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EDITORIAL

Joker in real life

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The practice of medicine combines art and science, and those of us who enjoy the privilege of being medical professionals are rewarded with both professional and altruistic satisfaction in tending to the society we serve.

Many physicians share a passion for cinema and through this art, we try not only to distract our minds after bearing the great responsibilities our profession entails, but also, to learn from the characters that are presented in a film, whether reality or fiction.

Joker is undeniably an exceptional film, although the city, the characters, and the situation presented situation are totally fictitious, we cannot help but relate the film to what we are currently facing in our world today.

From the moment that the film begins, the main character reacts with laughter to the overwhelming social pressure, in which aggression, the lack of respect for the individual, bullying, mockery, and the enjoyment of others suffering, appear as social characteristics of a sick community. As medical doctors, we can recognize pathological characteristics in the main character, whom to justify his unreasonable, irrational, and uncontrollable laughter, displays a simple card with a warning that he suffers from a neurological problem that produces his spontaneous hilarity.

The explanation presented is that the main character suffers a history of severe cranial trauma with altered consciousness that had a permanent effect, leaving the Joker with a disorder of inappropriate response which manifests as laughter.

Bilateral frontal damage can affect the bilateral corticonuclear system, causing the so-called pseudobulbar syndrome or loss of continence of emotions syndrome. Those who suffer from this syndrome can present a laugh or cry that is excessive and totally out of place, although it is difficult to believe that the person who suffers damage from the corticonuclear pathway (which regulates the motor nuclei of the brain stem, cranial nerves: III, IV, V, VI, VII, IX, X, XI, and XII) does not concomitantly suffer damage the corticospinal pathways. In the case of the Joker, in a manner uncharacteristic for such a brain-damaged patient, the character manages to dance down some stairs with enviable balance while wearing huge clown shoes.

In our professional practice, we had the honor of caring for a 35-year-old patient with Behcet's disease who presented these characteristics and that, during the development of his illness, suffered the loss of his 12-year-old daughter. At the funeral, our patient started laughing so uncontrollably and excessively that he decided to leave the funeral to avoid the judging eyes of those present who did not understand his laugh as a symptom of his condition in such an unfortunate scene.

Neurological involvement is a rare manifestation; it is one of the most serious causes of long-term morbidity, commonly associated to parenchymal affectation[1-3].

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Fiction intertwined with reality and sometimes confusion overcomes us when our brain is injured and we are suffering from an inflammatory process as seemingly irrelevant as a simple urinary infection (often delirium is associated with this combination).

The reality of our patient produces both pathos and hope that humanity still exists in the face of societal violence. Our patient's reaction, unlike that of the Joker's, expresses his consciousness of his inappropriate behavior. Certainly, the actors, film directors, and the extras that cooperated to make Joker passionately lived each scene of such a great work of art. However, nothing compares to the physician's privilege of living our day-to-day interactions with both science and the art of medicine.

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ORIGINAL ARTICLE

Attention deficit disorder, comorbidity, and treatment at the Hospital Psiquiátrico Infantil Dr. Juan N. Navarro, Mexico City

Juan C. Reséndiz-Aparicio[1], María del P. Poza-y Díaz[2], Esmeralda Arriaga-Cruz[2], Inés A. Nogales-Imaca[2], Dalia M. Becerra-Alcántara[2], Ernesto Rodríguez-Rodríguez[1], and Michel Gutiérrez-Ceniceros[1]*

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Abstract

Background: *Attention deficit hyperactivity disorder (ADHD) is the main motive for consultation at the Hospital Psiquiátrico Infantil.* **Materials and methods:** *Prospective study analyzing patients with ADHD for 2 months.* **Results:** *Recruited 555 patients, average age 8.7 (± 1.66) years, 485 (87.4%) males and 70 (12.6%) females. The most frequent subtype was combined in 440 (79.3%). We observed high comorbidity (68.1%), with externalizing disorders 143 (25.8%) patients and internalizing disorders 136 (24.5%). Epilepsy was found in eight patients. The most commonly used medications were methylphenidate for 485 cases (87.4%), followed by risperidone 45 (8.1%), fluoxetine 32 (5.8%), and without drug treatment 31 (5.6%). Mood stabilizers in 102 patients (18.4%), 32% received more than one drug. The most frequent combinations were methylphenidate with valproate, methylphenidate with risperidone, and methylphenidate with fluoxetine.* **Conclusions:** *Males attend more frequently, and the most frequent subtype is combined. Comorbidity presented in almost 70%, most predominantly with the oppositional defiant disorder. Methylphenidate is the most commonly used drug in monotherapy or in combination.*

Key words: *Attention deficit hyperactivity disorder. Comorbidity. Treatment. Methylphenidate.*

Trastorno por déficit de atención, comorbilidad y tratamiento en el Hospital Psiquiátrico Infantil Dr Juan N. Navarro, Ciudad de México

Resumen

Antecedentes: *TDAH es el principal motivo de consulta en el Hospital Psiquiátrico Infantil.* **Métodos:** *Analizamos pacientes con TDAH (DSM-5), durante dos meses.* **Resultados:** *Reclutamos 555 pacientes, edad promedio de 8.7 (± 1.66) años, varones 485 (87.4%) y mujeres 70 (12.6%). El subtipo más frecuente, combinado 440 pacientes (79.3%). Observamos alta comorbilidad (68.1%), los trastornos externalizados en 143 pacientes (25.8%) y los internalizados 136 (24.5%). Epilepsia se encontró en 8 pacientes. Medicamento más empleado metilfenidato en 485 (87.4%), después risperidona 45 (8.1%), fluoxetina 32 (5.8%), sin tratamiento farmacológico 31 (5.6%). Modulador del afecto 102 pacientes (18.4%). El 32% recibían más de un fármaco. Combinaciones más frecuentes metilfenidato con valproato, metilfenidato con risperidona y metilfenidato con*

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fluoxetina. **Conclusiones:** *Los varones acuden con mayor frecuencia, el subtipo más frecuente fue combinado. La comorbilidad ocupó casi el 70%, predominando el trastorno oposicionista desafiante. Metilfenidato es el fármaco de mayor uso en monoterapia o en combinación.*

Palabras clave: *TDAH. Comorbilidad. Tratamiento. Metilfenidato.*

Introduction

Attention deficit hyperactivity disorder (ADHD) is the neurodevelopmental disorder of greatest prevalence worldwide. It is estimated to affect 5-7% of children and adolescents, and about 3% of the adult population[1,2].

Polanczyk et al. reviewed 154 studies that utilized the DSM-5 classification, like ICD-10, in patients 18 years old or younger, concluding that the global prevalence is 5%. In addition, they concluded that the variations in prevalence observed in various studies could be attributed to different methods and statistics employed[3].

In our setting, ADHD is considered to be the number one reason to seek attention in the psychiatric service. At the Hospital Psiquiátrico Infantil Dr. Juan N. Navarro (Children's Psychiatric Hospital Dr. Juan N. Navarro), according to statistics from 2016, the incidence reported was 1.3 new cases per day, with 476 new cases per year. This adds up to 19.1% of the global demand for said institution, as registered in the update of the clinical guides for ADHD of this institution in 2018. It is also considered to be the neurodevelopmental disorder of greatest prevalence in the pediatric neurology service[4].

In the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association), the prevalence is considered to be between 3 and 5%. However, these numbers vary depending on the population studied, the methods used and the inclusion criteria required. Recently, a higher prevalence has been observed, reaching up to 17.1%[5,6].

There are still no conclusive biological markers specific for ADHD. However, recent studies have revealed the participation of a group of 105 genes that show statistical significance for their association with ADHD[7]. The clinical variations are established in function of the symptomatic dominance of hyperactivity-impulsiveness, inattentiveness, or both[8,9].

The concept of concomitant morbidity was coined in the context of chronic diseases to refer to any new clinical entity in addition to the existing one and was quickly adopted to describe the coexistence of two or more mental disorders[9]. Studies in child and adolescent psychopathologies have shown that concomitant morbidity frequently constitutes the rule and that there is an average of 2.5 coexisting psychiatric diagnoses, in clinics treating Mexican adolescents[10].

The existence of comorbid disorders associated with ADHD constitutes an essential determiner in its evolution and prognosis[11], and even in its therapeutic algorithm. Recent data indicate that over half of the people diagnosed with ADHD fulfill the criteria for one or more additional neuropsychiatric disorders[12].

Epidemiological research shows high comorbidity of ADHD with externalizing disorders, such as conduct disorder (CD), oppositional defiant disorder (ODD), or both, as well as with internalizing disorders, especially major depressive disorder and anxiety disorder, as well as dysthymic disorder and bipolar disorder. There are a number of studies that emphasize the direct impact of said comorbidities on poor academic abilities, which in turn are prognostic and risk factors for internalizing disorders[13].

In CD, there are reiterated aggressive and criminal conducts that violate the basic rights of other people or important social rules. Half of the patients with ADHD can be associated with an ODD or CD[14].

Various studies agree that around 30% of the children with ADHD also have an associated affective disorder (major depression, bipolar disorder, or dysthymic disorder). Bipolar disorder is a disease that presents more commonly than had been thought in pediatrics[15].

There does not seem to be a specific pattern of association between the different subtypes of anxiety disorders and the different subtypes of ADHD[16]. Studies indicate that the clinical factors that better predict the chronicity of these diseases in children are: concomitant morbidity, being female, and presenting at an older age during childhood[17].

Another important group of comorbidities includes learning disorders, where we find that the rates of the association are estimated to be that one in every four children with ADHD has a learning disorder[18].

These symptoms are exponential in the context of a patient with ADHD and it is estimated that there is a correlation between them of 11-52%, according to different studies. Together, they tend to worsen academic performance, which can affect emotional well-being and determine future professional performance[19,20].

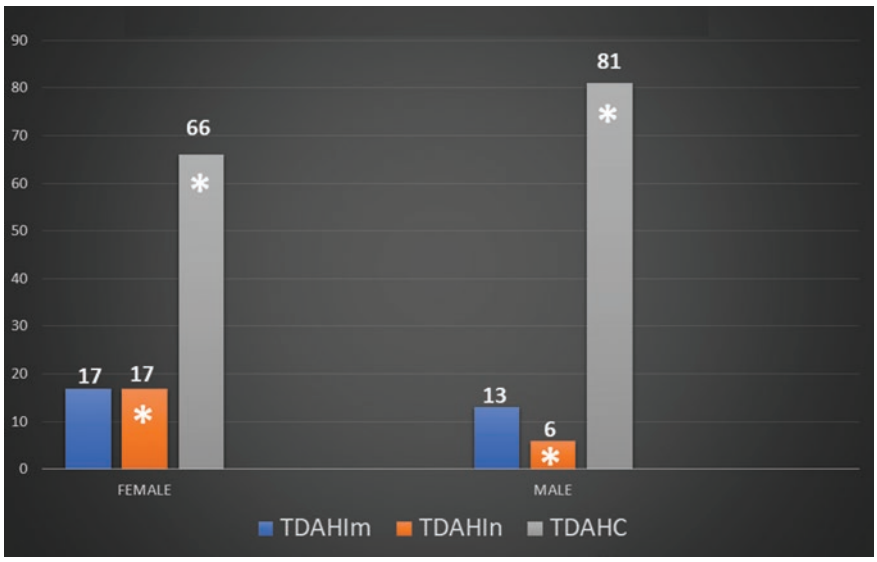

Figure 1. Distribution by gender and attention deficit hyperactivity disorder (ADHD) subtype.
*Significant difference ($p > 0.05$). ADHDImp subtype: predominantly hyperactive-impulsive; ADHDIn subtype: predominantly inattentive; ADHDC subtype: combined.

Children with ADHD may have an increased risk of presenting epileptic seizures. It is estimated that around 15% can develop epilepsy. Diverse studies suggest that 30-40% of children with epilepsy present ADHD, in contrast to 7-9% in the general population[21,22]. However, epilepsy does not constitute, *per se*, a contraindication for treatment of ADHD, including the use of stimulants. Methylphenidate is effective for the majority of children and adolescents with ADHD and comorbid epilepsy, without an increase in the risk of seizures[23].

Methylphenidate is the most commonly used medication for the treatment of ADHD, and currently, shows better tolerance since the introduction of extended-release presentations[24]. Atomoxetine is used as first-line therapy for ADHD and is particularly useful when the patient has comorbidity with tics, anxiety, or depressive symptoms[25].

Among the atypical antipsychotics, risperidone is considered the drug of choice for the pharmacologic treatment of aggressive behavior associated with ADHD, in the case of comorbidity with CD, as well as with tics and Tourette syndrome[26].

There are also non-neuropsychiatric comorbidities associated with ADHD, as demonstrated in a number of European studies that have described an increase in the risk of developing metabolic and cardiovascular diseases such as diabetes, obesity, and hypertension, with a subsequent risk of disease from renal failure, among others[27].

The objective of this study is to identify the main comorbidities of ADHD and the treatments implemented since this condition is within the main causes of consultation in our institution. This is a report of local experience in an institution dedicated to child psychiatry and neurodevelopmental neurology.

Materials and methods

We carried out a prospective 2-month study on patients that regularly attend the clinics that treat school-age patients at the Hospital Psiquiátrico Infantil Dr. Juan N. Navarro in Mexico City with the main diagnosis of attention deficit disorder based on DSM-5. For the purpose of this article, we abbreviate attention deficit disorder as ADHD, the predominantly inattentive subtype as ADHDIn, the predominantly hyperactive-impulsive subtype as ADHDImp, and finally, the combined or mixed subtype as ADHDC. For the analysis of results, we divided the age groups between pre-school children (4-6 years old), schoolchildren from 7 to 11 years old, pre-adolescents (12 and 13 years old), and adolescents from 14 to 18 years old. We created a database that contained age, gender, hospital registration number, attention deficit disorder subtype,

electroencephalogram (EEG) results, family history of epilepsy, treatment used, and finally, whether there are any comorbid disorders and what these were according to DSM-5. We excluded children with clinical evidence of mental retardation, and when there was clinical doubt, we reviewed the intellectual capacity test (WISC-IV) results from the medical records. If the test was missing, it was administered before including the patient in the database. During the 2 months of the study, from Monday to Friday, the patient's data were given to the doctors in the outpatient service that attended school-age patients between 6 and 12. Later, patients ages 4 and 5 who attended these clinics were added to the database, as well as one patient who turned 13 on the day of his appointment.

Results

A total of 555 patients between the ages of 4 and 13 were recruited, with the average age being 8.7 ± 1.6 years, predominantly male, with 485 boys (87.4%) and 70 females (12.6%). The most frequent subtype of ADHD was the mixed or combined attention deficit disorder, with 440 patients, representing 79.3% of the sample and a significant predominance of males. This was followed by the predominantly hyperactive-impulsive subtype in 74 patients (13.3%) and the inattentive subtype in 41 patients (7.4%), for which there was a significant difference in favor of females being 17% female versus 6% male (Fig. 1). When dividing the patients by age group, we found that the preschoolers (4-6 years old) and the pre-adolescents (12-13 years old) were the minority, while the most frequent where the school-age children, that is, between 7 and 11 years old. When differentiating the population by age, gender, and subtype (Table 1), we observe that, in general, the males are being attended and diagnosed at the Hospital at a younger age with respect to the females.

In terms of clinical doubt of intellectual capacity, only five intelligence tests were required, which resulted in total scores above 95 points, normal for the patients, and without significant interscalar differences.

We found a positive medical history of epilepsy in 43 patients, representing 7.7%. EEGs were not carried out for 55.8% of the patients, which is 310 children when the attending physician did not believe them necessary. For the remaining 245 patients, the results from this study are normal for 112 cases (20.2%), while 133 patients (24%) showed abnormal findings, only for data from slowing, unstructured background rhythms and other non-specific abnormalities, with the exception of some patients that presented with some form of comorbid epilepsy.

A total of 378 patients (68.1%) presented comorbidities. Of these, 312 had only one comorbidity, 51 patients had

Table 1. Distribution by age group, gender, and ADHD subtype

	Male	Female
Preschool (4-6 years)		
ADHDImp	5	2
ADHDIn	1	0
ADHDC	27	7
Total	33	9
School-age (7-11 years)		
ADHDImp	56	10
ADHDIn	25	10
ADHDC	348	36
Total	429	56
Adolescents (12-13 years)		
ADHDImp	1	0
ADHDIn	3	2
ADHDC	19	3
Total	23	5

ADHDImp subtype: predominantly hyperactive-impulsive; ADHDIn subtype: predominantly inattentive; ADHDC subtype: combined.

