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Manual for the Extrapyramidal Symptom Rating Scale (ESRS)

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Abstract

The Extrapyramidal Symptom Rating Scale (ESRS) was developed to assess four types of drug-induced movement disorders (DIMD): Parkinsonism, akathisia, dystonia, and tardive dyskinesia (TD). Comprehensive ESRS definitions and basic instructions are given.

Factor analysis provided six ESRS factors: 1) hypokinetic Parkinsonism; 2) orofacial dyskinesia; 3) trunk/limb dyskinesia; 4) akathisia; 5) tremor; and 6) tardive dystonia. Two pivotal studies found high inter-rater reliability correlations in both antipsychotic-induced movement disorders and idiopathic Parkinson disease.

For inter-rater reliability and certification of raters, $\geq 80\%$ of item ratings of the complete scale should be ± 1 point of expert ratings and $\geq 70\%$ of ratings on individual items of each ESRS subscale should be ± 1 point of expert ratings.

During a cross-scale comparison, AIMS and ESRS were found to have a 96% (359/374) agreement between TD-defined cases by DSM-IV TD criteria. Two recent international studies using the ESRS included over 3000 patients worldwide and showed an incidence of TD ranging from 10.2% (2000) to 12% (1998).

ESRS specificity was investigated through two different approaches, path analyses and ANCOVA PANSS factors changes, which found that ESRS measurement of drug-induced EPS is valid and discriminative from psychiatric symptoms.
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1. Introduction

Antipsychotics are a well-recognized treatment of schizophrenia, but the risks associated with their use require sensitive measures of drug-induced extrapyramidal symptoms (EPS) or drug-induced movement disorders (DIMD) (Chouinard, 2004). Parkinsonian

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symptoms interfere with cognition and social rehabilitation, and EPS resemble symptoms associated with psychotic illness: bradykinesia and facial mask resemble blunted affect and motor retardation; akathisia may be confounded with agitation, anxiety and insomnia; dystonias and dyskinesias with mannerisms and schizophrenic motor disturbances. Finally, both akathisia and tardive dyskinesia have been linked with suicide in schizophrenia (Margolese et al., 2001). Thus, because of the common features of EPS and schizophrenic symptoms, patients receiving antipsychotics need to be evaluated for treatment-emergent movement disorders by using one of the standardized rating scales such as the Extrapyramidal Symptom Rating Scale (ESRS) (Chouinard et al., 1980), AIMS (Guy, 1976) or Simpson–Angus (Simpson and Angus, 1970).

The ESRS was originally developed for epidemiological studies of tardive dyskinesia in schizophrenic outpatients on long-term classical anti-D_2 antipsychotic medications (Chouinard et al., 1979b, 1988) and first used in clinical trials in 1976 (Chouinard and Annable, 1976). Its sensitivity and validity was established through clinical trials with oral antipsychotics (Chouinard and Annable, 1982), depot antipsychotics (Chouinard et al., 1982, 1989), various antiParkinsonian drugs (Chouinard et al., 1979a,c, 1987; De Montigny et al., 1979), antimanics (Chouinard et al., 1983, 1985), various CNS drugs (Chouinard et al., 1977, 1978) and placebo (Chouinard et al., 1987; Chouinard, 1990). Since then it has been widely used in multi-center clinical research on antipsychotics (for example (Chouinard et al., 1993; Chouinard, 1995; Jeste et al., 2000; Meltzer et al., 2003)) and to differentiate schizophrenic symptoms from drug-induced EPS (Chouinard et al., 2002, 2003; Marder et al., 1997; Moller et al., 1995). ESRS Parkinsonism ratings were found to be significantly (but with a small magnitude) correlated with both negative symptoms and disorganized thought at baseline in the USA–Canada risperidone trials (Marder et al., 1997; Moller et al., 1995). But ESRS changes did not correlate with changes in clinical outcome following drug treatment as measured by PANSS (Marder et al., 1997). In other words, clinical improvement was independent from EPS changes as measured by the ESRS. Path analysis on ESRS also found that there is only a weak influence of EPS changes on negative symptom changes of schizophrenia (Moller et al., 1995). These two studies showed the validity and specificity of ESRS measurement of DIMD from psychotic symptoms during clinical trials of antipsychotic agents carried out in 1989–1990, the era of classical and atypical antipsychotics.

2. Definitions

2.1. Parkinsonism

Drug-induced Parkinsonism consists of motor disturbances, which include: tremor, impaired gait/posture, postural instability, rigidity, reduced facial expression/speech, and bradykinesia. Sialorrhea is no longer included in the present ESRS version since it is less relevant as a Parkinsonian symptom in the era of atypical antipsychotics.

