração? Estômago? O resto do seu organismo? _____

SE SIM: Pode explicar? _____

Houve mudança da forma ou do tamanho da sua cabeça, ou do seu corpo ? _____

SE SIM: Por favor explique. _____

O que originou estas mudanças? _____

Dados sobre "Depressão" (G6)

Como esteve a sua disposição na semana passada: em geral bem, em geral mal? _____

SE "EM GERAL BEM": Houve, na semana passada, alturas em que se tenha sentido triste, ou infeliz? _____ SE SIM, PASSE À PERGUNTA SEGUINTE:

SE "EM GERAL MAL": Há algo em particular que o entristeça? _____

Quantas vezes se sente triste? _____

Qual tem sido a intensidade dessa tristeza ? _____

Tem chorado ultimamente? _____

O seu sono tem sido de alguma forma afectado pelo seu estado de humor? _____

O seu apetite foi afectado por isso? _____

Tem participado menos em actividades por causa do seu humor? _____

Tem tido por vezes ideias de fazer mal a si próprio? _____

SE SIM: Algumas ideias em acabar com a sua vida? _____

SE SIM: Tentou suicidar-se? _____

Dados sobre "Sentimentos de culpa" (G3) e Grandiosidade (PS)

Se tivesse que se comparar a uma pessoa dita normal, como é que se acharia: um pouco melhor, talvez um pouco pior, ou semelhante? _____

SE PIOR: Pior em que aspectos? _____

Como se sente, exactamente, em relação a si próprio? _____

SE MELHOR: Melhor em que aspectos? _____

SE SEMELHANTE: Acha-se especial nalguns aspectos? _____

SE SIM: Em que aspectos? _____

Considerar-se-ia a si próprio dotado? _____

Tem talentos ou capacidades que a maioria das pessoas não têm? _____

SE SIM: Por favor explique. _____

Tem alguns poderes especiais? _____

SE SIM: Quais são? _____

De onde vêm esses poderes? _____

Tem percepções extrasensoriais (PES), ou consegue ler a mente de outras pessoas? _____

É muito saudável? _____

SE SIM: Por favor explique. _____

Acha que pode ser considerado muito esperto? _____

SE SIM: Porque é que acha isso? _____

Descrever-se-ia a si próprio como famoso? _____

Algumas pessoas reconhecê-lo-iam da TV, da rádio, ou dos jornais? _____

SE SIM: Pode-me falar disso? _____

É uma pessoa religiosa? _____

SE SIM: Está próximo de Deus? _____

SE SIM: Deus incumbiu-o de algum papel, ou fim especial,? _____

Pode acontecer que seja um dos mensageiros, ou anjos de Deus? _____

SE SIM: Como mensageiro (anjo) de Deus, que poderes especiais tem? _____

Considera-se, talvez, a si próprio como sendo Deus? _____

Tem alguma missão especial na vida? _____

SE SIM: Qual é a sua missão? _____

Quem o designou para essa missão? _____

Alguma vez fez algo errado - algo sobre o que se sinta mal, ou culpado? _____

SE SIM: Exactamente até que ponto isso o incomoda agora ? _____

Acha que merece ser castigado por isso? _____

SE SIM: Que tipo de castigo acha que merece? _____

Já tem pensado em se castigar a si próprio? _____

SE SIM: Já alguma vez agiu de acordo com esses pensamentos de se auto-punir? _____

Dados sobre "Desorientação" (GlO)

Pode-me dizer a data de hoje (i.e., o dia, mês, e ano)? _____

Qual é o nome do sítio onde estamos agora? _____

(Se estiver hospitalizado) Em que enfermaria está? _____

Qual é a morada do local onde está agora? _____

Se alguém precisar de lhe telefonar, para que número deve essa pessoa ligar? _____

Qual é o nome do médico que o está a tratar? _____

(Se estiver hospitalizado) Pode-me dizer que pessoas há mais na equipa, e o que fazem? _____

Sabe quem é actual Presidente da República? _____

Quem é o nosso Primeiro Ministro? _____

Quem é o Presidente da Câmara desta cidade? _____

Dados sobre "Dificuldade com o Pensamento Abstracto" (N5)

Vou agora dizer umas quantas palavras, e gostaria que me dissesse em que medida elas são importantes. Vamos começar, por exemplo, com as palavras "maçã" e "banana." O que lhe fazem lembrar – o que é que têm em comum?