Table 2. Comorbidity of internalizing and externalizing disorder, according to DSM

	Number of patients	Percentage
Depressive dis. (grouped)		
Mild depression	8	1.4
Moderate depression	26	4.7
Severe depression	1	0.2
Recurrent depression	8	1.4
Dysthymia	14	2.5
Total	57	10.2
Bipolar dis. (5/7 with ADHD)		
Total	7	1.3
Anxiety dis. (grouped)		
Anxiety dis.	4	0.7
Generalized anxiety dis.	29	5.2
Mixed anxiety-depressive dis.	15	2.7
Unspecified anxiety dis.	13	2.3
Obsessive compulsive dis.	2	0.3
Post-traumatic stress	2	0.3
Total	65	11.7
Mixed adjustment dis.		
Total	7	1.3
Total internalizing dis.	136	24.5
Conduct dis.	20	3.6
Oppositional defiant dis.	123	22.2
Total externalizing dis.	143	25.8

Dis.: disorder.

Table 3. Comorbidities according to DSM-5

	Number of patients	Percentage
Learning dis.		
Dyslexia	21	3.8
Dyscalculia	1	0.2
Dysgraphia	2	0.3
Mixed learning dis.	49	8.8
Total	73	13.6
Elimination dis.		
Enuresis	21	3.8
Encopresis	13	2.3
Total	34	6.1
Inadequate family support		
Total	33	5.9
Communication dis.		
Total	15	2.7
Epilepsy		
Total	8	1.4
Asperger syndrome		
Total	5	0-9
Separation anxiety		
Total	4	0.7
Headaches		
Total	3	0.5
Sexual abuse		
Total	2	0.3
Chronic motor tic dis.		
Total	1	0.2
Total comorbidity	378	68.1
Without comorbidity	177	31.9

Dis.: disorder. The number of patients with at least one comorbidity reached almost 70% of the sample population.

Table 4. Pharmacological treatment used for ADHD management

Medication*	Number of patients	Percentage
Methylphenidate	485	87.4
Risperidone	45	8.1
Fluoxetine	32	5.8
Sertraline	24	4.3
Atomoxetine	22	4.0
Valproate	6	1.1
Imipramine	5	0.9
Paroxetine	1	0.2
Haloperidol	1	0.2
Imipramine	1	0.2
No treatment	31	5.6

*Some patients took more than one of these medications.

Table 5. Antiepileptic drugs used as mood or impulse stabilizers

Medication	Number of patients
Valproate	66
Carbamazepine	19
Oxcarbazepine	4
Topiramate	2
Lamotrigine	1
Levetiracetam	1
Phenytoin	1
Total	102 (18.4%)

two, three were found in 12 patients, and three patients presented four comorbidities associated with ADHD. In this population, and in agreement with DSM-5, we found internalizing disorders in 136 patients (24.5%): depressive disorders in 57 (10.3%), bipolar disorder in 7 (1.3%), anxiety disorder 65 (11.7%), and adjustment disorders with mixed anxiety-depression in 3 (1.3%) (Table 2). Comorbid externalizing disorders expressed as CDs found in 20 individuals (3.6%) and ODD in 123 (22.2%), representing 25.8% (143), affected patients.

Other frequent comorbid disorders were learning disorders found in a total of 73 patients (13.6%), elimination disorders in 34 (6.1%), and communication disorders in 15 (2.7%). The remaining comorbidities are shown in table 3. We observed that only eight patients, representing 1.4% of the sample, were found to have comorbid epilepsy with ADHD, of which seven were diagnosed before 4 years of age. Etiology was unknown in four cases and was structural in four cases. Focal epilepsy was found in six of the eight patients, three initiating in the frontal lobe and three in the temporal lobe.

An interesting finding was that five of the seven patients presenting bipolar disorder where of the ADHDImp subtype (hyperactive-impulsive).

The medications used were justified based on the results obtained from the comorbidity detected in these patients with attention deficit disorder. The most common medication employed was methylphenidate, in 485 patients (87.4%), followed by risperidone for

Table 6. Drug combinations: breakdown of combination therapy

Medication	Patients	Percentage
Two drugs	161	29
Three drugs	17	3
Total	178	32
MPH + VPA	37	6.7
MPH + RIS	28	5.0
MPH + FLX	26	4.7
MPH + SER	21	3.8
MPH + CBZ	18	3.2
RIS + VPA	16	2.9
MPH + OXC	4	0.7
MPH + IMI	3	0.5
ATX + VPA	2	0.4
ATX + RIS	2	0.4
MPH + LTG	1	0.2
MPH + LEV	1	0.2
MPH + PRX	1	0.2
MPH + ATX	1	0.2

MPH: methylphenidate; VPA: valproate; RIS: risperidone; FLX: fluoxetine; SER: sertraline; CBZ: carbamazepine; OXC: oxcarbazepine; IMI: imipramine; ATX: atomoxetine; LTG: lamotrigine; LEV: levetiracetam; PRX: paroxetine.

Table 7. Combination of three drugs

Medication	Number of patients	Percentage
MPH + VPA + RIS	7	1.3
MPH + RIS + FLX	2	0.4
RIS + VPA + ATX	2	0.4
MPH + RIS + TPM	2	0.4
ATX + FLX + VPA	1	0.2
MPH + VPA + SER	1	0.2
MPH + RIS + CBZ	1	0.2
MPH + FLX + PHT	1	0.2

MPH: methylphenidate; VPA: valproate; RIS: risperidone; FLX: fluoxetine; ATX: atomoxetine; TPM: topiramate; SER: sertraline; CBZ: carbamazepine; PHT: phenytoin.

45 (8.1%), fluoxetine for 32 (5.8%), sertraline 24 (4.3%), and atomoxetine 22 (4%), (Table 4), while 31 patients did not receive any pharmacologic treatment, representing 5.6% of the population studied. Antiepileptic drugs were used as a mood or impulse modulators in 102 patients (18.4%), valproate being the most common, as shown in table 5.

A total of 178 patients (32%) received more than one medication. A combination of two drugs was observed in 161 children (29%) and the use of three drugs in 17 (3%) cases. The three most frequent combinations were methylphenidate with valproate, methylphenidate with risperidone, and methylphenidate with fluoxetine, followed by other combinations, as shown in tables 6 and 7. Most (6 of 8) of the patients diagnosed with epilepsy and ADHD were treated with valproate and methylphenidate.

The most common association found was between ADHD and ODD (123 patients). The subtypes of attention deficit disorder in this group were ADHDImp in 14, ADHDIn in 2, and ADHDC in 107 patients. Most were treated with a combination of methylphenidate and risperidone or valproate.

Conclusions

Our institution receives a patient population of ADHD that is predominantly male. This is not surprising since, in general, it is well known that childhood psychopathologies are more frequent in this gender, especially when considering school-age patients, which were the focus of this study. Based on the DSM-5 criteria for subtype classification, we observed that almost 80% of these patients fulfilled the requirements for both inattentiveness and hyperactivity, thus being included in the combined or mixed subtype of ADHD. The literature indicates that the predominantly hyperactive-impulsive is more frequent in males, although we did not find a significant difference for this group. However, we did find a significant prevalence of the predominantly inattentive subtype for females, data that is consistent with the literature.

We consider that the EEG should not be used routinely, although we found unspecific abnormalities more frequently in patients with more comorbidities. This should be studied further to determine whether there is a real association. We consider that the EEG is not useful as a diagnostic, prognostic, or treatment factor, nor for pharmacologic decisions, as has been determined for other childhood psychiatric disorders[28].

Without a doubt, comorbidity in the patient with ADHD is a general rule, as evidenced in our study, since we found that 70% of the patients had at least one comorbidity and could present up to four comorbidities associated with ADHD. As expected, for patients with

a greater number of comorbidities, the treatment costs are increased[29]. Externalizing disorders were most frequently associated with ADHD, mainly represented by ODD, for which there is a genetic component but which becomes more evident when there is improper family management. Thus, it is difficult to establish what percentage of the symptoms correspond to genetic make-up and what part corresponds to family management or dynamics. However, it is known that these patients have more severe symptoms, greater social dysfunction, and a more deteriorated quality of life[30]. The comorbidities with internalizing disorders made up a quarter of the associations with ADHD, and the educational learning disorders presented in more than 13% of the population, which, added to the attention problem causes educational failure for these children. A vicious circle is frequently found in these cases, since when a child presents with ADHD and learning disabilities there is an educational failure which leads to frustration and could, on the one hand, lead to anxiety or mood problems or, on the other hand, to behavioral problems. The important part is to help them break this circle and convert it into a virtuous circle.

Although there is a study, cited in a number of publication, on a group of patients in Iceland[31], where the authors concluded that ADHD is associated with a greater risk of unprovoked seizures and must be considered as a risk factor for epilepsy, we did not find such a risk. Our study showed that the frequency of epilepsy in children with ADHD without an intellectual disability was similar to that of the general population in our country[32]. Thus, we consider that ADHD is not always a risk factor to present epilepsy. The type of epilepsy, the etiology, and the pharmacological management of this group of patients with ADHD and epilepsy were similar to that for patients with epilepsy and without ADHD in this age group.

The most used medication in our institution is methylphenidate, a first-line treatment for the treatment of ADHD in the Mexican algorithms and around the world. It is the drug of choice at our hospital due to the high rate of effectiveness, availability, and experience in its use. Another of the drugs, used as second-line treatment in various algorithms, is atomoxetine; however, this drug was used with lower frequency since the cost of the medication in our country was a factor, in some cases. Risperidone was used for an important number of cases for comorbidity management, especially to modulate impulsive and aggressive behavior, frequently observed in ODD, which predominated in our population. Selective serotonin reuptake inhibitors are used to treat comorbidities with mood disorders and anxiety which, as previously stated, were frequently associated with ADHD.

When analyzing the large numbers of associated comorbidities, we can understand the great amount of medications used. We have to consider that this hospital is a high specialty facility that concentrates these cases; thus, our patient sample is from a population with treatment difficulties. Ideally, every patient with ADHD should be approached in a multidisciplinary manner with the involvement of parents, teachers, psychologists, therapists, family counselors, social workers, and even society. In the case of requiring pharmacological management, this must be started with a single drug and only use a second when required due to the comorbidity and when the patient does not respond adequately.

An interesting observation was that, of the seven patients with comorbid bipolar disorder, five presented the hyperactive-impulsive subtype. This leads us to question whether there may be a superposition of symptoms in these patients, remembering that we have an obligation to detect the possibility of comorbidity in these cases or to carry out a differential diagnosis between the two entities since children with bipolar disorder are frequently rapid cyclers with high levels of irritability and have a chronic clinical evolution[33].

Study limitations

The results found are similar to those already reported in the world literature; however, they are of institutional relevance since they provide a situational diagnosis to establish diagnostic guides for our target population. A cross-sectional study will be considered in the future.

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The present investigation has not received any specific scholarship from the public, commercial, or non-profit agencies.

Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

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ORIGINAL ARTICLE

Electroencephalographic activity during sentence production in healthy and schizophrenic men

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Abstract

Background: *Schizophrenia is a psychiatric disorder marked by hallucinations, delusions, cognitive deficit, apathy, and thinking disorders. Speech disturbance is one of the main diagnostic criteria during acute periods of schizophrenia. In addition, abnormalities of brain language areas have been consistently described in schizophrenic individuals. The aim of this study was to describe the linguistic performance and cerebral activity during sentence production using word pairs with high or low semantic relatedness.* **Material and methods:** *We recorded electrical brain activity (electroencephalography [EEG]) of 15 healthy men and 11 men with disorganized schizophrenia while they were producing sentences with high and low relatedness word pairs.* **Results:** *The results showed significant differences; participants in both groups had significant longer latencies to produce sentences with low than with high relatedness word pairs. Furthermore, sentences formed with low relatedness pairs were significantly longer than those formed with high relatedness word pairs in both groups. EEG parameters also showed differences; in healthy subjects, we found enhancement of absolute alpha rhythm over the occipital leads during the period preceding sentence production with high relatedness word pairs.* **Conclusion:** *In contrast, in schizophrenia patients producing sentences with high relatedness word pairs, it was theta and beta rhythms that were enhanced in frontal regions.*

Key words: *Semantic relatedness. Verbal fluency. Electroencephalography. Absolute power.*

Actividad electroencefalográfica durante la producción de oraciones en hombres sanos y con esquizofrenia

Resumen

Antecedentes: *La esquizofrenia es una enfermedad caracterizada por alucinaciones, déficits cognitivos, apatía y alteraciones del pensamiento. Uno de los principales criterios diagnósticos durante los periodos agudos son las alteraciones del lenguaje. El objetivo de este trabajo fue describir el desempeño lingüístico y la actividad cerebral durante la producción de oraciones usando pares de palabras con alta y baja relación semántica.* **Material y métodos:** *Registramos la actividad eléctrica (EEG) de 15 hombres sanos y 11 pacientes con esquizofrenia desorganizada mientras producían oraciones con pares de palabras con alta y baja relación semántica.* **Resultados:** *Los resultados mostraron diferencias significativas; ambos grupos*

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tuvieron latencias más largas al producir oraciones usando palabras con baja relación semántica. Además, estas oraciones fueron significativamente más largas, que aquellas formadas usando palabras con alta relación semántica, en ambos grupos. El EEG también mostró diferencias; en los sujetos sanos hubo un aumento del ritmo alfa en el occipital durante el periodo previo a la producción de oraciones con alta relación semántica. **Conclusiones:** *En contraste, en los pacientes con esquizofrenia fueron los ritmos teta y beta los que incrementaron en regiones frontales al producir este tipo de oraciones.*

Palabras clave: *Cercanía semántica. Fluidez verbal. EEG. Poder absoluto.*

Introduction

In patients with schizophrenia, language disorder has been considered a diagnostic indicator of the illness[1]. Particularly, abnormalities in connections between words and concepts are the most representative sign of thought disorder[2-4].

Some studies have showed that schizophrenic patients have deficits in tasks involving semantic relations between words[5,6]. Building sentences with highly semantically related words lead to fast activation of their inner representation in working memory (WM)[7]. Sentence production involves cognitive processes that are based on the integration of activity in multiple brain regions, particularly associative cortical sites[8,9].

One technique widely used to study brain mechanisms of cognitive impairments in patients with mental disorders is electroencephalography (EEG)[10]. EEG studies indicate that between 50% and 60% of patients with schizophrenia show slowing of alpha rhythm, although 15% of them show beta activity between 13 Hz and 18 Hz and 10% of the patients have paroxysmal EEG changes[11].

Some authors have used EEG to describe the brain functioning that underlies cognitive task performance in schizophrenic patients[12]. Most of the symptoms are evident while patients are solving daily life problems; cognitive researchers are aware of this problem and have developed experimental conditions that simulate life demands, such as arithmetical problem-solving[13]; memory retrieval[14]; syntactical language organization, and communication fluency[15].

In this study, we analyzed the EEG during sentence production in schizophrenic and healthy men. Our objective is to identify possible changes in brain electrical activity in healthy and schizophrenic subjects during the construction of sentences using word pairs with high and low semantic relatedness. We predicted that sentence production using low relatedness word pairs requires more verbal processing and WM capacity than using high relatedness word pairs, and this would be associated to differences in EEG patterns in schizophrenic patients compared to healthy men.

Methods

The study was carried out in accordance with the Helsinki Declaration and was approved by the Faculty of Psychology Institutional Review Board at the Universidad Autónoma de Puebla (Puebla, Mexico).

Participants

We analyzed the brain electrical activity of 11 men in the acute phase of disorganized schizophrenia and 15 healthy men. Patients were recruited from the Rafael Serrano Psychiatric Hospital in Puebla, México, and healthy men were selected by advertisement. All subjects were right-handed according to the Annette scale[16]. Mean age of healthy men was 32.5 years (standard deviation [SD] = 4.2) and 31.7 years (SD = 3.2) for schizophrenic subjects. Educational level of healthy men was 6.5 years (SD = 2.3) and schizophrenic subjects was 6.1 (SD = 1.4). Patients' mean age of schizophrenia onset was 31.3 (SD = 0.6) and the mean duration of illness was 6.0 months (SD = 0.1).

All of the patients had between mild and moderate illnesses according to their scores on the Scale for the Assessment of Positive Symptoms[17] (mean score = 16.5, SD = 12.8, range = 0.41). Patients were evaluated 1 day after they were admitted to the hospital to avoid changes in their clinical status. All participants were native, monolingual Spanish speakers who never learned any other language. No history of head trauma, substance abuse, or addiction was recorded. After a complete description of the study, written informed consent was obtained from all participants and their relatives.

Stimuli and task

Thirty pairs of highly related words (e.g., table chair) and 30 pairs of low-related words (e.g., dog lock) were collected from the previous work[18]. Each participant was instructed to construct a sentence using the pair of words involved without changing the order of words or modifying the word itself (e.g., chairs instead of

chair). We presented 33 pairs of words for each of the two conditions: low-related and high-related words.