2.1.1. Tremor

Tremor is either present at rest (labeled as a ‘resting tremor’, which frequently decreases with directed and purposeful movement) or may be accentuated by the patient’s posture or action (labeled as ‘postural tremor’ or ‘action tremor’, respectively, which, when severe, may interfere with feeding). Tremor is rhythmic, oscillates along an axis, and is either low in frequency (3–4 cpm) and high in amplitude, or high in frequency (10–12 cpm) and low in amplitude. Body parts involved include tongue, jaw/chin, lips, head, and upper and lower limbs. Pill rolling tremor (a classical Parkinsonian tremor present at rest) can occur after several years of antipsychotic drug treatment and looks as if the patient is rolling a pill between his fingers and thumb. It is understood that tremors observed in this population may originate from a variety of conditions such as familial idiopathic benign tremor, idiopathic Parkinson’s disease (IPD), or lithium toxicity.

2.1.2. Impaired gait/posture

Impaired gait/posture includes two aspects of Parkinsonian symptoms. Impaired gait manifests itself initially by decreased pendular movement, ending in an inability to walk or with festination (short accelerating steps to catch up with the patient’s center of gravity) and freezing on turning. Impaired Parkin-

sonian posture starts with a flexed head (slightly stooped posture, not quite erect), which may be normal for elderly persons, and then a stiff posture. A bent spine and stooped posture may be the predominant symptom in patients with idiopathic Parkinson's disease (IPD). The cause of this bent spine might represent either dystonia or rigidity. The patient may also lean to one side.

2.1.3. Postural instability

Postural instability or impaired balance, is common in IPD, especially as the illness progresses, leading to falls and loss of independence. Postural instability appears to be multi-factorial, reflecting both sensory and motor aspects of postural control. Balance is needed to keep the body in an upright position in both the sitting and erect positions and while performing voluntary actions. Clinical measurement of postural control is done through standardized testing of postural instability. A single objective measure is impossible due to the complex interrelation between balance and postural instability. Rating scales have used similar procedures of sudden pushing and/or pulling to measure postural instability. Patients exhibiting this symptom have difficulty assuming an erect posture when suddenly pushed and/or pulled from the back and in more severe cases even without pushing. This procedure focuses on the motor component of postural instability since the test is performed under normal sensory conditions (eyes opened).

2.1.4. Rigidity

Rigidity refers to stiffness or rigidity of muscles. This rigidity, defined as resistance to passive movement, is usually evident during manipulation of the patient's limb/s. Passive movement of a patient's limb (either arm or leg upon physical examination) may demonstrate smooth resistance (like trying to bend a lead pipe—"lead-pipe" rigidity) or ratchet-like jerks called "cogwheeling," which is the combination of rigidity with tremor. Cogwheeling is probably best elicited by a slow rotation of the wrist or elbow through a full range of motion.

2.1.5. Reduced facial expression/speech

Reduced facial expression/speech or "facial mask" is apparent in subjects showing little or no emotion. In this condition, smiling, blinking and spontaneous eye movements are less frequent, giving rise to a staring expression. In its more severe form, the patient has difficulty frowning, speech is slurred and lips may be parted. This is different from blunted affect and reduced expressed emotion, which are features of deficit schizophrenic symptoms. The behavioral characteristics of blunted affect consist of a lack of manifest emotion, when there is no muscular disability to block or decrease spontaneity of expressed emotion. In contrast, a Parkinsonian facial mask is caused by both rigidity and bradykinesia of facial muscles, which cause the physical disability inhibiting emotional expression. This latter condition is a physical rather than emotional disability, and its features are described in the scale through gradual decrease in facial expressiveness and speech: decreased smiling, blinking, and slurred speech.

2.1.6. Bradykinesia/hypokinesia

Bradykinesia/hypokinesia consisting of slowed, reduced voluntary movements is best seen in the patient's slowness to initiate movement. Voluntary and spontaneous movements are decreased both in frequency and amplitude. The patient may also find their volitional movement suddenly and unexpectedly stopped while performing repetitive, simultaneous movements or carrying out routine tasks and be unable to follow through to complete the action. Bradykinesia may also prevent patients from interrupting a fall when trying to catch their balance. It may be difficult to distinguish between drug-induced bradykinesia and negative symptoms of schizophrenia, such as motor retardation or lack of spontaneity. Differentiation is further complicated when the same patient manifests both conditions. A bradykinetic Parkinsonian depression syndrome induced by anti-D_2 antipsychotics has been described by Rifkin et al. (1975) and is differentiated from motor retardation related to the psychotic illness by its response to antiParkinsonian anticholinergic drugs and/or to a decrease in antipsychotic dosage. Furthermore drug-induced bradykinesia is often more marked in the early morning (as in IPD), and many patients with drug-induced bradykinesia feel the need to take their antiParkinsonian medication in order to overcome morning feelings of slowness, lethargy and apathy.