SE RESPONDER "SÃO AMBAS UM FRUTO": Bem. E agora destas...?
(Seleccione outros três items da lista "Semelhanças", do Apêndice A. com níveis variados de dificuldade)

SE É DADA UMA RESPOSTA QUE É CONCRETA, TANGENCIAL, OU IDIOSSINCRÁTICA, COMO P. EX.: "AMBAS TÊM CASCA," "SÃO AMBAS PARA COMER," "SÃO PEQUENAS" OU "OS MACACOS GOSTAM DELAS": Está bem, mas ambas são fruta. Agora o que se passa com ... e ... : o que parecem estas?
(Escolha outros três items da lista "Semelhanças", do Apêndice A com vários níveis de dificuldade)

APÊNDICE A

Items para semelhanças na avaliação de "Dificuldades com o pensamento abstracto"

1. O que têm de comum uma bola e uma laranja?
2. Maçã e banana ?
3. Lápis e caneta?
4. Um tostão e dez tostões?

5. Mesa e cadeira?
6. Tigre e elefante?
7. Chapéu e camisola?
8. Autocarro e combóio?

9. Braço e perna?
10. Rosa e tulipa?
11. Tio and primo?
12. O Sol e a Lua?

13. Pintura e poema?
14. Topo da montanha e vale?

Nota ao Apêndice A: As semelhanças são em regra avaliadas, seleccionando quatro items com diferentes níveis de dificuldade (i.e., seleccionando um item de cada quarteto do conjunto). Ao usar a PANSS longitudinalmente, os items devem ser sistematicamente alterados, com sucessivas entrevistas, de modo a fornecer selecções diferentes dos vários níveis de dificuldade, minimizando assim a repetição.

Notas relativas às respostas sobre semelhanças:

_____

_____

_____

15. Ar e água?
16. Paz e prosperidade?

Faça um círculo em redor das semelhanças escolhidas.

Provavelmente já ouviu a expressão: "Quem não tem cão, caça com gato." O que quer isto de facto dizer? Há um dizer muito antigo: "A capa não faz o livro." Qual é o verdadeiro significado deste provérbio?

(Escolha mais outros dois provérbios da lista do Apêndice B, com vários níveis de dificuldade.)

APÊNDICE B

Items para a INTERPRETAÇÃO DE PROVÉRBIOS na avaliação de "Dificuldade com o Pensamento abstracto"

O que quer dizer:

1. "Seco que nem um carapau"
2. "Quem não tem cão, caça com gato"
3. "Mais vale sê-lo, do que parecê-lo"
4. "Quem corre por gosto não cansa"

5. "Quem vê caras não vê corações"
6. "Quem tudo quer, tudo perde"
7. "Nem tudo o que luz é ouro"
8. "Mais vale prevenir do que remediar.

9. "Depois da tempestade vem a bonança"
10. "A galinha da minha vizinha é sempre melhor do que a minha"
11. "Mais vale um pássaro na mão do que dois a voar"
12. "Uma andorinha não faz a Primavera"

13. "Candeia que vai à frente alumia duas vezes"
14. "Água mole em pedra dura tanto dá até que fura"
15. "Em tempo de guerra não se limpam armas"
16. "Quem tem telhados de vidro não atira pedras ao do vizinho"

Nota ao Apêndice B: A interpretação dos provérbios é geralmente avaliada pela selecção de quatro items a níveis diferentes de dificuldade (p.ex., um item seleccionado de cada quarteto do conjunto completo). Ao usar a PANSS longitudinalmente, os items devem ser sistematicamente alterados nas entrevistas sucessivas, de modo a fornecer diferentes selecções dos vários níveis de dificuldade, minimizando assim a repetição.

Notas às respostas aos provérbios:

Faça um círculo em volta dos provérbios escolhidos..

Dados sobre "Falta de Senso Crítico e de Insight" (G12)

Há quanto tempo está internado ?

Porque veio para o hospital (clínica, etc.)?

Precisava de estar internado ?

SE NÃO: Tinha algum problema que necessitava tratamento?

SE SIM: Acha que tinha um problema psiquiátrico ou mental?

SE SIM: Porquê?...que acha que tinha um problema psiquiátrico ou mental?

SE SIM: Em quê que isso consiste? Pode-me falar disso? _____

SE SIM: Em sua opinião precisaria de tomar medicamentos? _____

SE NÃO:

(Se está medicado:) Porque está então a tomar medicamentos? _____

(Se não está medicado:) Porque está ainda internado? _____

SE SIM: Porquê?... Os medicamentos ajudam-no? _____

Nesta altura tem alguns problemas psiquiátricos ou mentais? _____

SE NÃO: Porque razão está ainda internado? _____

SE SIM: Explique, por favor. _____

Até que ponto é que esses problemas são graves? _____

(Se está hospitalizado:)

Está pronto para ter alta? _____

Pensa que vai continuar a tomar medicamentos depois de ter alta ? _____

Quais são os seus planos para o futuro? _____

Quais são os seus objectivos mais significativos? _____

Bom, isto é tudo o que tinha para lhe perguntar. Tem alguma pergunta que gostasse de me fazer?
Muito obrigado pela sua colaboração.