Experimental procedure

Each subject received the instruction that after hearing the pair of words, they must construct a sentence using the pair of words without changing them. The experimental session began by asking the participant to close his eyes. Over the next 5 min, the participants sat with their eyes closed to record resting brain activity. Each test began with the presentation of one pair of words, previously recorded, through headphones. When the subject was ready to state his sentence, he began to speak. The next pair of words was given 5-6 s after the end of sentence articulation. Pairs of high- and low-related words were presented in pseudo-random order.

EEG data acquisition and analysis

EEG was recorded with an EEG device (Nicolet Viking EEG) according to the international 10-20 system from the following leads: Fp1, Fp2, F3, F4, F7, F8, Fz, T3, T4, T5, T6, C3, C4, Cz, P3, P4, Pz O1, O2, and Oz referred to linked earlobes. The sampling rate was 128 Hz. Amplifiers had a bandpass from 0.5 Hz to 30 Hz. For analysis, cerebral electrical activity was selected during the period from the beginning of word presentation to the start of the first oral articulation in each word pair. This period was defined in EEG with physiological markers (quick mouth movement). The sentences were recorded for posterior linguistic analysis.

We eliminated those EEG epochs with movement artifacts. Electromyography and EOG derivative from the movement of the chin, mouth, and eyes was indicated and marked. The final analyzed EEG period was 120 s in all participants. We used the fast Fourier transformation to estimate the power spectra. We analyzed the absolute power EEG rhythms in the following frequencies bands: delta (1-3.5 Hz), theta (4-7.5 Hz), alpha (8-12.5 Hz), beta 1 (13-18.5 Hz), beta 2 (19-24.5), and beta 3 (25-30 Hz).

Behavioral data analysis

The analysis is based on the comparison of values between the group of healthy subjects and the group of patients with schizophrenia. The response variables were the latencies (time in seconds) and length of sentences (number of words) constructed using high and low relation word pairs. Due to the different number of subjects in each group, we used the Mann–Whitney U test to compare the latency between groups and between the two stimulus conditions (high and low word pair relatedness). For statistical analysis and graphical representations, we used the program Prism 5 for Windows (GraphPad Software Inc., San Diego, USA, 2002).

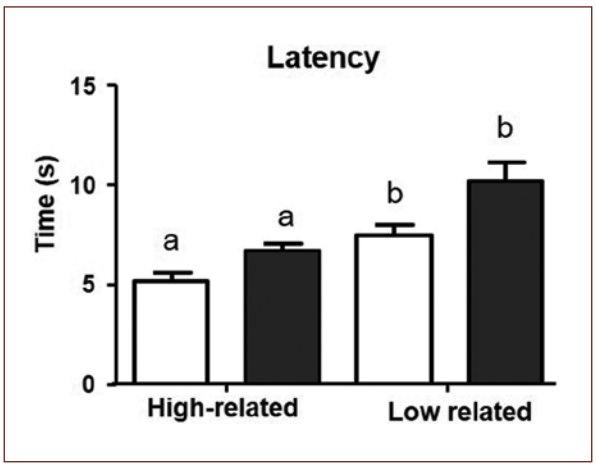

Figure 1. Comparison of latency to produce sentences between healthy (white) and schizophrenic (black) men with high and low relatedness word pairs. Data are means ± standard deviation (n = 15 healthy and n = 11 schizophrenic men). Letters indicate significant differences. Details of statistics are given in the text.

Results

In healthy subjects, the latency for constructing sentences with high relatedness word pairs was 5.1 s (± 0.37 SD) and with low relatedness pairs was 7.4 s (± 0.52 SD). Subjects with schizophrenia constructed sentences using pair of high relatedness word pairs in 6.7 s (± 0.30 SD) and low relatedness pairs in 10.1 s (± 0.97 SD).

Kruskal–Wallis (KW) test showed significant differences in the latency to produce sentences (KW = 47.75, $p < 0.0001$), *post hoc* Dunn's multiple comparison tests showed that this difference depended only on word pair relatedness (Fig. 1).

We counted the number of words utilized to construct sentences. Healthy subjects incorporated 5.86 (± 0.91 SD) words in sentences with high relatedness word pairs and used 7.8 words (± 0.91 S.D) to form sentences with low relatedness pairs. Subjects with schizophrenia incorporated 7 (± 1.0 S.D) words in

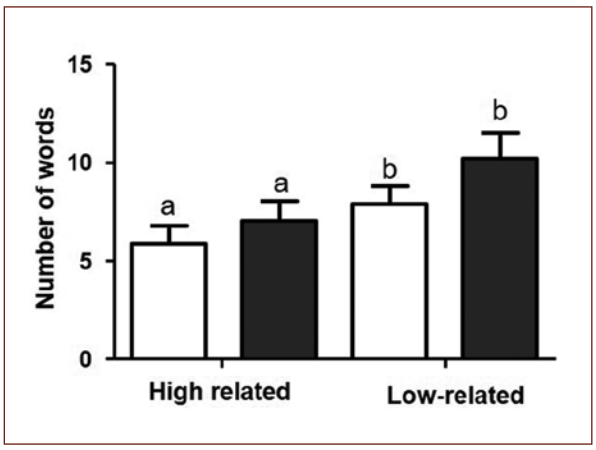

Figure 2. Difference in number of words used to produce sentences between healthy (white) and schizophrenic (black) men, with high and low relatedness word pairs. Data are means ± standard deviation (n = 15 healthy and n = 11 schizophrenic men). Letters indicate significant differences. Details of statistics are given in the text.

sentences with high relatedness pairs and 10.18 words (± 1.3 SD) in sentences with low relatedness pairs.

KW test showed significant differences in the number of words to construct sentences (KW = 35.92, $p < 0.0001$), *post hoc* Dunn's multiple comparison tests showed that this difference depended only on word pair relatedness (Fig. 2).

EEG data

EEG data were compared between groups using the Mann–Whitney U-test to assess the statistical significance of the difference in the absolute power of each EEG band. During the construction of sentences with high relatedness word pairs, healthy subjects showed significant higher absolute power in delta and alpha rhythm than schizophrenic patients. However, schizophrenic patients showed significantly higher absolute power in theta, beta 1, beta 2, and beta 3 rhythms compare to healthy subjects (Fig. 3).

During the construction of sentences with low relatedness word pairs, schizophrenic patients showed significant higher absolute power in delta, theta, and beta rhythms, while healthy subjects exhibited significantly higher alpha rhythm (Fig. 4).

Topographical analysis

Construction of sentences with highly related word pairs induced a different distribution of absolute power between the control and schizophrenic groups. The absolute power of alpha rhythm was increase in healthy subjects over the occipital leads. The absolute power of theta and beta rhythms is increase over the frontal and central leads in schizophrenic patients (Fig. 5).

Construction of sentences with low relatedness word pairs also induced different distribution of absolute power between the groups. In healthy subjects, we found enhancement of alpha rhythm, especially in occipital regions, as well as theta power in frontal areas. Schizophrenic patients showed an increase in absolute power in theta band in frontotemporal areas. In addition, a diffuse increase of absolute power in beta band appeared in schizophrenic patients (Fig. 6).

Discussion

There is extensive literature about deficits in verbal functioning in schizophrenia, showing various abnormalities in verbal production, comprehension, and cerebral lateralization of language[19]. Several functional magnetic resonance imaging studies using language paradigms also show abnormal processing in verbal fluency tasks and loss of left hemisphere lateralization in the temporal and frontal lobes of patients with chronic schizophrenia[20].

Some authors Ford and Mathalon[21] have argued that EEG measures of coherence indicate interdependence of activity in the frontal speech production and temporal speech reception areas during speech in control subjects, but not in schizophrenia patients. These data suggest that a corollary discharge from frontal areas fails to alert the auditory cortex that they are self-generated, leading to the misattribution of inner speech to external sources.

Wynn et al.[22] found no differences between schizophrenic patients and controls in the ability to form global objects from local elements, during visual integration tests. This is relevant to our tests because we asked patients and control subjects to form coherent sentences (global object) from isolated words (local elements). The cognitive effort required for that kind of tasks involves information sorting (word pairs), to generate a coherent order. Schizophrenic patients have difficulty maintaining thematic consistency. In our study, patients formed sentences with no morphological deficits, but which were thematically incoherent. To construct a sentence, using pairs of word, it is necessary to maintain the words in the short-term memory while seeking a context in which to put them, as well as constant monitoring to avoid mistakes[23]. Short-term memory and

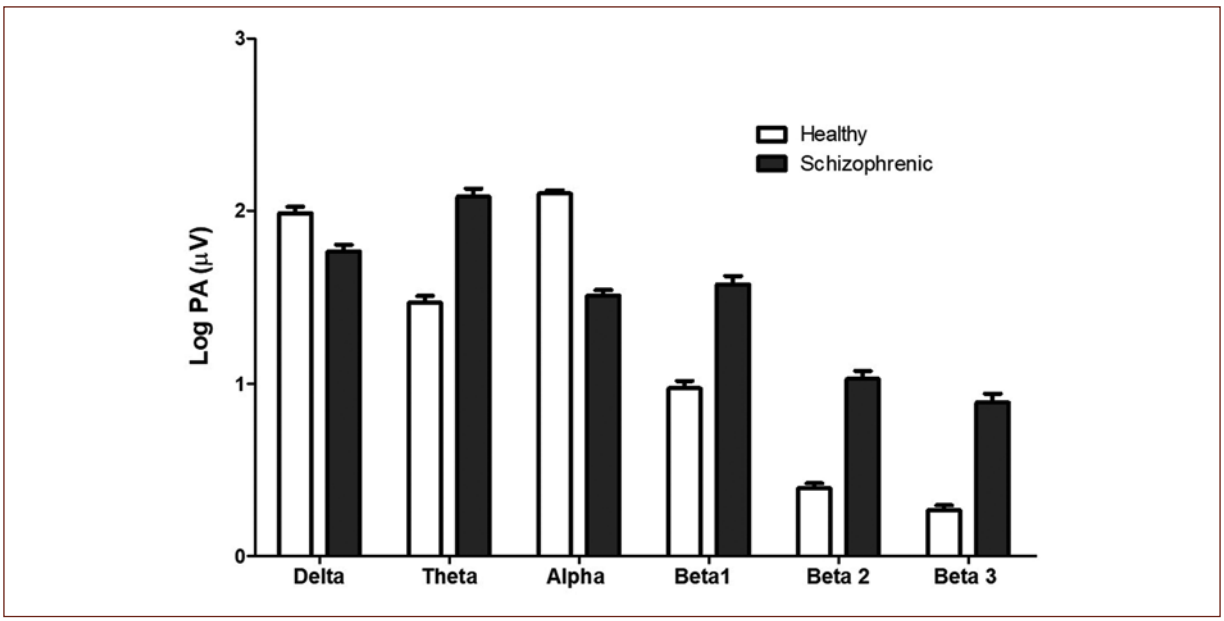

Figure 3. Comparison of the absolute power (Log PA) obtained during sentence production using highly related word pairs. Details of statistics are given in the text.

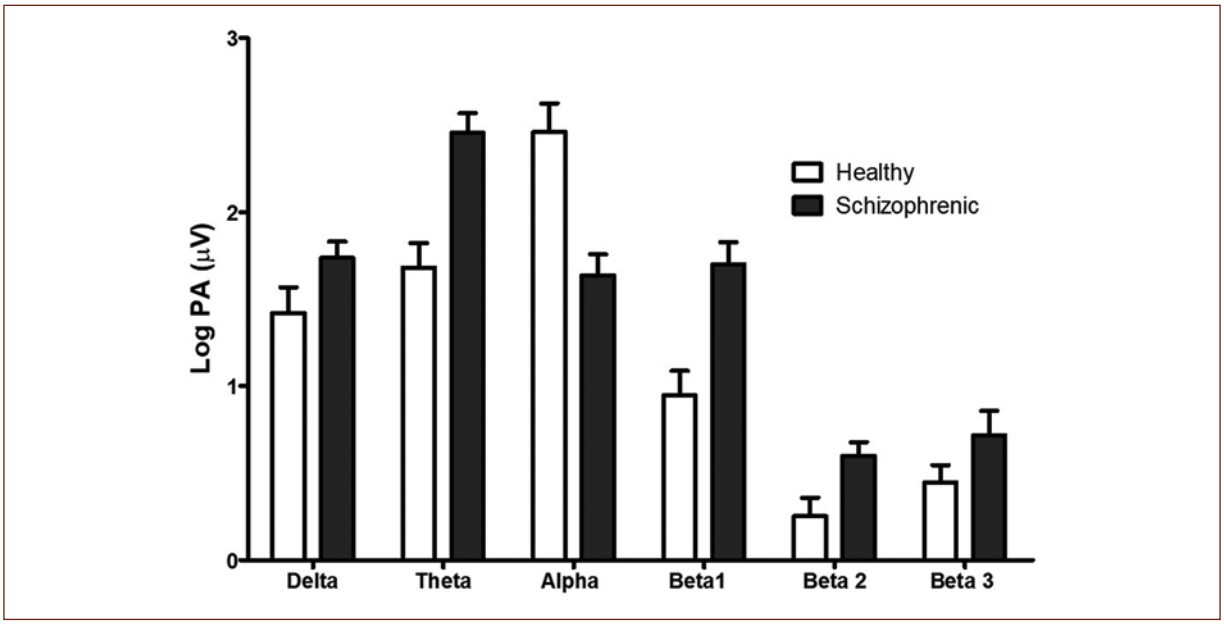

Figure 4. Comparison of the absolute power (Log PA) obtained during sentence production using low relatedness word pairs.

monitoring are functions associated with the work of the frontotemporal and frontoparietal cortex[24-26].

Expression of language is a complex process and involves a distributed network in cortical regions. Our results demonstrate that when control subjects form sentences with highly related word pairs, absolute power over theta and beta bands is more expressive on frontopolar and frontal-inferior regions, respectively. Lin et al.[27] suggested that theta power increases during longer latencies; furthermore, alpha-band oscillations are suggested

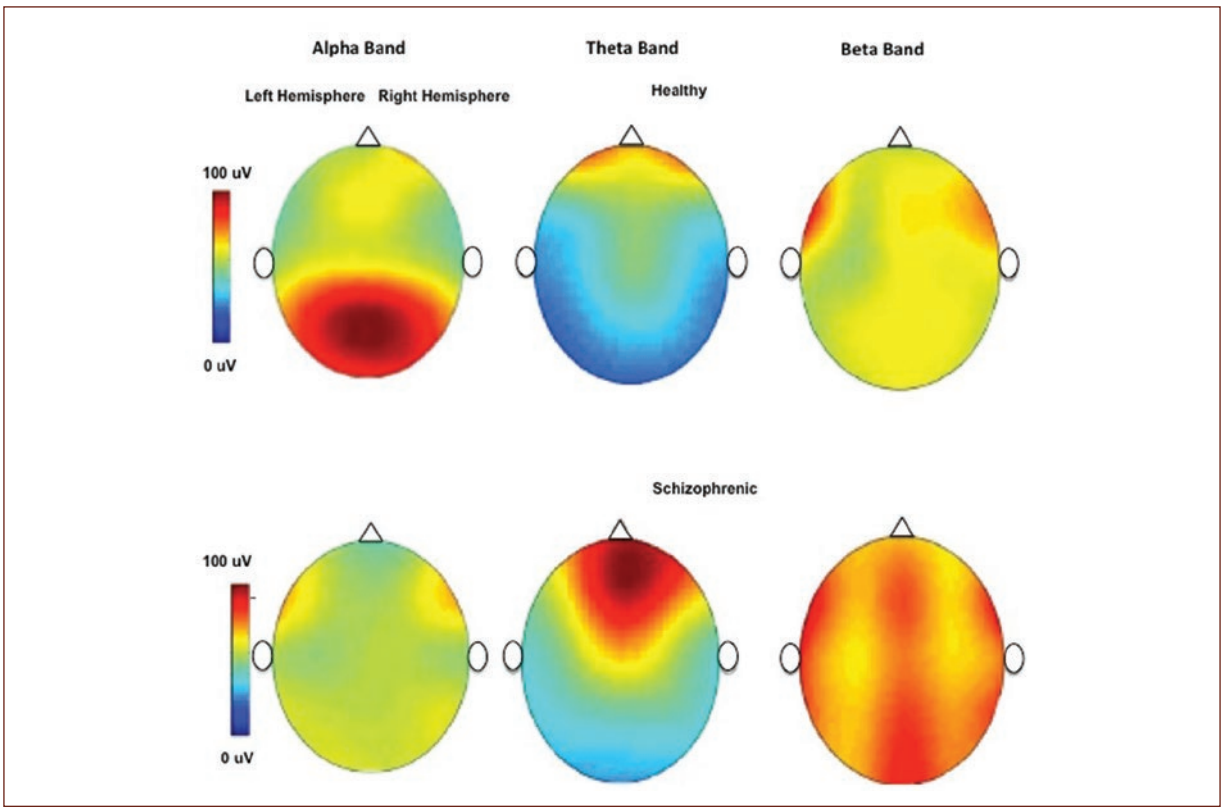

Figure 5. Brain mapping while producing sentences with high relatedness word pairs.