2.2. Akathisia

Akathisia consists of subjective feelings of inner restlessness with the urge to move, and/or objective movements such as restless movement of one extremity, fidgeting, changing position, rocking while standing or sitting, lifting feet as if marching on one spot, crossing/uncrossing legs while sitting, and inability to sit down for long periods with pacing back. Terminology used by the patient to describe these feelings may often be confusing and even idiosyncratic. If terms such as "restlessness" are used, they must be distinguished from anxiety, insomnia, attention deficit disorder or restless leg syndrome. Akathisia may be acute/sub-acute and disturbing for the patient leading to possible suicide or aggressive behavior (homicide), or chronic/tardive with only the motor components present. As with other tardive movement disorders, patients may be unaware of the tardive motor form of akathisia.

2.3. Dystonia

Dystonia is a movement disorder in which muscles are contracted and contorted, sometimes accompanied by repetitive jerking or twisting movements, resulting in the patient's assuming abnormal postures or positions. Dystonia is usually first seen during action and in more advanced cases both at rest and during action. It may be evidenced as sustained muscle contractions with minimal effort to overcome or as forceful contractions that can only be overcome with effort, best seen in acute dystonia. Dystonias may occur with few associated movements or may be seen as a movement ending in a sustained abnormal posture or contracture. Dystonias may affect any part of the body including the tongue, jaw (clenching/bruxism), eyes (blepharospasm/oculogyration), face (grimacing), larynx (hoarseness/choked voice), pharynx, arms, legs, trunk (bending) and neck (head turning). Oculogyration is seen acutely and is typical of drug-induced dystonia. Dystonia may be acute (of short/recent duration) or chronic (tardive). Acute dystonia is of sudden onset, recurrent, associated with distress and/or pain, and evidenced by forceful contractions that can only sometimes be overcome with effort. Acute dystonia usually requires immediate treatment. In contrast, chronic or tardive dystonia is an abnormal posture of hands, arms, feet or trunk; it could be short lasting (generally a few seconds), of small amplitude and not distressing to the patient. It is of a persistent nature and usually develops insidiously. It should be differentiated from mannerisms and abnormal postures originating from the schizophrenic illness.

Tardive dystonia could progress over time and may be associated or mixed with other movement disorders, most commonly with tardive dyskinesia (dyskinetic-dystonia or dystonic-dyskinesia, depending which is predominant). As with tardive dyskinesia, the patient may be unaware of chronic forms of dystonia.

2.4. Dyskinesia

Dyskinesia is characterized by movements that are repetitive, purposeless, and involuntary. The patient may have dyskinetic movements of the arms, legs, and trunk, as well as a variety of different movements of the face, jaw (chewing/biting), tongue (protrusion/fly catching), and lips (smacking/pursing/puckering). Antipsychotic-induced dyskinesias typically involve the bucco–linguo–masticatory (BLM) region. Finger movements may occur and make it appear as though the patient is playing an invisible guitar or piano. Virtually any muscle group may be involved including those controlling respiration and swallowing. Like with other tardive types of DIMD, patients are not necessarily aware of the movements.

3. Examination procedure and description of the scale

The ESRS consists of four subscales and four CGI-S scales:

I) a questionnaire of EPS or DIMD
II) an examination of Parkinsonism and akathisia
III) an examination of dystonia
IV) an examination of dyskinesia
V) to VIII) clinical global impression severity (CGI-S) scales of tardive dyskinesia, Parkin-

sonism, dystonia and akathisia. For the ESRS manual and scoring sheet, see Appendix. For a summary of the examination procedure that follows, see Table 1.

Instruction 1: Patient is asked to remove his/her shoes, to remove anything from his/her mouth (except dentures) and to sit facing the examiner on a chair with no armrests.