PANSS

1) Subescala positiva

P1	Delírios	1.....2.....3.....4.....5.....6.....7
P2	Desorganização conceptual	1.....2.....3.....4.....5.....6.....7
P3	Comportamento alucinatório	1.....2.....3.....4.....5.....6.....7
P4	Excitação	1.....2.....3.....4.....5.....6.....7
P5	Grandiosidade	1.....2.....3.....4.....5.....6.....7
P6	Desconfiança / Perseguição	1.....2.....3.....4.....5.....6.....7
P7	Hostilidade	1.....2.....3.....4.....5.....6.....7

Subtotal ☐☐

2) Subescala negativa

N1	Embotamento afectivo	1.....2.....3.....4.....5.....6.....7
N2	Isolamento afectivo	1.....2.....3.....4.....5.....6.....7
N3	Contacto pobre	1.....2.....3.....4.....5.....6.....7
N4	Isolamento social passivo/apático	1.....2.....3.....4.....5.....6.....7
N5	Dificuldades com o pensamento abstracto	1.....2.....3.....4.....5.....6.....7
N6	Ausência de espontaneidade e de fluxo na conversa	1.....2.....3.....4.....5.....6.....7
N7	Pensamento estereotipado	1.....2.....3.....4.....5.....6.....7

Subtotal ☐☐

3) Subescala de psicopatologia geral

G1	Implicações psicossomáticas	1.....2.....3.....4.....5.....6.....7
G2	Ansiedade	1.....2.....3.....4.....5.....6.....7
G3	Sentimentos de culpa	1.....2.....3.....4.....5.....6.....7
G4	Tensão	1.....2.....3.....4.....5.....6.....7
G5	Maneirismos e postura	1.....2.....3.....4.....5.....6.....7
G6	Depressão	1.....2.....3.....4.....5.....6.....7
G7	Lentificação motora	1.....2.....3.....4.....5.....6.....7
G8	Não cooperação	1.....2.....3.....4.....5.....6.....7
G9	Conteúdo invulgar do pensamento	1.....2.....3.....4.....5.....6.....7
G10	Desorientação	1.....2.....3.....4.....5.....6.....7
G11	Atenção reduzida	1.....2.....3.....4.....5.....6.....7
G12	Ausência de juízo e de "insight"	1.....2.....3.....4.....5.....6.....7
G13	Perturbação da vontade	1.....2.....3.....4.....5.....6.....7
G14	Controlo deficientes dos impulsos	1.....2.....3.....4.....5.....6.....7
G15	Preocupação	1.....2.....3.....4.....5.....6.....7
G16	Evicção social activa	1.....2.....3.....4.....5.....6.....7