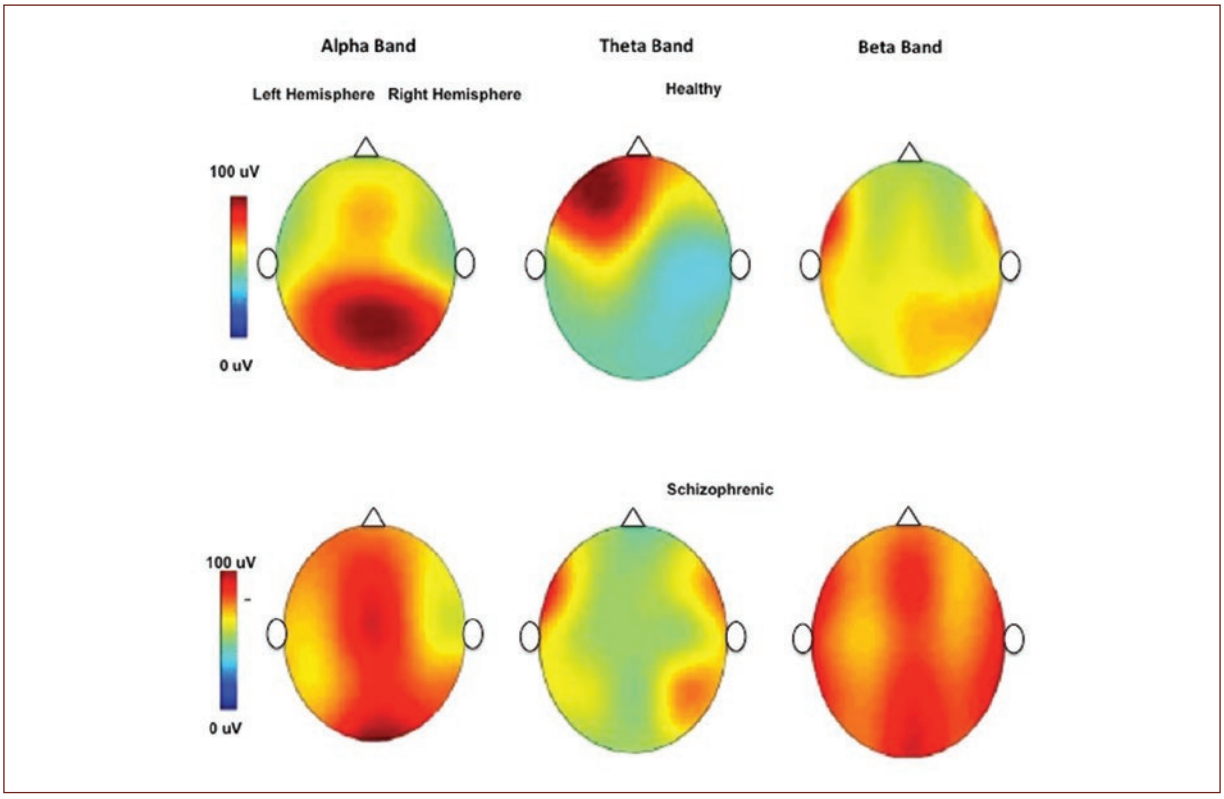

Figure 6. Brain mapping while producing sentences with low relatedness word pairs.

to be closely associated with attentional selection, specifically anticipatory and temporal attention[28].

In schizophrenic patients, the absolute power of the theta band increased in the frontotemporal regions in both hemispheres with an extension to the right parietal region. The beta band also increased diffusely. Doesburg et al. suggested that oscillatory synchronization and cross-frequency interactions are mechanisms of functional integration among distributed brain areas that support expressive language processing[29].

Theta activity has been found over frontal regions when subjects form images during mental task performance[30]. We believe that a sentence forming task involves organizing images, but in more complex tasks, the images may be less structured. On the other hand, beta activity is associated with sensory information analysis and decision-making because the task implies a goal-oriented behavior. The assumption behind this idea is that the motor system initiates active movement preparation on the reception of stimulus input[31]. Language production in schizophrenia is disordered and filled with irrelevant pieces of information and derailments. Such erratic discourse may be linked to the inability to use pragmatic rules, attention, action planning, ordering, and sequencing[32].

Finally, we consider that sentence production using high and low relatedness word pairs could be used to explore different cognitive process, such attention, WM, executive functions, as well as the search for coherence. We believe that in the area of neuropsychological rehabilitation, particularly for schizophrenic patients, it is necessary to create methods to solve problems in discourse construction, looking into different cognitive processes that are required for generating meaning in patients' speech.

Conclusion

There are significant differences in behavior and EEG activity during sentences production, using low and high relatedness words. Specifically, absolute power is increased in patients with schizophrenia over the theta, and beta rythms. We consider that producing sentences with high or low relatedness words could be used for new experimental paradigms.

Differences in EEG patterns in schizophrenic patients compared to healthy men.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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ORIGINAL ARTICLE

Efecto de la empatía sobre el procesamiento cortical temprano y tardío de rostros

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Resumen

Antecedentes: *La empatía depende, en gran medida, de la capacidad de procesar las emociones que son expresadas en el rostro de la otra persona.* **Objetivo:** *El objetivo del presente estudio fue evaluar las diferencias en el curso del tiempo del procesamiento cognitivo de rostros con expresiones de alegría, neutras e ira en personas con baja y alta empatía.* **Método:** *El estudio se llevó a cabo con 60 participantes distribuidos en dos grupos (baja y alta empatía), los cuales observaron rostros con expresiones de alegría, neutras e ira mientras se registraba los potenciales relacionados a eventos P100, N170 y LPP, como indicadores de la atención temprana, codificación del estímulo como un rostro humano y activación y enganche atencional.* **Resultados:** *No se encontraron diferencias significativas entre grupos en el componente P100. El potencial N170 fue mayor en el grupo con alta empatía y el LPP fue mayor ante expresiones de ira en el grupo con baja empatía.* **Conclusiones:** *Los resultados sugieren que la empatía no tiene un efecto en la respuesta de atención temprana hacia los rostros, pero sí aumenta el reconocimiento del estímulo como un rostro humano y que las personas con baja empatía tienen mayor enganche atencional ante expresiones de ira.*

Palabras clave: *Empatía. Rostros. P100. N170. LPP.*

The effect of empathy on early and late cortical face processing

Abstract

Background: *Empathy depends, to a large extent, on the ability to process the emotions that are expressed in the faces of other people.* **Objective:** *The objective of the present study was to evaluate the differences in the time course of cognitive processing of happy, neutral and angry faces in subjects with low and high empathy.* **Method:** *The study was carried out with 60 participants divided into two groups (low and high empathy), which observed happy, neutral and angry faces while recording the events related potentials (ERP) P100, N170 and LPP, as indicators of early attention, encoding of the stimulus as a human face and activation and attentional engagement.* **Results:** *No significant differences were found between groups in the P100 component. The N170 ERP was higher in the high empathy group and the LPP was higher to angry faces in the*

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low empathy group. **Conclusions:** *The results suggest that empathy does not have an effect on the response of early attention to faces, but it does increase the recognition of the stimulus as a human face and subjects with low empathy have greater attentional engagement to expressions of anger.*

Key words: *Empathy. Faces. P100. N170. LPP.*

Introducción

Una de las habilidades fundamentales para la interacción social y la comunicación emocional es la empatía[1,2], la cual se define como la habilidad para entender y responder a los mensajes emocionales de otros[3]. La empatía está dividida en dos componentes: la empatía afectiva, que es un proceso en donde la percepción de una emoción en otra persona genera una reacción emocional en sintonía con la percibida, y la empatía cognitiva, que es la habilidad para inferir de forma precisa la emoción del otro[4].

La forma de comunicación más básica de las emociones es por medio de las expresiones faciales[5], las cuales tienen una función biológica y afectan de forma diferencial al observador. Se ha demostrado que las expresiones faciales generan respuestas de mímica y contagio emocional, por ejemplo, las expresiones faciales de alegría generan activación del músculo cigomático y las expresiones de ira la activación del músculo corrugador[6,7], incluso cuando las expresiones son vistas por periodos de tiempo muy cortos en donde no hay conciencia de la expresión observada[8]. Sin embargo, el contagio emocional producto de la observación de expresiones emocionales en el rostro se ha encontrado solamente en personas con alta empatía afectiva, las cuales son las que presentan mayor actividad de los músculos cigomático y corrugador ante expresiones de alegría e ira respectivamente[9,10].

A nivel central el procesamiento de rostros humanos se ha asociado con varios potenciales relacionados a eventos (PRE), principalmente con el componente N170, el cual es un potencial temprano negativo que ocurre en la región parietal-temporal y es un indicador fiable de las etapas tempranas de codificación de las características faciales[11,12]. El PRE P100 también se ha asociado al procesamiento temprano de rostros, el P100 es un potencial positivo que sirve como indicador de atención temprana y ocurre en la región occipital-parietal[13]. El P100 aumenta ante la observación de rostros humanos[14], lo que sugiere la relevancia biológica de las características del rostro. Finalmente, el componente LPP es un potencial positivo tardío que se genera en la región parietal-occipital después de 300 ms y se asocia a activación y atención sostenida hacia diferentes estímulos, entre ellos los rostros humanos, que generan enganche atencional por su relevancia motivacional[15].

La expresión emocional en el rostro modula la magnitud de algunos PRE, lo que sugiere un aumento o disminución en el procesamiento cognitivo de los rostros, por ejemplo, se ha encontrado que las expresiones de ira y miedo generan un aumento en el LPP[16]. Sin embargo, la evidencia no es concluyente con respecto al efecto de la expresión emocional en los PRE P100 y N170. Por ejemplo, Batty y Taylor[11] no encontraron diferencias significativas en el P100 ante rostros con distintas expresiones emocionales, sin embargo, Smith, et al.[16] encontraron que los rostros de miedo generan mayor amplitud del P100 en comparación con los rostros neutrales. Con relación al componente N170, se ha encontrado que las expresiones de miedo e ira generan mayor amplitud en comparación con las expresiones neutrales[11,17], aunque otras investigaciones no han encontrado estos mismos datos[16]. Las diferencias en los resultados de los componentes P100 y N170 pueden deberse al uso de distintos estímulos faciales, los cuales pueden variar con relación al nivel de activación temprana que generan en el observador y al nivel de empatía de los participantes.

Pocos estudios han evaluado el efecto de la empatía sobre el procesamiento cortical de los rostros y sus resultados no son concluyentes. Las investigaciones en este campo sugieren que a mayor empatía, mayor respuesta atencional ante los rostros, lo que se refleja en la correlación positiva encontrada entre el nivel de empatía y el aumento en los potenciales N170 y LPP ante rostros con expresiones de alegría, ira, sorpresa, miedo y tristeza[18,19]; sin embargo, los resultados no son sólidos sobre las posibles diferencias entre grupos con baja y alta empatía. Adicionalmente, estas investigaciones no han utilizado rostros con expresiones neutrales, lo que limita sus conclusiones, ya que no se sabe si el aumento en los PRE es producto de las expresiones emocionales o si este fenómeno ocurre ante el rostro humano en general. Tampoco se ha evaluado el procesamiento temprano del rostro por medio del componente P100 en personas con baja y alta empatía, el cual es un indicador de la fase más temprana de atención.

Por lo anterior, el objetivo del presente estudio fue evaluar las diferencias en el curso del tiempo del procesamiento cognitivo de rostros humanos con expresiones de alegría, neutras e ira en personas con baja y alta empatía, para lo cual se utilizó como indicadores neurofisiológicos los PRE P100, N170 y LPP, como indicadores de la atención temprana, codificación del estímulo como un rostro humano y activación y enganche atencional.

Método

Participantes

El estudio se desarrolló con 60 participantes con edades entre 18 y 26 años, los cuales fueron divididos en dos grupos según su puntaje en el índice de reactividad interpersonal[20] (IRI) y en especial en sus dos escalas principales: toma de perspectiva, la cual mide empatía cognitiva, y preocupación empática, que mide empatía afectiva. Cada grupo estuvo conformado por 30 participantes, el grupo de personas con baja empatía (15 mujeres y 15 hombres, con una edad promedio de 21.10 años, (desviación estándar [DE]: 2.11) y el grupo de personas con alta empatía (14 mujeres y 16 hombres, con una edad promedio de 21.82 años (DE: 2.53). No hubo diferencias significativas entre grupos en la edad de los participantes ($t_{(55)}$: –1.16; p = 0.25), ni en la distribución de hombres y mujeres ($\chi^2_{(1)}$: 0.01; p = 0.88). Los puntajes en las escalas del IRI en cada grupo se presentan en la tabla 1. Se excluyeron participantes con reporte de enfermedades neurológicas, que estuvieran bajo tratamiento farmacológico o con problemas de visión no corregidos. Todos los participantes firmaron el formato de consentimiento informado y el estudio fue aprobado por el Comité de Ética de la institución.

Tabla 1. Puntajes promedio (desviación estándar) en las escalas del índice de reactividad interpersonal (IRI) en el grupo de personas con baja y alta empatía

Escala del IRI	Baja empatía	Alta empatía	p
Toma de perspectiva	15.39 (4.48)	19.00 (3.90)	0.003
Escala de fantasía	12.64 (4.37)	15.48 (5.38)	0.034
Preocupación empática	13.39 (3.15)	20.27 (1.90)	< 0.001
Estrés personal por empatía	11.21 (5.31)	11.44 (4.85)	0.806
Total IRI	52.64 (12.02)	66.20 (10.85)	< 0.001

Estímulos

Se utilizaron 24 imágenes de rostros a color del instrumento NimStim[21]. Ocho mostraban expresiones de alegría, ocho expresiones neutrales y ocho expresiones de ira. Cada expresión emocional fue representada por cuatro hombres y cuatro mujeres. Los modelos utilizados en el experimento fueron aquellos que tenían rasgos latinos (cabello oscuro, ojos café o negros). Para cada una de las expresiones emocionales se utilizaron las imágenes de los mismos modelos, con el objetivo de evitar sesgos de atractivo físico en alguna de las emociones. Los estímulos fueron presentados en una pantalla plana de 19 pulgadas sobre un fondo negro localizada a 60 cm aproximadamente del participante. Cada imagen tuvo un tamaño de 480 × 480 píxeles.

Cada estímulo se presentó dos veces con la restricción de no mostrar dos veces seguidas una misma expresión emocional. Se organizaron cuatro órdenes de presentación de estímulos diferentes, los cuales fueron distribuidos de forma equilibrada entre todos los participantes. En general el experimento tuvo un total de 48 ensayos. Cada uno inició con una pantalla negra y una cruz de fijación «+» en el centro durante 500 ms, posteriormente aparecía el rostro durante 2 segundos y finalizaba con un intervalo entre estímulos variable (pantalla negra) entre 3 y 5 segundos. La presentación de los estímulos se programó en el *software* E-Prime 2.0 (*Psychology Software Tools*, PA, EE.UU.).

Registro del electroencefalograma

La actividad electroencefalográfica (el EEG) se registró de forma continua mediante un equipo BioSemi ActiveTwo de 32 canales (BioSemi, Amsterdam, Países Bajos). La ubicación de los electrodos se hizo por medio de un gorro con las coordenadas del sistema internacional 10/20. Durante la adquisición de los datos, la tasa de muestreo fue de 1024 Hz, cada canal se referenció al promedio de la actividad de los 32 canales y se mantuvo la impedancia por debajo de 20 kΩ. Para identificar los parpadeos y movimientos oculares se registró el electrooculograma por medio de dos electrodos ubicados a un centímetro debajo de la pupila del ojo derecho para los movimientos verticales y otro ubicado a un centímetro del canto del ojo izquierdo para los movimientos horizontales.

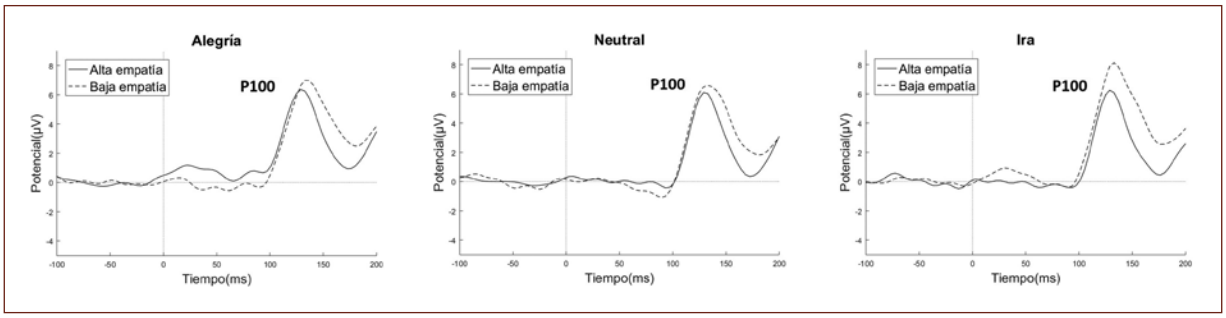

Figura 1. *Grand average* del potencial relacionado a eventos P100 en personas con baja y alta empatía ante rostros alegres, neutrales y con ira. Ubicación PO3, PO4, O1, Oz y O2.