The removal of shoes can be omitted if an assessment of lower extremity dyskinetic movements is not required. In clinical trials it is completed unless clinically inappropriate for the patient (often patients do not feel comfortable removing their shoes) or it can be delayed until the testing of postural stability. Removing food and gum from the mouth is necessary in order to assess bucco–labial, lingual and jaw movements. The armless chair is essential for detection of tremors, decreased spontaneous movements, dyskinesia and akathisia.

Instruction 2: Complete the questionnaire.

The questionnaire rates subjective DIMD, i.e., Parkinsonism, akathisia, dystonia, and dyskinesia, as reported by the patient and which are experienced at periods other than the time of examination during the last week. For demented patients or autistic children, a nurse or key relative may also provide information in relation to the questionnaire. The questionnaire permits the evaluator to spend time with the patient to observe spontaneous DIMD.

Instruction 3: Observe facial expressiveness, speech, akathisia, dystonia and dyskinesia while completing the questionnaire and while completing items 4, 5, and 6.

Items in the objective examination are assessed during the course of standard tests of neurological examination (there is no new procedure to be learned by the physician when the physician is the examiner).

Instruction 4: Patient is asked to extend both arms forward, with palms down and eyes closed.

This test of posture tremors along with observing the patient's tremors at rest and the copying of a spiral with each hand (Instruction 6) is part of an overall assessment of tremors, which includes rest, posture and action tremors. Eyes are kept closed so that the patient is unable to correct if there is a lateralized neurological lesion.

Instruction 5: The patient is asked to carry out pronation and supination of both hands as fast as possible and to perform rapid alternate movements of both wrists simultaneously. Repeat as necessary.

Both tests are useful in the evaluation of tardive dyskinesia, as well as in the rating of slowness and difficulty in initiating movement. For bradykinesia, these two tests were selected because the initiation of several repetitive movements can be observed and for one test simultaneous movements of both wrists permit the detection of impaired ability to perform simultaneous tests. The inability to stop a movement should also be observed. For TD, the

Table 1
Summary of the ESRS examination procedure

1. Patient is asked to remove their shoes (omitted if judged clinically inappropriate or when patient hesitates, or delayed after patient has walked (after # 7). The patient is asked to remove anything from their mouth (except dentures). The patient is asked to sit facing the examiner on a chair with no armrests.
2. Complete the questionnaire.
3. Observe facial expressiveness, speech and dyskinesia while completing the questionnaire and while completing items 4, 5, and 6 below.
4. Patient is asked to extend both arms forward, with palms down and eyes closed.
5. The patient is asked to carry out pronation and supination of both hands as fast as possible, and to perform rapid alternate movements of both wrists. Repeat as necessary.
6. While the patient sits facing the examiner on a chair with no armrests about 1 foot (approx. 30 cm) from a table with his upper body turned, the patient is asked to copy a spiral with each hand and to write the name of his town, province/state and country.
7. Patient is asked to walk a distance of 12–15 feet (4–5 m) away from, and then back towards the examiner. Repeat as necessary.
8. Patient is asked to stand erect with eyes open with feet slightly apart (1–2 cm). The examiner pushes the patient on each shoulder, the back and pushes the chest or pulls from the back while asking the patient to keep his balance.
9. Carry out the examination of the muscular tonus of the four limbs.

oral–facial region is observed while the patient is performing pronation–supination and alternate movement tests; these voluntary movements help to uncover buccal–labial–masticatory and lower extremity dyskinesias.

Instruction 6: While the patient sits facing the examiner on a chair with no armrests about 1 foot (approx. 30 cm) from a table with his/her upper body turned, the patient is asked to copy a spiral with each hand and to write the name of his town, province/state and country.

This test permits the assessment of action tremors through graphic oscillation, and dyskinetic movements may be unmasked or augmented when the patient completes Instruction 6, for the test is performed under some emotional tension and uses other voluntary muscle groups. In this regard, it is important to encourage the patient to concentrate on the task requested.

Instruction 7: Patient is asked to walk a distance of 12–15 feet (4–5 m) away from, and then back towards, the examiner. Repeat as necessary.

This permits the evaluator to rate gait and posture. Absence of or a decrease in unilateral or bilateral pendular moments is observed. Abnormalities of posture are also looked for: flexed head, stiff posture, stooped posture. TD and/or chronic dystonia of upper limbs and trunk are looked for while the patient is walking.

Instruction 8: Patient is asked to stand erect with eyes open and feet together or slightly apart (1–2 cm). The examiner pushes the patient gently but firmly (strongly if necessary) on each shoulder (for lateropulsion), the back (for anteropulsion), and pushes the chest or pulls from the back (for retropulsion) while asking the patient to keep his balance and resist. Preferably, the patient removes his/her shoes before the test.