Subtotal ☐☐☐

Score total ☐☐☐

Appendix E: Visual Scale

0 1 2 3 4 5 6 7 8 9

Menos Desagradável

Mais Desagradável

Appendix F: Sound list of Newcastle Battery of Unpleasant Sounds

		0= least unpleasant	1	2	3	4	5	6	7	8	9= most unpleasant			0= least unpleasant	1	2	3	4	5	6	7	8	9= most unpleasant
1	Angle_grind1	0	1	2	3	4	5	6	7	8	9	39	Fork_glass_4	0	1	2	3	4	5	6	7	8	9
2	Angle_grind_2	0	1	2	3	4	5	6	7	8	9	40	Frog1	0	1	2	3	4	5	6	7	8	9
3	Anteater	0	1	2	3	4	5	6	7	8	9	41	Glassbreaking	0	1	2	3	4	5	6	7	8	9
4	Applause	0	1	2	3	4	5	6	7	8	9	42	Gorilla	0	1	2	3	4	5	6	7	8	9
5	Baby cry	0	1	2	3	4	5	6	7	8	9	43	Guitar_1	0	1	2	3	4	5	6	7	8	9
6	Baby laugh	0	1	2	3	4	5	6	7	8	9	44	Guitar_2	0	1	2	3	4	5	6	7	8	9
7	Bear2	0	1	2	3	4	5	6	7	8	9	45	Hippo	0	1	2	3	4	5	6	7	8	9
8	Blackboard_chalk_1	0	1	2	3	4	5	6	7	8	9	46	Howlin_wolf	0	1	2	3	4	5	6	7	8	9
9	Blackboard_chalk_2	0	1	2	3	4	5	6	7	8	9	47	Junglebird2	0	1	2	3	4	5	6	7	8	9
10	Blackboard_nails_1	0	1	2	3	4	5	6	7	8	9	48	Knife_bottle_1	0	1	2	3	4	5	6	7	8	9
11	Blackboard_nails_2	0	1	2	3	4	5	6	7	8	9	49	Lamb	0	1	2	3	4	5	6	7	8	9
12	Brake_double	0	1	2	3	4	5	6	7	8	9	50	Leopard1	0	1	2	3	4	5	6	7	8	9
13	Bubblingwater	0	1	2	3	4	5	6	7	8	9	51	Lion2	0	1	2	3	4	5	6	7	8	9
14	Bull frog	0	1	2	3	4	5	6	7	8	9	52	Lioncub	0	1	2	3	4	5	6	7	8	9
15	Buzzer	0	1	2	3	4	5	6	7	8	9	53	Macaca	0	1	2	3	4	5	6	7	8	9
16	Camel	0	1	2	3	4	5	6	7	8	9	54	Mixer_glass_1	0	1	2	3	4	5	6	7	8	9
17	Cat_screaming	0	1	2	3	4	5	6	7	8	9	55	Multiple_babies	0	1	2	3	4	5	6	7	8	9
18	Catpurr2	0	1	2	3	4	5	6	7	8	9	56	Panther	0	1	2	3	4	5	6	7	8	9
19	Clarinet_honk	0	1	2	3	4	5	6	7	8	9	57	Phone_ringing	0	1	2	3	4	5	6	7	8	9
20	Clarinet_squeak	0	1	2	3	4	5	6	7	8	9	58	Pig_	0	1	2	3	4	5	6	7	8	9
21	Cougar	0	1	2	3	4	5	6	7	8	9	59	Puffer	0	1	2	3	4	5	6	7	8	9
22	Doggrowl	0	1	2	3	4	5	6	7	8	9	60	Record_scratch_1	0	1	2	3	4	5	6	7	8	9
23	Dolphinclicks	0	1	2	3	4	5	6	7	8	9	61	Reving_Engine	0	1	2	3	4	5	6	7	8	9
24	Domesticcat	0	1	2	3	4	5	6	7	8	9	62	Ruler_bottle_1	0	1	2	3	4	5	6	7	8	9
25	Eagle2	0	1	2	3	4	5	6	7	8	9	63	Ruler_bottle_2	0	1	2	3	4	5	6	7	8	9
26	Electric_drill_2	0	1	2	3	4	5	6	7	8	9	64	Running water_short	0	1	2	3	4	5	6	7	8	9
27	Electric_drill	0	1	2	3	4	5	6	7	8	9	65	Smallwaterfall	0	1	2	3	4	5	6	7	8	9
28	Elephant	0	1	2	3	4	5	6	7	8	9	66	Spade_drag_1	0	1	2	3	4	5	6	7	8	9
29	Falcon	0	1	2	3	4	5	6	7	8	9	67	Spade_drag_2	0	1	2	3	4	5	6	7	8	9
30	Femalescream_2	0	1	2	3	4	5	6	7	8	9	68	Spade_drop_1	0	1	2	3	4	5	6	7	8	9
31	Femalescream	0	1	2	3	4	5	6	7	8	9	69	Thunder1	0	1	2	3	4	5	6	7	8	9
32	Film_projector	0	1	2	3	4	5	6	7	8	9	70	Thunder2_	0	1	2	3	4	5	6	7	8	9
33	Firealarm	0	1	2	3	4	5	6	7	8	9	71	Tire_skids	0	1	2	3	4	5	6	7	8	9
34	Fork_bottle_1	0	1	2	3	4	5	6	7	8	9	72	Violin	0	1	2	3	4	5	6	7	8	9
35	Fork_bottle_3	0	1	2	3	4	5	6	7	8	9	73	Wasp_1	0	1	2	3	4	5	6	7	8	9
36	Fork_bottle_4	0	1	2	3	4	5	6	7	8	9	74	Waterflow	0	1	2	3	4	5	6	7	8	9
37	Fork_glass_1	0	1	2	3	4	5	6	7	8	9	75	Zeb	0	1	2	3	4	5	6	7	8	9
38	Fork_glass_3	0	1	2	3	4	5	6	7	8	9												

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