Procesamiento de los datos del EEG

La señal del EEG se procesó en Matlab a través del *toolbox* EEGLab[22] y de *scripts* diseñados específicamente para el estudio. Inicialmente se disminuyó la tasa de muestreo a 256 Hz y se aplicó un filtro de banda entre 0.1 y 40 Hz. Se segmentó el registro en intervalos de 1,100 ms (100 ms preestímulo y 1,000 ms postestímulo) y se corrigieron los artefactos producto de los movimientos oculares con el algoritmo de Gratton, Coles y Donchin[23]. Se identificaron los valores extremos (+/– 70 μV) en cada canal y se rechazaron los ensayos que tuvieran cuatro o más canales con estos valores; en total se eliminó el 3.8% de los ensayos.

Se analizaron la amplitud y la latencia de los PRE P100 y N170 en las regiones en donde la actividad suele ser mayor[16,24]. El P100 se registró en una ventana de tiempo entre 100 a 200 ms en la región parietal-occipital y occipital (electrodos PO3, PO4, O1, Oz y O2). El N170 se registró en la región parietal (electrodos P7 y P8), con una ventana de tiempo entre 150 a 250 ms. El potencial LPP se analizó por medio del área bajo la curva (ABC), debido a que al ser un potencial lento no se identifica un pico claro, lo que disminuye la validez de los análisis de amplitud y latencia[24]. El LPP se registró en las zonas parietal y parietal-occipital (electrodos P3, Pz, P4, PO3 y PO4) en una ventana de tiempo entre 300 y 700 ms.

Medidas de autorreporte

Para la división del grupo de participantes en personas con baja y alta empatía se utilizó la versión del IRI[20] validada en Colombia[25]. El IRI es un instrumento compuesto por 28 ítems, está dividido en cuatro subescalas que miden empatía cognitiva y empatía afectiva. Las dos escalas principales del IRI son «toma de perspectiva» (empatía cognitiva) y «preocupación empática» (empatía afectiva).

Para la evaluación subjetiva de la emoción se utilizó el maniquí de autoevaluación (*Self-Assessment Manikin* [SAM]). El SAM es un instrumento desarrollado por Bradley y Lang[26], para evaluar las dimensiones de la emoción (valencia, *arousal* y dominancia). El SAM está conformado por tres escalas, una para cada dimensión, las cuales utilizan cinco figuras humanoides que indican diferentes niveles de intensidad y niveles intermedios entre cada figura. El puntaje en cada escala va de 1 a 9. El SAM ha mostrado niveles apropiados de validez en población colombiana[27].

Análisis estadístico

El análisis de los potenciales P100, N170 y LPP se hizo a través de un ANOVA mixta de medidas repetidas, con el factor intersujeto «grupo» (baja y alta empatía) y con los factores intrasujeto «emoción» (alegría, neutral e ira) y «ubicación» (electrodos de cada PRE). El análisis de las medidas subjetivas de la emoción (valencia, *arousal* y dominancia) se hizo mediante un ANOVA mixto de medidas repetidas 2 × 3, con el factor grupo como variable intersujeto y la emoción como variable intrasujeto. Se aplicó la corrección Greenhouse-Geisser en todos los casos para corregir cualquier violación de la esfericidad en los datos. La comparación de pares *post hoc* se hizo con la corrección Bonferroni. El nivel de significancia para todos los análisis fue de $p < 0.05$ y se reporta el tamaño del efecto[28] (η_p^2; pequeño ≥ 0.01, medio ≥ 0.06 y grande ≥ 0.14). Todos los análisis fueron realizados en el programa estadístico SPSS® 20.0

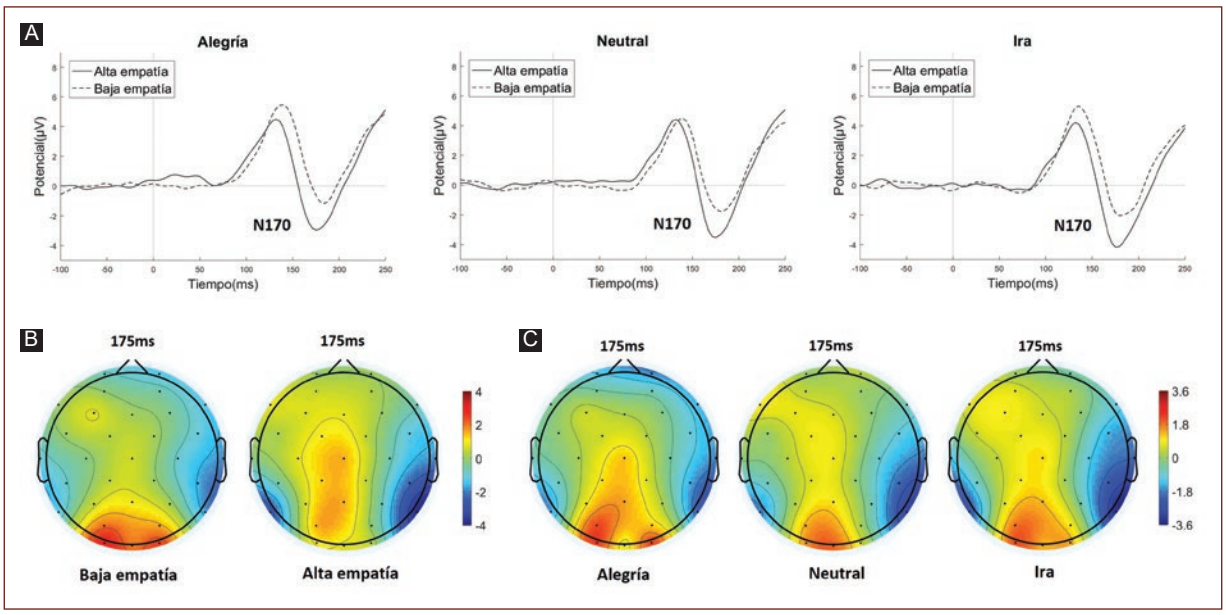

Figura 2. A: *grand average* del potencial relacionado a eventos N170 en personas con baja y alta empatía ante rostros alegres, neutrales y con ira. Ubicación P7 y P8. **B:** mapas topográficos de la actividad cortical a los 175 ms para cada grupo. **C:** mapas topográficos de la actividad cortical a los 175 ms para expresiones de alegría, neutrales e ira.

Resultados

P100

Con respecto a la amplitud del potencial P100, el ANOVA reveló un efecto principal significativo para ubicación ($F_{(4,232)}$: 36.06; p < 0.001; η_p^2: 0.38). El P100 fue mayor en la región occipital (O2, Oz y O1), en comparación con la región parietal-occipital (PO3 y PO4) (todas las p < 0.001). No se encontró ningún otro efecto principal o de interacción significativos (todas las p > 0.11). Con relación a la latencia del P100 no se encontró ningún efecto significativo (todas las p > 0.09) (Fig. 1).

N170

El ANOVA para la amplitud del potencial evocado N170 encontró un efecto principal significativo para grupo ($F_{(1,58)}$: 5.05; p = 0.02; η_p^2: 0.08) y emoción ($F_{(2,116)}$: 4.82; p = 0.01; η_p^2: 0.07) (figura 2). En general, la amplitud del N170 fue mayor (más negativo) en el grupo con alta empatía en comparación con el grupo con baja empatía y las expresiones de ira generaron una mayor amplitud del N170 en comparación con las expresiones de alegría (p = 0.008). No hubo otros efectos significativos (todas las p > 0.17).

En relación con la latencia del N170, el ANOVA reveló un efecto principal significativo para ubicación ($F_{(1,58)}$: 6.00; p = 0.01; η_p^2: 0.09), la latencia en el hemisferio derecho (electrodo P8) fue menor que en el hemisferio izquierdo (electrodo P7). No se encontró ningún otro efecto principal o de interacción significativo (todas las p > 0.22).

LPP

El ANOVA para el ABC del potencial evocado LPP encontró un efecto principal y de interacción significativos para emoción ($F_{(2,116)}$: 4.77; p = 0.01; η_p^2: 0.07), ubicación ($F_{(4,232)}$: 36.85; p < 0.001; η_p^2: 0.38) y grupo × emoción ($F_{(2,116)}$: 4.61; p = 0.01; η_p^2: 0.07) (Fig. 3). En general, los rostros de ira y alegría generaron mayor LPP que los rostros neutrales, lo que se refleja en una tendencia cuadrática y significativa de los datos ($F_{(1,58)}$: 9.37; p = 0.003; η_p^2: 0.13). El LPP fue mayor en los electrodos PO3 y PO4 en comparación con P3, Pz y P4 (todas las p < 0.001). Con respecto a la interacción grupo × emoción, se encontró que en el grupo de participantes con baja empatía el LPP fue mayor ante los rostros de ira en comparación con los rostros neutrales y alegres (ambas p < 0.05).

Medidas de autorreporte

En la tabla 2 se muestran los puntajes en valencia, *arousal* y dominancia para cada una de las

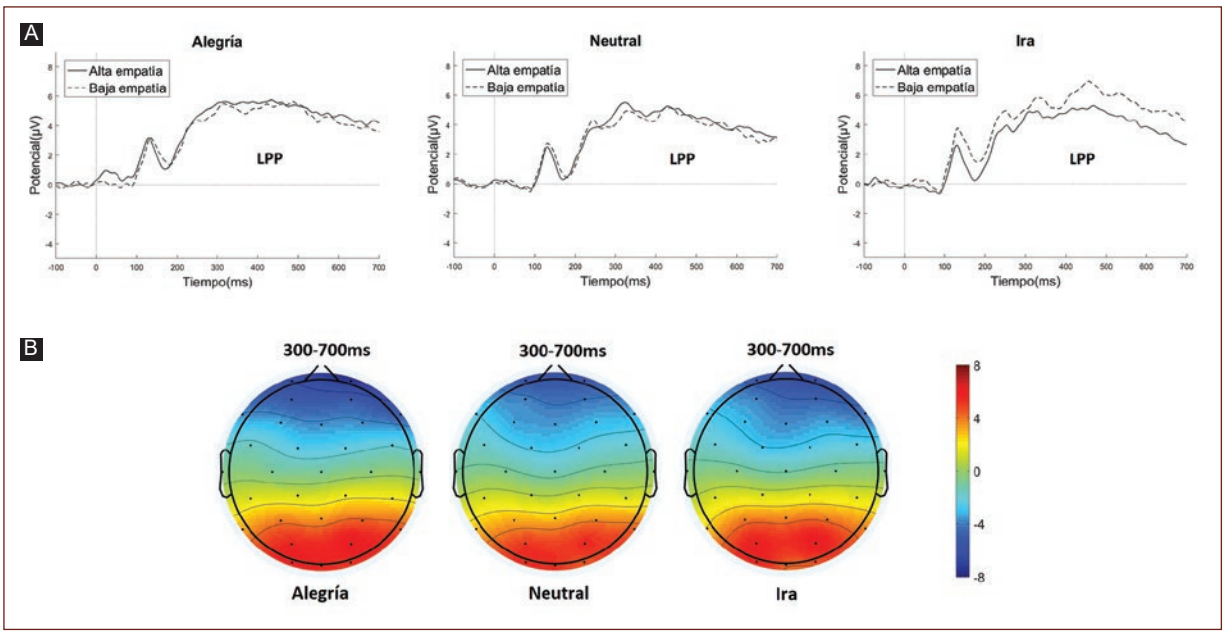

Figura 3. A: *grand average* del potencial relacionado a eventos LPP en personas con baja y alta empatía ante rostros alegres, neutrales y con ira. Ubicación P3, Pz, P4, PO3 y PO4. **B:** mapas topográficos de la actividad cortical promedio de los 300 a 700 ms para expresiones de alegría, neutrales e ira.

expresiones emocionales. El ANOVA para la dimensión de valencia identificó un efecto principal significativo para emoción ($F_{(2,110)}$: 82.28; $p < 0.001$; η_p^2: 0.59). Las expresiones de ira generaron estados afectivos negativos, las expresiones de alegría estados afectivos positivos y las expresiones neutrales estados afectivos neutrales (todas las $p < 0.001$). No se encontraron otros efectos principales ni de interacción significativos (todas las $p > 0.62$). Para la dimensión de *arousal* el ANOVA encontró un efecto principal significativo para emoción ($F_{(2,110)}$: 6.56; $p = 0.002$; η_p^2: 0.10). Las expresiones de ira generaron mayor activación que las expresiones neutrales ($p = 0.002$). No se encontraron otros efectos principales ni de interacción significativos (todas las $p > 0.29$). Por último, para la dimensión de dominancia, el ANOVA nuevamente encontró un efecto principal significativo para emoción ($F_{(2,110)}$: 3.36; $p = 0.04$; η_p^2: 0.05). Las expresiones de ira generaron menor percepción de control en comparación con las expresiones de alegría ($p = 0.05$). No se encontraron otros efectos principales ni de interacción significativos (todas las $p > 0.71$).

Tabla 2. Puntajes promedio (desviaciones estándar) en valencia, *arousal* y dominancia ante cada expresión emocional

	Alegría	Neutral	Ira
Valencia	6.38 (1.52)	4.68 (1.01)	3.74 (1.47)
Arousal	4.03 (1.73)	3.60 (1.89)	4.28 (1.83)
Dominancia	7.18 (1.71)	7.00 (1.87)	6.72 (1.76)

Discusión

El presente estudio utilizó técnicas neurofisiológicas para evaluar en el curso del tiempo las posibles diferencias en el procesamiento cognitivo de rostros humanos con expresiones de alegría, neutras e ira en personas con baja y alta empatía. Los resultados no mostraron diferencias significativas en el componente P100, lo que sugiere respuestas similares de atención temprana hacia los rostros en ambos grupos, sin embargo, sí se observaron diferencias en el procesamiento posterior, el potencial N170 es mayor en las personas con alta empatía, lo que sugiere una mayor codificación o reconocimiento de las características faciales. También se identificaron diferencias en el enganche atencional en las personas con baja empatía, las cuales respondieron con mayor atención sostenida ante las expresiones de ira.

La ausencia de diferencias significativas entre grupos en el P100 sugiere que la respuesta de atención inicial hacia los rostros no se ve influenciada por el nivel de empatía de las personas, lo que coincide con

las conclusiones del estudio de Herrmann, et al.[14] relacionadas con la alta relevancia biológica y motivacional de los rostros, los cuales generan una mayor respuesta de atención temprana en comparación con otros tipos de estímulos. En conjunto, estos resultados sugieren que la primera respuesta atencional hacia el rostro es un proceso muy básico mediado más por variables de orden evolutivo que de aprendizaje individual. Tampoco hubo diferencias en el P100 con relación al tipo de expresión emocional, estos mismos resultados se han reportado previamente[11], lo que indica que la primera respuesta atencional hacia el rostro no parece estar modulada por la emoción expresada.

Los resultados en el componente N170 sugieren un mayor procesamiento atencional y de reconocimiento del rostro humano en las personas con alta empatía. Resultados similares han sido reportados previamente[18,19], lo que indica que el procesamiento detallado del rostro (sus características, rasgos, expresiones) aumenta la posibilidad del reconocimiento emocional y la generación posterior de un estado afectivo en sintonía con la expresión observada, es decir, una respuesta de empatía afectiva. Este mecanismo ha sido previamente descrito en los estudios sobre contagio emocional[29,30] y empatía[9], en donde el proceso inicia con la percepción del rostro del otro individuo, continua con la respuesta de mímica facial que sirve como mecanismo de retroalimentación para la propia persona y la induce a un estado emocional similar, lo que finaliza en una respuesta de empatía afectiva.

Este proceso a nivel neurobiológico estaría soportado por el sistema de las neuronas espejo que valida la teoría de la simulación como mecanismo para el desarrollo de la empatía[31,32]. Los estudios con neuroimagen han mostrado que el sistema de las neuronas espejo en los humanos se encuentra conformado por una red compleja de áreas visuales en las regiones occipital, parietal y temporal y dos regiones predominantemente motoras (parte anterior del lóbulo parietal inferior y el sector del lóbulo frontal conformado por el córtex premotor ventral más la región posterior del giro frontal inferior)[33,34]. La estructura de esta red neuronal indica que gran parte del proceso se da en la región parietal, en donde el potencial N170 ocurre con mayor amplitud[11,16,24] y en donde se registró el potencial N170 en este estudio (electrodos P7 y P8), siendo menor la latencia en el hemisferio derecho.