This test evaluates postural stability. The examiner should be ready to catch the patient from falling especially if the patient has an obvious impairment of balance at rest before testing. For patients who are already unstable, the test is completed gently.

Instruction 9: Carry out the examination of the muscular tonus of the four limbs.

Both limbs are examined as a pair in order to observe differences between the left and right side. Patient is asked to relax. Both arms are simultaneously rotated to permit examination of shoulders and, subsequently, elbows and wrists. Left and right knees are then successively moved and a comparison between the two sides made. Examination of hips and ankles does not provide more sensitivity and can be disturbing to psychotic patients. As with IPD, proximal joints are the most affected and rigidity may be more present in one part and/or one side of the body.

4. Scoring instructions

4.1. Questionnaire for Parkinsonism, akathisia, dystonia and dyskinesia

For the subjective examination (subscale I of the ESRS) scoring is on a 4-point scale (0=Absent; 1=Mild, 2=Moderate, 3=Severe). The evaluator takes into account the verbal report of the patient on: 1) the frequency and duration of the symptom during the day; 2) the number of days the symptom was present during the last week; and, 3) the subjective evaluation of the intensity of the symptom by the patient. When rating subjective EPS, severity is assessed over the last 7 days. One inquires about how persistent symptoms have been on the most typical day in the past 7 days.

4.2. Examination: Parkinsonism and akathisia

Both tremors and rigidity (items 1 and 4) are scored on a 7-point item scale (0=none–6=severe) for each part of the body, which are scored as separate items. The ESRS and the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn and Elton, 1987) rate each part of the body separately for tremors and rigidity, since, in both drug-induced Parkinsonism and IPD, the symptoms can be seen initially in one limb and when it progresses it may involve several limbs, thus increasing the number of items in each scale, but permitting the rating of severity in each part of the body involved.

Ratings for tremors are made taking into account two axes: the amplitude of the movement and the number of times with which it is observed during the

interview. Assessment of tremors includes rest, posture and action tremors. Ratings of the other items of Parkinsonism and akathisia are recorded on a 7-point item scale (0=absent–6=most severe) with anchor points.

One difficulty in the rating of abnormal movements was to include both the amplitude of the abnormal movement (the higher the amplitude, the more severe the disorder) and the frequency that an abnormal movement is observed (the more frequent, the greater the severity). Thus, it appeared necessary to rate hyperkinetic disorders, tremors and dyskinesia, on a two-axis dimension to take into account that a small amplitude tremor seen frequently is as pathological as a larger amplitude tremor seen less frequently.

4.3. Examination: dystonia

Both acute and chronic dystonic movements are scored on a 7-point item scale (0=absent–6=most severe). Each body part is rated separately including right upper limb, left upper limb, right lower limb, left lower limb, head, jaw, tongue, lips, face, trunk and other (any other area).

4.4. Examination: dyskinesia

Dyskinetic movements at each site (tongue, jaw, bucco–labial, trunk, upper and lower extremities, and others {any other area including face}) are evaluated as individual items. They are rated similarly to tremors. Involuntary dyskinetic movements are repetitive, although not rhythmic and not oscillating along an axis, and their amplitude is usually greater with a low frequency cycle/s. Consequently we applied the same logic of a two-axis scale of amplitude and frequency as in the rating of tremors.

5. ESRS total and subtotal scores

5.1. ESRS Parkinsonism and akathisia scores in the era of classical antipsychotics

The score for Parkinsonism (including akathisia), ranges from 0 to 102 (17 items), and is based on all items of the Parkinsonism examination (subscale II): tremor (0–48), gait and posture (0–6), postural stability (0–6), rigidity (0–24), expressive automatic movements (0–6), bradykinesia (0–6), akathisia (0–6). In clinical trials, when establishing presence of Parkinsonism to initiate an antiParkinsonian medication, a score of 3 or greater is required on at least one of the above listed items including the 8 items of tremor or the 4 items of rigidity. When establishing the presence versus absence of Parkinsonism, a score of 2 on 2 items or a score of 3 or greater on one item is required to establish the presence.

Subscores: Two subscores were formed using the objective examination of Parkinsonism: a hypokinesia factor, ranging from 0 to 42, calculated as the sum of items: gait and posture (0–6), rigidity (0–24), expressive automatic movements (0–6), and bradykinesia (0–6); and a hyperkinesia factor, ranging from 0 to 54, calculated as the sum of items: tremor (0–48) and akathisia (0–6).