Los resultados con relación al efecto de la expresión emocional en el PRE N170 indican que las expresiones de ira aumentan su amplitud, lo que probablemente esté relacionado con una mayor relevancia conductual de la ira en comparación con la alegría. Estudios previos han mostrado que las expresiones de ira por sí solas logran activar el sistema motivacional defensivo, reflejado en la potenciación del reflejo de sobresalto, mientras que las expresiones de alegría, sin un contexto que las acompañe, no lo logran inhibir[35]. Esta diferencia se debe a que históricamente las expresiones de ira han evolucionado como señales de peligro en sí mismas y el organismo se prepara para responder automáticamente ante ellas[36].

Los resultados en el LPP indican, como era esperable, un mayor enganche atencional ante las expresiones de ira y alegría en comparación con los rostros neutrales. Múltiples estudios han mostrado que el LPP es sensible al *arousal* generado por los estímulos, lo que indica que se produce una mayor respuesta de atención sostenida (mayor magnitud del LPP) hacia estímulos emocionalmente relevantes y un menor LPP ante estímulos neutrales[15,16].

También se encontró que las personas con baja empatía respondieron con un mayor LPP ante las expresiones de ira en comparación con las demás expresiones. Estos resultados no fueron encontrados en las investigaciones previas en donde se estudió la relación entre empatía y LPP[18,19], sin embargo, puede estar relacionado con la mayor relevancia conductual de las expresiones de ira[35,36], que lleva a que incluso las personas con baja empatía centren su atención en esta expresiones. Este resultado también podría ser coherente con la hipótesis de la relación entre empatía, regulación emocional y agresividad[37], ya que si las personas con baja empatía se enganchan atencionalmente con las expresiones de ira podrían tener mayores dificultades para regularse emocionalmente y generar, posteriormente, una respuesta de agresión.

Finalmente, los resultados en las medias de autorreporte no mostraron diferencias significativas entre grupos en ninguna de las dimensiones de la emoción (valencia, *arousal* y dominancia), lo que sugiere que la percepción de la experiencia emocional puede ser similar en personas con baja y alta empatía cuando observan rostros alegres, neutros y con ira, es decir, que se experimenta, por ejemplo, una valencia positiva ante los rostros alegres y aversiva ante los rostros con ira en ambos grupos. Sin embargo, la empatía es la capacidad para entender y experimentar una emoción en sintonía con la observada[3,4], por lo cual se requiere una experiencia emocional más precisa que solamente la

percepción de la valencia (apetitiva o aversiva), el *arousal* y la dominancia, por lo cual, las dimensiones de la emoción no son, necesariamente, indicadores precisos de empatía.

Los resultados del presente estudio deben analizarse tomando en cuenta varias limitaciones. Primero, solamente se estudiaron tres expresiones faciales (alegría, neutra e ira), por lo cual futuras investigaciones deberán analizar las posibles diferencias entre las demás emociones. Segundo, la muestra estuvo conformada por personas con baja y alta empatía, sin embargo, no hubo un grupo que estuviera ubicado en niveles intermedios de empatía, el análisis de este tercer grupo permitirá comprender mejor el procesamiento cognitivo de las expresiones emocionales. Finalmente, el estudio aborda la empatía afectiva como un solo constructo con dos polos (baja y alta), sin embargo, estudios recientes han propuesto que la empatía afectiva podría ser dividida en dos tipos (resonancia afectiva y disonancia afectiva)[38]. La primera hace referencia al concepto tradicional de empatía afectiva y la segunda a personas que sienten lo opuesto a lo que observan (p. ej., placer ante el dolor ajeno o rabia ante la felicidad del otro), futuros estudios podrán utilizar esta nueva forma de evaluar la empatía afectiva en conjunto con técnicas neurofisiológicas para investigar el procesamiento de rostros.

Conclusiones

En conjunto, los resultados del presente estudio sugieren que la empatía no tiene un efecto en la respuesta de atención inicial ante los rostros humanos (P100), sin embargo, sí tiene un efecto sobre el reconocimiento de las características del rostro (mayor N170 en personas con alta empatía). Finalmente, las personas con baja empatía generan mayor enganche atencional (mayor LPP) hacia las expresiones de ira.

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Conflicto de intereses

Los autores declararan no tener conflictos de interés.

Responsabilidades éticas

Protección de personas y animales. Los autores declaran que los procedimientos seguidos se conformaron a las normas éticas del comité de experimentación humana responsable y de acuerdo con la Asociación Médica Mundial y la Declaración de Helsinki.

Confidencialidad de los datos. Los autores declaran que en este artículo no aparecen datos de pacientes.

Derecho a la privacidad y consentimiento informado. Los autores declaran que en este artículo no aparecen datos de pacientes.

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RESEARCH ARTICLE

A multidisciplinary clinic for amyotrophic lateral sclerosis patients in Northeast Mexico

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Abstract

Amyotrophic lateral sclerosis (ALS) is a late-onset neurodegenerative disorder characterized by rapid deterioration and selective death of motor neurons (MNs) in central nervous system. There is no effective therapy for ALS patients. Riluzole, only slightly delays disease progression. Edaravone was FDA approved as an intravenous therapy, however, this drug is expensive and has been applied in few cases in our country. There is compelling evidence patients who attend an ALS multidisciplinary clinic experience improved survival. An ALS multidisciplinary clinic was launched in our institution and adapted to our healthcare system. It is described the processes involved in the evaluation of patients in an all day long session where ALS patients are evaluated by several professionals from different specialties specially trained in the needs of subjects living with this disorder. We consider that this model of healthcare for patients with ALS may be useful in another healthcare institutions in our country.

Key words: *Amyotrophic lateral sclerosis. Multidisciplinary clinic. Mortality. Survival.*

Clínica multidisciplinaria para pacientes con esclerosis lateral amiotrófica en el Noreste de México

Resumen

Esclerosis Lateral Amiotrófica (ELA) es una enfermedad neurodegenerativa caracterizada por rápido deterioro y muerte selectiva de neuronas motoras en el sistema nervioso central. No existe tratamiento efectivo para los pacientes con ELA. El Riluzole solo prolonga discretamente la sobrevida. El Edaravone aprobado por la FDA como tratamiento intravenoso, es costoso y solo ha sido utilizado en algunos pacientes en nuestro país. Existe evidencia en los últimos años que el manejo multidisciplinario de los pacientes con ELA mejora la sobrevida. En nuestra institución efectuamos la apertura de la clínica multidisciplinaria para ELA. Describimos los procesos involucrados en la evaluación de los pacientes en una sesión durante todo un día, donde los pacientes son evaluados por médicos de diferentes especialidades y con entrenamiento en la evaluación de pacientes con ELA Consideramos que este modelo de atención para el cuidado de los pacientes que sufren este trastorno neurológico es útil y podría ser aplicado en otras instituciones del sector salud de nuestro país.

Palabras claves: *Esclerosis lateral amiotrófica. Clínica multidisciplinaria. Mortalidad. Sobrevida.*

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Introduction

Amyotrophic lateral sclerosis (ALS) is a late-onset neurodegenerative disorder characterized by rapid deterioration and selective death of motor neurons (MNs) in cerebral cortex, brain stem, and spinal cord.[1,2] Clinical features are attributable to the superimposition of motor deficit occurring by damage in upper motor neurons (UMN) and lower motor neurons (LMN). Motor phenotypes are highly heterogeneous and defined by, 1) the body region of onset; 2) the relative mix of UMN and LMN involvement; and 3) the rate of progression.[3] According to different series, mean survival of ALS patients ranges from 15.7 months to 47 months after presentation.[4-7]

At present, there is no effective therapy for ALS patients.[6-10] Riluzole, until recently was the only medication approved by the FDA. However, this drug only slightly delays disease progression.[3,6,7] Two years ago Edaravone was FDA approved as an intravenous therapy for ALS patients.[11] However, this drug is expensive and so far, has been applied in very few cases in our country. Non-invasive ventilation (NIV) confers a survival and quality of life benefits in patients with ALS. It remains unclear whether gastrostomy improves survival, as there have been no randomized controlled trials.[9]

Multidisciplinary clinic has been settled in a number of countries (Ireland, Holland, Italy, England, USA). There is compelling evidence that those who attend in a multidisciplinary clinic experience improved survival.[9-14] The processes by which survival advantage is conferred remain unclear. Services through a network clinic, did not demonstrate a survival benefit for ALS patients attending or being referred to a centralized clinic.[9] In our country, the common clinical approach to patients with ALS provided by the social security system is through network clinic and referred to a second or third level hospital to be evaluated and managed by neurologist without multidisciplinary health care team of professionals trained in the needs of ALS subjects.[6,7] In the private healthcare system, usually patients suffering of motor neuron symptoms are initially evaluated by a general practitioner, orthopedist and traumatologist and finally those patients are sent to a neurologist that usually request other healthcare specialists (neurophysiologist, respiratory therapist, physical therapist and neuroradiologist) to establish the diagnosis of definite ALS and suggest and initial management. However, an appropriate follow-up by a multidisciplinary health care team is usually missing. In Mexican population, it has been reported that the mean interval between clinical onset to clinical diagnosis is 13.9 months (ranges from 1 to 42 months) including ALS patients evaluated in social security system and in private practice healthcare system.[6]

Primary ALS clinic

The school of medicine and the Hospital San Jose of the Tecnológico de Monterrey started in 2005 an ALS care clinic for the evaluation and management of patients with ALS. At that time, in this care clinic participated a neurologist with specialist expertise in ALS, a psychologist, two residents of the neurology residence program, two neuroscience researchers and one pulmonary physician. Since information about demographic characteristics of Mexican ALS patients was lacking, after this clinic commencement, we settled a population-based epidemiological study to define the clinical and demographic characteristics of Mexican ALS patients.[6] Referred and interested patients with motor neuron disease were evaluated between June 2005 and May 2010. Patients who were born and were residing in Mexico were included in a retrospective and longitudinal study. From 141 patients that were evaluated in that period, 85 were Mexicans and only 65 of them fulfilled the El Escorial clinical and neurophysiological criteria for definite ALS. Two cases (3.3%) were classified as having familial ALS (fALS). Most of the Mexican patients (65%) came from regions with the highest socioeconomic status.[6] The explanation for this finding was related to the location of this ALS clinic into a private hospital. After this information was obtained, we started to progress this clinic to the concept of multidisciplinary care model for ALS subjects and adjust our benchmark approach to patients with ALS.

Healthcare system in Mexico

There are three healthcare systems in Mexico: 1) the social security system subsidized by workers, entrepreneurs and government funding; 2) the ministry of health system includes hospitals and academic institutions including national institutes of health that are supported by federal and state government contributions; and 3) the private healthcare system including hospitals and outpatient´s clinics held by private insurance companies, private insurance service providers and payment capacity by individuals. Services through a network clinic in these systems usually referred patients with possible ALS or motor neuron disease to a third level of attention hospitals for evaluation by neurologist, so far, our country did not have multidisciplinary clinic for ALS patients.

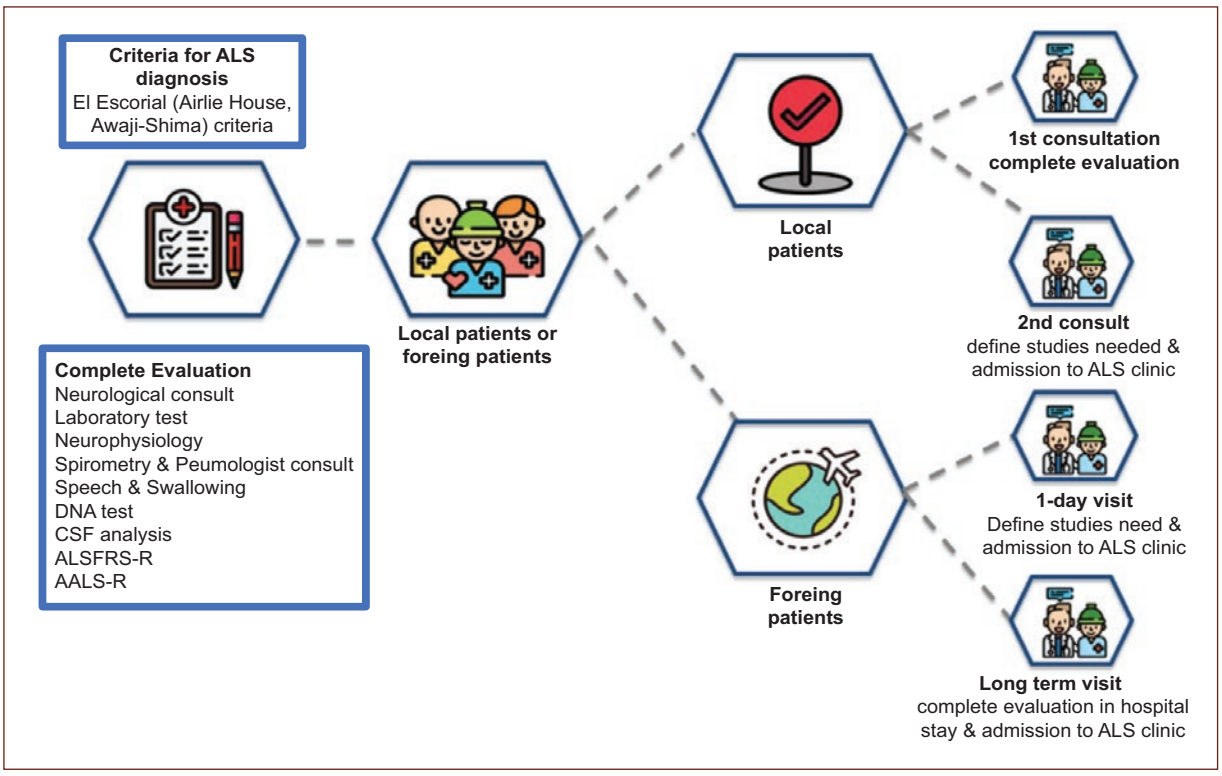

Figure 1. A schematic representation of ALS multidisciplinary clinic at Neurology and Neurosurgery Institute, TecSalud at the Tecnológico de Monterrey. ALSFRS-R: ALS Functional Rating Scale Revised, AALS-RS: Appel ALS Rating Scale.

Multidisciplinary ALS clinic

The multidisciplinary health care model for ALS incorporates professionals specially trained in the needs of subjects living with this disorder, allowing them to receive care from each discipline during a single visit. The care team involves a neurologist, physical therapist, occupational therapist, respiratory therapist, nurse, dietitian, speech language pathologist, social worker and mental health professional. There are a number of multidisciplinary ALS clinics in USA that are ALS Association Certified Treatment Centers of Excellence.[14] In European Union there are also a number of countries having multidisciplinary clinics for ALS patients including Ireland, Holland, Italy, England, Switzerland, Portugal, Belgium and other European countries.[8-10,12] In USA since 1998, the ALS association´s national network of Certified Treatment Centers of Excellence has provided the evidence-based system for the multidisciplinary ALS care centers. Each ALS clinic must meet the ALS Association's clinical care and treatment standards, which are based on the American Academy of Neurology practice parameters, more than one hundred ALS clinics are certified in USA.[14]

After Dr. Stanley Appel invite us for attending his ALS multidisciplinary clinic in the neurology service at the Methodist hospital in Houston Texas USA, we witnessed the processes involved in the evaluation of ALS patients in the first ALS multidisciplinary clinic started in USA during the last century. After this visit, we acquired from Dr Appel the methodology to establish an ALS multidisciplinary clinic in our institution according to our private healthcare system. We consider to establish a model of health care that may be also useful in the social security system and ministry of health system in Mexico. Dr. Appel ALS multidisciplinary clinic has a team of 21 professionals from 11 specialties that are attending ALS patients in an all day long session at least 6 hours duration once a month. ALS patients are evaluated by several professionals from different specialties.

TecSalud ALS multidisciplinary clinic

During the last year we started working in adapt our healthcare system to an ALS multidisciplinary clinic as a care model for ALS patients useful to our institution as well as to other institutions and hospitals in our country. Since patients suffering of motor neuron symptoms or

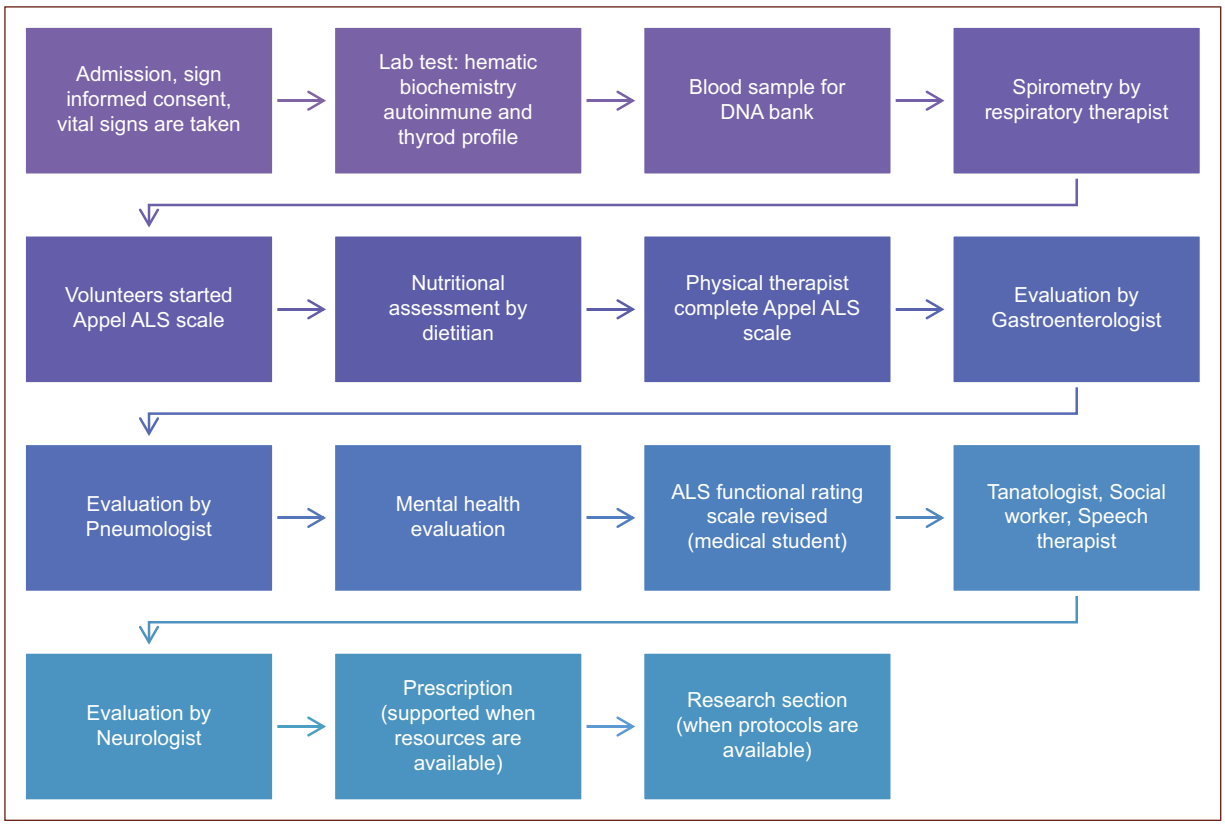

Figure 2. Patient flow diagram attending the TecSalud ALS Multidisciplinary Clinic.

definite ALS are sent to our institution from our location, other states of Mexico and abroad, we decided to present different options for evaluation patient from our location (local) outside or abroad (foreign) (figure 1). However, a complete evaluation is required to establish the diagnosis of definite ALS according to El Escorial (Arlie House and Awaji-Shima) clinical and neurophysiological criteria. Patients with ALS are sent to TecSalud ALS Multidisciplinary Clinic that are evaluated in half a day session every three months. The patients are assessed by a team of 14 professionals (Physical Therapist, Speech Therapist, Dietitian, Psychologist, Mental Health, Gastroenterologist, Pneumologist and Neurologists) from 8 specialties. Six volunteers participate accomplishing upper extremities muscle strength items from the Appel ALS scale.[15] Fifteen medical students collect demographic information, collect samples to the DNA blood bank, help physicians from different specialties in the evaluation of patients and in fulfilling the ALS functional rating scale revised. The participation of senior students of the school of medicine at the Tecnológico de Monterrey under supervision from professionals specially trained in the needs of subjects living with disorder, help them to learn about diagnostic approach and follow up of ALS patients. The patients follow a pre-established order (figure 2).

During the present year (2019) the ALS multidisciplinary clinic performed four sessions. Thirteen patients were evaluated in the first session, 18 ALS patients in the second and third sessions and 20 patients in the last one. A total of 69 evaluations have been performed in 28 patients with definite ALS patients attended these four sessions at the TecSalud ALS multidisciplinary clinic. There were 11 females (age ranges 40 to 72 years, mean of 55.6 years old) and 17 males (age ranges 39 to 68 years mean of 58.7 years old). The patients came from different states of our country including Nuevo Leon, Coahuila, Tamaulipas, Jalisco, Zacatecas, Guanajuato and Baja California. The total costs of each session was supported by TecSalud and the physicians participating in the ALS multidisciplinary clinic, did not receive remuneration.

Conclusion

In conclusion, since there is no effective therapy for ALS patient[6] and the compelling evidence indicates that those patients who attend an ALS multidisciplinary clinic

experience improved survival[8-10,12-14]; an ALS multidisciplinary clinic has been settled in our institution. To our knowledge, this is the first ALS multidisciplinary clinic in Mexico. The processes by which survival advantage is conferred by this multidisciplinary approach remain unclear.[8] We consider that the survival improvement may be due to an early and appropriate nutritional and respiratory support established by professionals specially trained in different disciplines applied to the needs of ALS subjects. Our ALS multidisciplinary clinic adapted to our own healthcare system may be useful in another healthcare institutions in our country, adequate to improve life expectancy and quality of life in patients suffering of ALS.

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None.

Conflicts of interest

There are no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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REVIEW ARTICLE

Teaching neurology to "Millennials:" Basic concepts and recommendations

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Abstract

The generation currently studying medical specialization programs belongs to the so-called "Millennials". The characteristics of this generation provoke the need for a change or adjustment in the paradigm of the traditional teaching-learning environment. The objective of this review is to reaffirm some concepts about the main current models of teaching and learning, as well as certain techniques with the potential to benefit the learning of the current generation of medical specialty residents including the use of information and communication technologies. The concepts described include Bloom's taxonomy, Miller's pyramid, Dreyfus, skills acquisition, competency-based education model, active education and passive education, and evaluation recommendations. The revised strategies include flipped classroom, resident as teacher, resident as researcher, as well as the incorporation of technologies to it. The teacher-student dyad in medical specialties is characterized by a particular dynamic, in which the specific objective is the generation of new competent and professional doctors. Optimizing the teaching-learning environment according to the characteristics of the current generation is essential to achieve this goal.

Key words: *Teaching. Learning. Neurology. Millennials. Education.*

Enseñando neurología a los "Millennials": *Conceptos básicos y recomendaciones*

Resumen

La generación que actualmente cursa los programas de especialización médica pertenece a la denominada como "Milennials." Las características propias de dicha generación generan la necesidad de un cambio o ajuste en el paradigma del ambiente de enseñanza-aprendizaje tradicional. El objetivo de la presente revisión es reafirmar algunos conceptos sobre los principales modelos vigentes de enseñanza y de aprendizaje; así como de ciertas técnicas con el potencial de beneficiar el aprendizaje de la generación actual de residentes de especialidad médica incluyendo el uso de tecnologías de la información y comunicación. Los conceptos que se describen incluyen la taxonomía de Bloom, pirámide de Miller, adquisición de habilidades de Dreyfus, modelo de educación basado en competencias, educación

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activa y educación pasiva y recomendaciones sobre la evaluación. Las estrategias revisadas incluyen clase invertida, residente como profesor, residente como investigador, así como la incorporación de tecnologías a la misma. La diada profesor-estudiante en las especialidades médicas se caracteriza por una dinámica particular en la que el objetivo específico es la generación de nuevos médicos competentes y profesionales. El optimizar el ambiente de enseñanza-aprendizaje de acuerdo con las características propias de la generación actual es indispensable para lograr este objetivo.

Palabras claves: *Enseñanza. Aprendizaje. Neurología. Milennials. Educación.*

Introduction

A generational cohort consists of people of approximately the same age who share specific socio-historical experiences and who differ from those lived by groups that preceded or followed[1]. The "Generation Y" or "Millennials," those born between 1979 and 1994[2], have been stereotyped as self-centered, demotivated, disrespectful, and disloyal. On the other hand, this generational cohort also possesses a unique set of well-identified qualities[3]. Among the positive attributes of this generation are the tendency to work as a team, optimism, greater civil awareness, a desire for immediate access to technology, and efficiency[4].

According to the population pyramid of the National Institute of Statistics and Geography (INEGI), the "Millennials" represent around 35% of the Mexican population and many of them are already part of the country's workforce.

In the current context of postgraduate medical education, there is a coexistence between at least three generations, "Baby Boomers" (1946-1964), "Generation X" (1965-1978), and "Millennials." The next generation, the "Centennials" or "Generation Z" will be incorporated in the coming years.

Medical specializations are governed by a curricular plan called the Unique Medical Specialization Plan (Plan Único de Especializaciones Médicas [PUEM]), which defines the purposes to which academic action should be directed and the strategies to achieve its objectives. The PUEM contemplates that the student must dedicate 40 h/week for the realization of the academic activities (subjects) that comprise it and a minimum of 15 h/week of individual study. The specialty of neurology is considered to be usually 5 years long (2 years of internal medicine and 3 years of neurology) and the academic load is distributed as follows: healthcare work 7280 h (980 credits), medical care seminar 690 h (85 credits), research seminar 460 h (60 credits), and education seminar 230 h (30 credits). That is, 92.5% of the hours are dedicated to medical care, 5% to research, and 2.5% to education. The PUEM proposes an active teaching methodology focused on problem-solving.

The objective of this review is to reinforce some basic concepts of the teaching-learning process and competency-based learning and to suggest some specific teaching and evaluation models and techniques applicable to the field of neurology with particular emphasis on the generation of Millennials.

Bloom's taxonomy

The development of a curricular program has as its cornerstone the definition of the objectives. Since 1956, Benjamin Bloom and collaborators established a classification for the different objectives and skills that the teacher seeks to convey to his students. This classification of learning domains, better known as Bloom's taxonomy, is made up of three dimensions: affective, psychomotor, and cognitive. In turn, each of these dimensions or domains has different levels, which are hierarchical in nature, thus defining lower-order and higher-order levels[5].

The cognitive domain starts from the fact that it is first necessary to learn and remember the concept and then understands it. Once this is done, it is possible to apply this concept in an analysis, to finally evaluate an impact and generate a new product or result. A contribution of this taxonomy is the differentiation in the use of verbs as indicators of the objective.

The original classification has undergone several revisions as a reflection of the evolution and changes in educational theories. The 2001 revision stands out for the change from noun to verb to name the different categories and the inversion of the sequence of the last two higher-order levels[6].

Figure 1 shows Bloom's taxonomy and some examples of the verbs suitable for each level assessment. More recently, Bloom's taxonomy has been integrated with the Substitution, Augmentation, Modification, and Redefinition (SAMR) system; the latter is a model whose purpose is to facilitate the integration of Information and Communication Technologies (ICTs) in

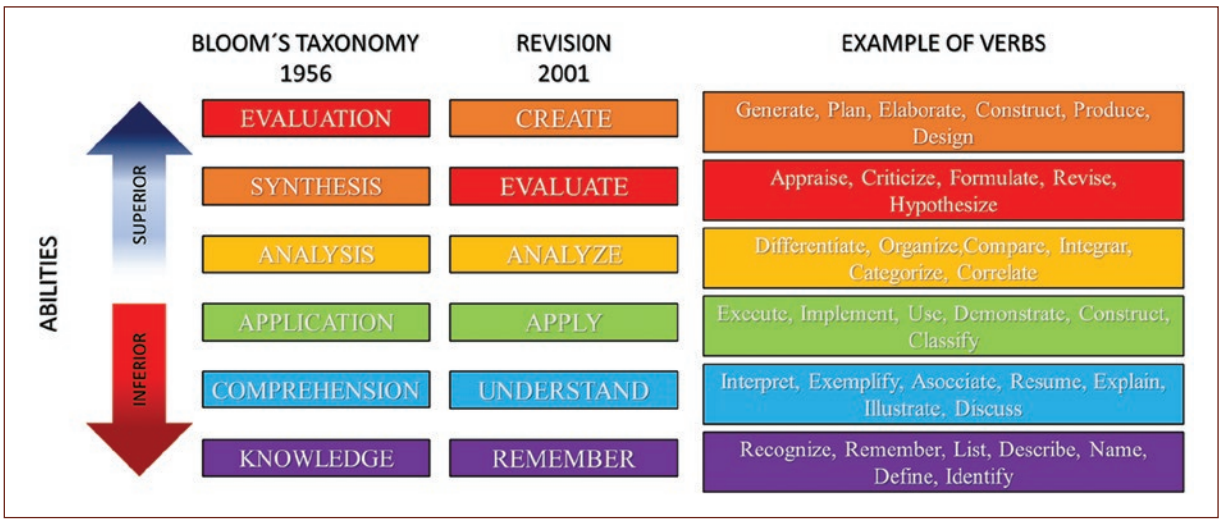

Figure 1. Bloom's taxonomy and examples of the verbs suitable for each level assessment.

education and will be described in greater detail in the corresponding section.

Miller's pyramid

The PUEM refers to the Miller pyramid as an integral part. This model is used for the evaluation of clinical competencies. It consists of four levels; two lower levels "Know" (knowledge) and "Know How" (describe) and two higher levels "Show how" (simulation) and "Do." Based on this categorization, a student can be classified as a novice or as an expert. Miller's pyramid, although useful, only includes knowledge and operational aspects, leaving aside other characteristics of competencies such as attitude and values. Recently, adjustments have been proposed to cover domains not evaluated[7]. At present, the evidence regarding the usefulness of this model in medical education is limited.

Dreyfus model of skill acquisition

A third approach uses the Dreyfus model of skill acquisition. The Dreyfus model consists of five levels: novice, advanced beginner, competent, proficient, and expert. However, when applying this model to medicine, the first two levels correspond to an undergraduate student, the third level to the resident, the fourth to the newly graduated specialist, and the last to the professional in the middle of his career. Perhaps, one of the most relevant limitations of this model is that the expert level works primarily on intuition and not on reasoning[8].

Kirkpatrick Model

The Kirkpatrick Model is used specifically for analyzing and evaluating the results of training and educational programs, thus making it suitable for neurology training assessment. It is based on four levels: Level 1 – reaction which measures how the student reacts to the training serving as a surrogate of satisfaction; Level 2 – learning analyses not only knowledge but also skills; Level 3 – behavior assesses if the training reflects in changes in how the student behaves; and Level 4 – results determine if the impact on the overall learning program and even on the organizational outcomes, the Kirkpatrick Model has been used extensively in medical education[9].

Competency-based education model

Competency-based education is a model that prioritizes knowledge learning and skills development without established time goals. That is, this model emphasizes how much students learn (learning-based system) instead of how long it takes to learn such knowledge and skills (time-based system)[10]. The foregoing still contrasts with the European Directive 2013/55/EU of Recognition of Professional Qualifications that still consider that the basic training of the doctor must consist of at least 5 years and a minimum of 5500 h of theoretical and practical teaching; parameters have not changed in the past 15 years.

In the field of medical education, there is no clear definition; however, there is consensus that the competence of the doctor must be multidimensional, dynamic,

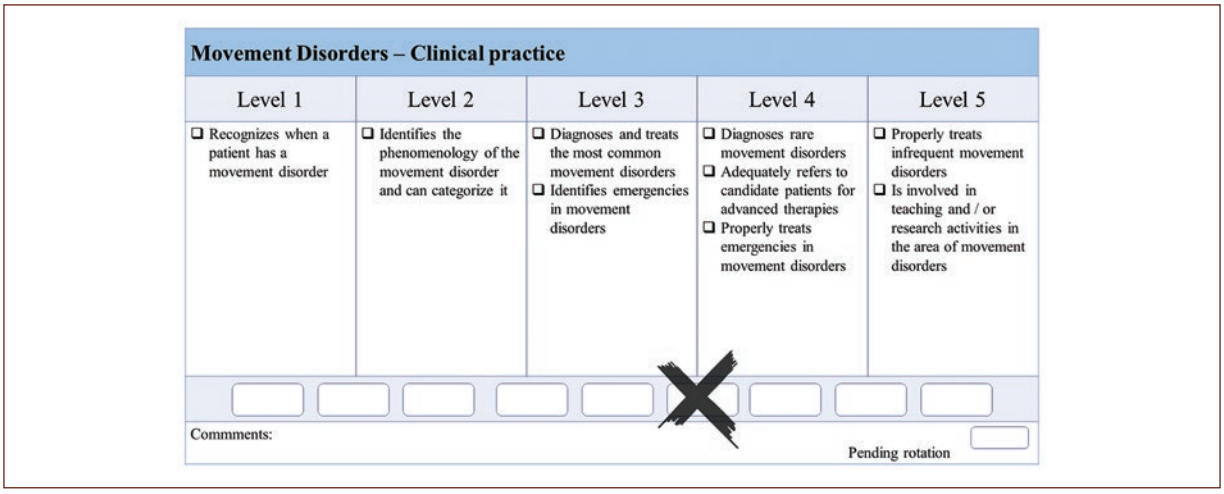

Figure 2. Example of competency-based education assessment through the use of milestones.

and contextual. The initial change in this education paradigm is to replace the question "What should the resident know?" To "What skills does the resident require?" Once these skills have been identified, the competencies (and their components) must be explicitly defined, set goals throughout the process as a reference, select the appropriate educational activities and methods, and design the instruments to assess the outcome. The Accreditation Council for Graduate Medical Education (ACGME) of the United States requires six basic competences: (1) medical knowledge, (2) patient care, (3) interpersonal communication skills, (4) professionalism, (5) practice-based learning and improvement, and (6) system-based practice[11]. These skills focused on neurosciences are in the curriculum of the American Academy of Neurology[12].