5.2. ESRS Parkinsonism and akathisia scores in the era of atypical antipsychotics

The Parkinsonism score, ranging from 0 to 96 (16 items), and the 2 factors (hypokinesia (0–42) and hyperkinesia (0–49) used now are similar to the previous ones (described in Section 5.1) minus one item: akathisia (0–6). The score for akathisia is separated from the Parkinsonism score and is based on the combined score of subjective akathisia (item 6 of the questionnaire) and objective akathisia (item 7 of the Parkinsonism/Akathisia objective examination). When establishing presence versus absence of akathisia, a total score of 3 or greater on the 2 items is required for presence.

5.3. Dystonia scores

The score for dystonia ranges from 0 to 60 (10 items), and is formed by including both acute and chronic dystonia, based on the dystonia examination (Subscale III). When establishing presence versus absence of dystonia, a score of 3 or greater on at least one item, or a score of 2 on 2 items is required to indicate presence of dystonia.

5.4. Dyskinesia and subtotal scores

Score for TD, ranging from 0 to 42, is based on the sum of all seven items in the TD objective examination. When scoring presence versus absence of TD, a score of 3 or greater on at least one item or a score of 2 on 2 items is required to indicate presence of TD. For tardive dyskinesia, scores for each item can be analyzed separately. A buccal–lingual–masticatory (BLM) subtotal, ranging from 0 to 18, is obtained from the sum of items 1, 2 and 3, and an extremities subtotal, ranging from 0 to 12, by adding the score for items 5 and 6.

5.5. ESRS total and subtotal scores for clinical trials and inter-rater reliability certification

For clinical trials, a total score for DIMD or EPS is formed based on all 41 items of the ESRS. It includes the 7 items of Subscale I (questionnaire), 17 items of Subscale II (Parkinsonism/Akathisia), 10 items of Part III (dystonia), and 7 items of Part IV (dyskinesia). For inter-rater reliability certification, the ESRS 41 item total score also includes the 4 CGI-S's and thus becomes ESRS 45 item total.

5.6. Clinical global impression of severity (CGI-S)

The clinical global impression of severity (CGI-S) of Parkinsonism, akathisia, dystonia, and tardive dyskinesia are rated according to results of the subjective questionnaire, examination subscales, and the evaluator's clinical experience by applying an 8 point rating (0: absent; 1: borderline; 2: very mild; 3: mild; 4: moderate; 5: moderately severe; 6: marked; 7: severe; 8: extremely severe). The 4 CGI-S's are analyzed as separate items.

6. Scale properties

6.1. Factor analysis

Annable et al. (1992) conducted principal components factor analysis with varimax rotation on the ESRS examination item scores of 305 schizophrenic outpatients treated with long-term anti-D_2 antipsychotics and assessed by a single neurologist who was experienced in the use of the scale. Six factors emerged accounting for 67.1% of the variance in the examination items of the scale, i.e., 1) hypokinetic Parkinsonism consisting of four items of subscale II: bradykinesia, facial mask, gait and posture, and rigidity (range score: 0–42); 2) orofacial dyskinesia consisting of four items of subscale IV: dyskinesias of the jaw, mouth and lips, tongue and face (other dyskinesia) (range score: 0–24); 3) trunk/limb dyskinesia consisting of three items of subscale IV items: dyskinesias of the trunk and the upper and lower extremities (range: 0–18); 4) akathisia consisting of the akathisia item of subscale II (range: 0–6); 5) tremor (subscale II) (range: 0–48); and, 6) tardive dystonia consisting of the 10 dystonia items of subscale III (range score: 0–60).

6.2. Inter-rater reliability studies

Two pivotal studies were carried out to establish the inter-rater reliability of the ESRS and a high inter-rater reliability was found in both antipsychotic-induced movement disorders (range of mean item correlation coefficients = 0.80–0.97) (Chouinard et al., 1980) and idiopathic Parkinson's disease (range $r = 0.88$–0.97) (Chouinard et al., 1984). In a first study, a neurologist and two psychiatrists independently rated 89 schizophrenic outpatients on long-term neuroleptic treatment. Inter-rater reliability coefficients were calculated for each item of the scale and ranged from 0.80 to 0.97 (Chouinard et al., 1980). In a second study, two neurologists independently rated 64 IPD patients (32 men and 32 women aged between 32 and 84 years) on treatment. Inter-rater reliability was assessed using analysis of variance intraclass correlation coefficients. Reliability was excellent for all divisions of the scale: questionnaire, $r = 0.97$; examination Parkinsonism $r = 0.95$; examination dystonia, $r = 0.88$; examination dyskinesia, $r = 0.96$ (Chouinard et al., 1984).

6.3. Inter-rater reliability certification studies

The scale has been evaluated for inter-rater reliability in several multi-center international studies through videotape training translated in 13

languages and was found to have a high inter-rater reliability. The following guidelines were first established by Stanley Kay for the PANSS and Guy Chouinard for the ESRS for the multi-center international studies of risperidone (Chouinard et al., 1993; Marder and Meibach, 1994). Since then, these guidelines have been followed for other multi-center studies (Clozapine, Risperidone-Consta, MAR, Amperozide, Zisprazidone, Olanzapine). For inter-rater reliability and certification of raters, the following requirements are necessary: 1) a minimum of 80% of the ratings on the individual items of the complete scale (ESRS 45 item including the 4 CGI-Ss) should be within ± 1 point of expert ratings and 2) a minimum of 70% of the ratings on the individual items included in each of the 4 ESRS subscales I–IV (questionnaire (7 items), Parkinsonism/akathisia (17 items), dystonia (10 items) and dyskinesia (7 items)) should be within ± 1 point of expert ratings. Note that for the ESRS items of rigidity, tremor, and dystonia, the reliability assessment treats the ratings on each part as separate items. Thus for subscale II Parkinsonism/akathisia examination, the evaluator is required to obtain 70% of 17 items within ± 1 point of the consensus ratings.

Expert ratings of ESRS during the actual patient examination and ratings done by other experts through video were found to be highly correlated. The problem of rating rigidity through a video was solved by a description of rigidity in terms of resistance to passive movement using ESRS anchor points. This method was found to be highly reliable between the ratings of the examiner and the expert rater using the video. In addition, for video inter-rater reliability and certification, the examiner not only described rigidity verbally, but his description was written on the video. This method proved very efficacious for training purposes and to achieve inter-rater reliability. On the other hand, the two pivotal inter-rater reliability studies were done with each of the experts examining patients with drug-induced movement disorder and IPD (Chouinard et al., 1980, 1984).

With practice the entire scale takes 10 min to complete and experts can complete it in 5 min, thus it takes a similar time to administer the ESRS and the AIMS. This is understandable since both scales, developed at the same time, follow a similar procedure. Filling in the scoring is longer with the ESRS than with the AIMS, since the ESRS is more comprehensive (it rates the 4 types of abnormal movements), has anchor points and includes a greater number of items. However, since it rates the 4 types of abnormal movements, it saves time when one has to administer another scale such as the Simpson–Angus. Recently, in a demonstration video with a normal volunteer, it took 15 min to administer the ESRS and 21 min to administer the AIMS–Simpson–Angus, and this was also found in the recent study comparing the ESRS and the AIMS (Gharabawi et al., in press).

6.4. Inter-scale reliability and cross-scale comparison: AIMS

A study was completed to determine the concordance between the Abnormal Involuntary Movement Scale (AIMS) and ESRS examination dyskinesia ratings, and to assess whether simplified TD criteria could be identified (Gharabawi et al., in press).

AIMS and ESRS examination TD items baseline data were collected between May 2002 and September 2003 in patients with schizophrenia or schizoaffective disorder included in two separate studies ($n=374$). Regression models explored the strength of relationships and were used to map ESRS and AIMS scores for corresponding items. The probability of AIMS-defined TD, using logistic regression models as a function of ESRS scores, identified simplified criteria for predicting AIMS-defined TD by ESRS scores.

A strong degree of association was found between corresponding scale items. Mapping of corresponding items defined "mild" as an AIMS score of 2 and an ESRS score of 2–3, and "moderate or worse" as an AIMS score of ≥ 3 and an ESRS score of ≥ 4. Using DSM-IV TD criteria, there was 96% (359/374) agreement between AIMS- and ESRS-defined cases of TD. The ESRS Clinical Global Impression-Severity of Dyskinesia (CGI-SD) was the best single predictor of AIMS-defined TD. An ESRS CGI-SD of ≥ 4 (95% CI: 3.61, 4.76) was associated with a $\geq 95\%$ probability of AIMS-defined TD.

The study demonstrated concordance and mapping between the AIMS and ESRS examination dyskinesia scores and identifies simplified criteria for TD. The ESRS CGI-SD predicted AIMS-defined TD. Since the two scales (AIMS and ESRS) have been used in most studies on antipsychotic-induced dyskinesias, this recent cross-scale comparison (Gharabawi et al., in press) provides strong evidence for comparable data between the two scales.