On the other hand, this same Accreditation Council has tools to evaluate the quality of the programs in different specialties through the fulfillment of milestones. The system consists of five levels; the teacher selects whether the resident already has the competencies of each level or is in the process of acquiring them[13]. Figure 2 shows the general goals for movement disorders as an example.

Active education and passive education

Broadly speaking, learning methods can be divided into passive and active. Passive learning is one that occurs when listening to the expert gives a lecture or conference. In this scenario, the resident does nothing but listen (convergent thinking). In active education, the teacher facilitates interaction and discussion (divergent thinking); the above empowers and motivates students resulting in a better learning process.

Within the active teaching strategies, the method called problem-based learning (PBL) has been the one that has traditionally been used in medicine. The problem-based method promotes critical thinking and communication skills and is useful when you have a small number of students[14]. At present, this is the method described in the PUEM. An alternative is the method called team-based learning (TBL); this method is more structured and is appropriate when you have a significant number of students as it works through creating small work teams. The TBL consists of three phases or modules: preparation before class (reading of pre-assigned material), assurance of learning (multiple-choice examination), and application of the concepts analyzed (discussion and consensus). This method has also demonstrated better academic performance and greater learning compared to the passive method[15]. Recently, it has been suggested to use a combination of both methods[16].

It is well recognized that Millennials are characterized by changing the focus of their attention if they are not interested in the subject. Therefore, active learning methods are the best choice.

The "flipped classroom"

Millennials are characterized by collaborative work, familiar with technology and driven by feedback. This is why the flipped classroom has been suggested as the ideal model to teach residents of this specific generation[17].

The educational model known as "flipped classroom" is to reverse the traditional teaching of sessions or classes. The time devoted to this activity should not focus on teaching a class based on textbooks or review articles, but rather focus on clarifying points of confusion, explaining the main concepts, and even encouraging the application of these concepts in hypothetical clinical settings. For this, it is required that residents complete basic learning at home beforehand. This model has been shown to improve levels of satisfaction while maintaining at least the same levels of knowledge acquisition as traditional methods[18].

More specifically, the flipped classroom educational model focuses on the development of higher-order thinking skills. Based on the Bloom's taxonomy described previously, this model privileges the levels of analyzing, synthesizing, and evaluating. In comparison, in the traditional model, the teacher transmits the knowledge to the residents during the class (lower-order levels knowledge and understanding), and the learning is passive. The resident is then responsible for developing skills individually and without home orientation that corresponds to the higher levels of applying, analyzing, evaluating, and creating. In contrast, in the flipped classroom model, the resident acquires knowledge at home asynchronously and at his own pace, while in class, jointly develops higher-order skills with the teacher.

From the point of view of the operatic program of a residency course, its content must be identified asynchronously. Conventionally, it is recommended that this knowledge is acquired through the reading of textbooks in a programmed way; however, it is currently necessary to include digital media such as blogs and podcasts previously identified by the tutor. Once this content is established, class sessions may follow a model of PBL, TBL, or audience response system.

On the other hand, it is recommended that the lectures or presentations given by the teacher are not to be completely eliminated; however, the objective is not to present the existing information in textbooks or review articles but to cement the knowledge that residents obtained asynchronously. It should be considered that only 5% of the material received at a lecture is properly retained and that the attention span is only about 15-20 min[19]. Therefore, it is suggested to divide the presentations into 15 min of class and 30 min of active learning[20]. For example, the Anesthesiology Program at Stanford University replaced the traditional 45 min classes at seven in the morning with 15 min classes supported with slides 3 times a week; the result was an increase in the quality of education[21].

At the undergraduate level of medicine, this model has been successful[22], although there are still some controversies as to whether the entire curriculum should use this model. A recent study showed that approximately 20% of students believe that 50% traditional model and 50% flipped classroom would be ideal; however, almost 70% of them felt that attending classes to review knowledge acquired at home should not be mandatory[23].

The PUEM contemplates the seminar modality focused on individual study and inquiry and analytical discussion in peer groups, for subsequent reflection. As previously mentioned, traditional classes are no longer considered very useful; however, a viable option is the update in the form of imparting them. Since Millennials prefer a less formal learning environment and appreciate interaction, it is advisable to use tools to include activities that required the participation of residents during presentations. There are free tools such as Google Forms or Pear Deck that can be integrated into PowerPoint presentations, Keynote, or Google Slides and provide results in real time.

Resident as teacher

It should not be forgotten that the word doctor comes from the Latin *docere*, to teach. That is, why another of the requirements of the ACGME is that the development of residents as educators is encouraged. The "resident as teacher" programs have been identified as such since the 1970s. However, the parameters to define its effectiveness have not been studied specifically until recently. In general, the benefits are both for students, usually medical students or residents of lower academic hierarchy, and for the resident who serves as a teacher[24]. In fact, a study conducted between 2007 and 2010 showed that the evaluation of medical students on a clinical rotation depends mainly on academic interaction with residents[25].

Feedback to residents about their ability to transmit knowledge to their peers is also relevant. One study showed that 94% of residents rated the feedback received immediately as very useful, and 91% of them mentioned that such feedback would impact the way they gave their presentations. The recommendations focused on the amount of content, focus on clinical reasoning, the use of visual support, and encouraging interaction[26].

The PUEM establishes time requirements that are equivalent to only 2.5% of the training; however, it is suggested to favor this role given the evidence

presented. In the case of the specialty in neurology, there are usually 1st year and 3rd year residents, to whom are added rotating other specialties, interns, and even students resulting in large groups. However, if the number of students is very small, the tutelary model can be favored.

Resident as researcher

As previously mentioned, medical specialty courses are also intended to involve the specialist in research. A fundamental part of this is the publication of scientific articles in peer-reviewed journals. It has been shown that 75% of residents who published an article during their training will continue publishing later. In contrast, only 55% of residents who did not publish during their residency published after the end of their residency[27]. Moreover, 71% of residents of curricular programs that actively contemplated research published compared to only 41% of programs focused solely on traditional education of knowledge and skills. In general, residents who published one or two articles during their training increased their number of publications to seven after the end of their residency. Another study conducted in urology residents of Canada reported that 94% had at least one publication during their residency, the average being four publications. However, 44% of them reported that publishing did not improve their competence in this area mainly due to issues such as lack of time and attention by a mentor and poor active participation in the investigation[28]. In the United States, a study of surgical residents graduated between 1993 and 2013 reported that 54% of residents had published at least one article as the first author. In addition, there was an increase of twice as many publications per resident as of 2003[29]. Finally, a study conducted at the Mayo Clinic from 2006 to 2012 found that the number of original articles published and the total number of publications during residency predicts better clinical performance not only in skills assessments such as the MiniCEX but also in the examination of knowledge of the corresponding specialty board[30].

Based on the above, specific programs have been developed. For example, the Penn State Hershey Medical Center Academic Resident Project contemplates the following actions: during the 1st year of residence, the resident is assigned a mentor (associate or principal professor) and a counselor (another faculty member) with whom a research project is chosen and the proposal is written. During the 2nd year, the project is completed and in the 3rd year, its results must be presented in the form of a manuscript that can be published along with a 10 min oral presentation[31].

A study in otorhinolaryngology residents showed that the implementation of a schedule restriction at a maximum of 80 h/week along with two rotations of 20-24 weeks in research resulted in the increase of one to five publications per resident[32]. The PUEM requires the preparation of a thesis as a termination requirement; it should be noted that in general, it is expected that around 30-40% of the specialty theses will be subsequently published as an original article[33].

On the other hand, it has been reported that < 30% of the papers presented at congresses by residents end up with the publication of an article in extense[34]. Finally, the previously cited studies agree that publishing during residency doubles the likelihood that the resident will be integrated into academic and research activities in the future. It is worth mentioning another of the Millennials stereotypes, not staying in the same job. In this regard, it has been shown that they are effectively better prepared for changes in their occupational area; however, this does not happen for those with high levels of education such as postgraduate studies[35]. Therefore, encouraging the continuation of studies with masters or doctorates in research can increase job stability.

A final aspect to consider in relation to publications is ethics. Millennials show a high concern for ethics and a search for role models. It has been reported that up to 57.3% of publications made by residents included an honorary authorship, euphemism for gift authorship. That is, more than half of the publications include coauthors who do not meet the international criteria to be recognized as such[36]. The above can subtract the interest of residents in the investigation and dissemination of it, so the teacher must always show an impeccable ethic. The PUEM only requires 5% of the total program time allocated to this activity; however, the benefits described justify a greater dedication to this area.

Assessment and evaluation of skills

Conventionally, the evaluation of skills is carried out through different methods, including the direct observation of procedural skills (DOPS) and clinical evaluation exercises (MiniCEX). The DOPS evaluates the resident while performing diagnostic and treatment procedures in clinical practice. The evaluator uses a structured checklist. In the MiniCEX, the resident's skills, attitudes, and behavior are evaluated before a routine clinical encounter with an approximate duration

of 15 min. It should be noted that the MiniCEX has shown a very good correlation with the Objective Structured Clinical Examination (OSCE), where knowledge, skills, behaviors, and attitudes are evaluated throughout a series of stations with different clinical scenarios[37]. Since the OSCE requires more time and resources, the MiniCEX is an acceptable option. In addition to the relative brevity of the assessment, the MiniCEX as well as the DOPS require that immediate feedback be offered to the resident. In the specific case of neurology, both instruments have proven useful[38].

Other methods include multi-source feedback (MSF or 360° evaluation) in which professionals working with the resident answer a structured form. In the case of Millennials, it is important to remember that it is a generation with a history of success, achievements, and self-confidence; as a result, they are accustomed to positive feedback. On the other extreme, the generations that precede them grew with the maxim "if there is no news, it is good news."

The methods mentioned above differ from formal written examinations where it is only possible to evaluate knowledge. In addition, formal oral examinations are characterized by poor content validity, high inter-rater variability, and grade inconsistencies[39].

Another recommended method for assessing skills is called Reporter, Interpreter, Manager, and Educator. At the reporter level, the resident is expected to be able to interrogate and explore, as well as present the clinical findings. At the interpreter level, it is expected to be able to use clinical reasoning, analyze, and prioritize differential diagnoses. At the manager level, the resident must generate reasonable patient-centered treatment options; finally, at the educator level, he is able to contribute to the education of patients, family members, and other members of the medical team[40].

Designing questions for evaluation

When generating the questions for evaluations, the six levels of Bloom's taxonomy should be considered: knowledge, understanding, application, analysis, synthesis, and evaluation. It should be considered that this taxonomy is hierarchical and that the terminology used corresponds to a level of complexity of the educational objectives. There are studies that compare performance among those who use the flipped classroom model or the traditional lecture model; some of them show superiority of the first[41], while others have shown no difference, including a study in a neuroanatomy course[42]. A recent study suggests that the difference or absence of this is related to the development of the questions since if there is no concordance between the question and the Bloom's level that is expected to evaluate. Thus, the results will be inadequate[43]. In summary, if the objective is to evaluate the flipped classroom model, questions aimed at higher-order levels should be used. On the other hand, if the model is traditional, a better evaluation will be obtained using questions directed at lower-order levels.

ICT

To properly understand the role of ICT, the concepts of synchronous and asynchronous formats must be defined. These terms are related to the online learning method used for educational materials and virtual training, included in courses, diplomas, masters, and doctorates. The above are encompassed under the term of e-learning. Broadly speaking, synchronous learning occurs when students and teachers are online while respecting pre-established schedules and duration times. The asynchronous one allows the student to access the didactic material when it suits him best, without restrictions of schedule or duration (although there are deadlines). Residents have been shown to prefer the asynchronous format over the synchronous in relation to e-learning, even placed alongside the traditional face-to-face class format[44]. The ACGME recommends that the program includes a combination of synchronous and asynchronous learning. The asynchronous component should cover at least 20% of the program and ideally should be monitored through a learning management system as described below[45].

The second aspect to consider is that with the involvement of ICTs in education, it has been necessary to establish new frameworks to guide the educator. The most recent model is the SAMR. It is a hierarchical model; the two lower levels are called potentiation and include substitution and augmentation. The upper two levels correspond to transformation and include modification and redefinition[46]. For example, at the substitution level, it is only necessary to change paper examination to one in digital format. On the augmentation level, electronic devices are used to improve the educational experience. At the modification level, a redesign of the way in which the material is presented (interactive simulations) is required, and in the redefinition level, new tasks are created that would result impossible to perform without the use of ICT.

Millennials are the first generation considered as digital natives, that is, they were born and grew up in a digital environment. At the same time, the Millennials

seek flexibility in their schedules to reach the balance between life and work. The above facilitate a paradigm shift of reserving learning moments only for scheduled sessions or during clinical activities as a visit step or outpatient consultation. The use of technology in smartphones or tablets such as messaging systems and social networks allows the delivery of brief and timely information at any time of the day. This can be done spontaneously or in a pre-established way. This information can be images or videos of quick visualization. A recent study evaluated the effect of using Twitter as part of a medical residency program in internal medicine. The authors created a specific account which was managed by two of the professors, as well as by the chief resident. The content of the publications was established in thirds: education of the residents, promotion of academic activities of the program, and promotion of other events. At the end of the academic year, 69% of residents indicated that this tool generally improved their medical education[47].

Another option is text messages or short message service (SMS). A study in urology residents compared learning through traditional classes compared to questions sent through SMS. Final grades and the level of satisfaction with learning were higher with the SMS method[48]. Recently, studies on the usefulness of other messaging systems such as WhatsApp have been published. The Duke Cardiology Program implemented a "WhatsApp group," in which clinical cases of interest and images were published under teacher supervision. About 66.7% of the students in the program participated actively and 85.7% said that the platform enriched the teaching process[49]. It is worth mentioning that the use of this platform was based on four rules: "what happens in WhatsApp, stays in WhatsApp," there is no consequence for wrong answers, it is only used during working days and hours, and there is a maximum of five cases per day to avoid fatigue in interactions.

Finally, the use of ICT with all its potential necessarily requires a platform for learning management system, generally known as LMS. The LMS allows to administer, distribute, and evaluate training activities. LMS costs for a residency or fellowship program can vary from free (Schoology) to hundreds of dollars per user (Blackboard, Canvas). However, on many occasions, academic or university institutions grant access to these systems (Moodle, Google Classroom). The National Institute of Neurology and Neurosurgery has its own LMN named as Neurocampus (www.neurocampus.cuaed.unam.mx), which through the LMS Moodle offers continuous medical education for its residents of specialty, subspecialty, and high specialty in virtual formats or mixed (blended education).

It is important to understand that it is currently considered that the responsibilities of the program to the resident and vice versa extend beyond the date of completion of the course. ICTs favor a learning ecosystem that allows these interactions to continue.

Conclusions

It should not be forgotten that generations are the product of the social environment, economic aspects, world and regional events, and technological changes, in which they grow. "Technological" generations such as Millennials and Generation Z require teaching-learning environments congruent with their needs. Diversity in educational models must be the norm, integrating multicultural talent. The models and techniques presented here are not exhaustive; the National University Autonomous University mandatory pedagogical training course for professors of medical specialties recommends additional tools such as assessment rubric, appreciation checklist, and portfolios. Recommendations on education for the high specialty courses have been also published elsewhere[50].

Mexico is an academic destination for the training of specialists, particularly from Central America and, more recently, from South America so that academic expectations force us to adopt modern teaching, learning, and evaluation models. Generation Y or Millennials are considered the generation with the highest level of education in history, and unlike Generation X, they tend to be more optimistic and literally believe that they can change the world. It is the responsibility of teachers to keep up to date in pedagogy and adopt the strategies with the highest probability of success to promote the development of skills and professionalization of their residents.

Declaration of conflicts of interest

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