6.5. Sensitivity and specificity of ESRS

Sensitivity of the ESRS was tested through different approaches comparing various antipsychotics and different types of antiParkinsonian and antidyskinetic medication. To illustrate the ESRS sensitivity, we selected the following double-blind controlled studies, which included small numbers of patients. In the Canadian risperidone study, comparing haloperidol, risperidone and placebo, significant differences in EPS measured by the ESRS were found between drugs and placebo with an N of 22 for placebo, risperidone 6 mg ($n=22$) and haloperidol ($n=21$) (Chouinard et al., 1993). Differences in the use of antiParkinsonian drug substantiated these Canadian results as well as the American risperidone study by Marder and Meibach (1994). Sensitivity in the treatment of drug-induced Parkinsonism was also tested using placebo, an anticholinergic antiParkinsonian and L-Dopa. The ESRS was particularly sensitive in detecting EPS differences (Parkinson score $p<0.001$ and hypokinesia score $p<0.01$) between placebo ($n=24$), L-Dopa ($n=26$) and procyclidine ($n=24$), the standard anticholinergic antiParkinsonian drug (Chouinard et al., 1987). In Tourette patients, the ESRS proved to be very sensitive in detecting EPS differences (Parkinson score $p<0.004$ and hypokinesia factor $p<0.006$) between risperidone 2.5 mg ($n=23$) and placebo ($n=23$) (Dion et al., 2002). The sensitivity of the ESRS was also seen in detecting differences ($p<0.01$) between olanzapine ($n=21$) and haloperidol ($n=23$) for ESRS Parkinson (Purdon et al. 2000).

Moller et al. (1995) investigated if the differences in drug effects between risperidone and haloperidol on PANSS negative symptoms were secondary to the drug effects on PANSS positive, ESRS extrapyramidal symptoms (total score of ESRS examination subscales II, III and IV), and PANSS depressive symptoms by means of an analysis of the data from the USA–Canada risperidone placebo double-blind randomized clinical trial of 523 schizophrenic patients (Chouinard et al., 1993; Marder and Meibach, 1994). Regression analyses in the total sample and within treatment groups confirmed a relationship between changes in negative symptoms and the other variables studied ($R2=0.50$–0.51, $p<0.001$). Only depressive symptoms did not contribute significantly to these results ($p>0.10$). However, path analysis showed that the greater mean change ($p<0.05$) of negative symptoms with risperidone compared to haloperidol could not be explained by the correlations between favorable effects on PANSS positive and/or ESRS symptoms. Furthermore, the relationship between a shift in ESRS extrapyramidal symptoms and a shift in PANSS negative symptoms was not found to be statistically significant [R: 0.19 for both risperidone 6 mg ($p=0.09$) and haloperidol ($p=0.13$)] and confirmed the weak effect of ESRS symptoms on PANSS negative symptoms changes produced by drug treatment in comparison to the strong effects (R: 0.51 for risperidone 6 mg and R: 0.45 for haloperidol $p<0.01$) of PANSS positive symptoms on PANSS negative symptom changes.

Marder et al. (1997) investigated whether there was an association between two ESRS measurements (ESRS Parkinsonism examination and CGI-S-Parkinsonism) and the five PANSS factors by using Pearson product–moment correlations during the placebo washout period and in the placebo treated patients. ESRS Parkinsonism examination and CGI-S-Parkinsonism scores at selection and baseline (before and after the washout period) for all patients and at 1, 2, 4, 6, and 8 weeks for the placebo group were found to be significantly correlated with Factors 1 (negative symptoms) and 3 (disorganized thought), but the magnitude was small (a correlation of .15 explaining 2% of the variance). The other three factors were clearly unrelated to ESRS Parkinsonism. These results confirm earlier results (Moller et al., 1995) using a different statistical approach. The specificity of the ESRS through PANSS factor changes/improvement was then investigated to see if the occurrence of ESRS extrapyramidal symptoms had an effect on the change/

improvement scores of the five PANSS factors in patients receiving 2, 6, 10, 16 mg/day of risperidone versus haloperidol. Among all the possible comparisons, none were statistically significant, indicating that treatment related changes in the 5 PANSS factors were not related to ESRS changes. When patients were stratified as to whether or not they received antiParkinsonian medications, no effects of the presence of antiParkinsonian drug were found on PANSS changes, nor did the presence of antiParkinsonians modify the lack of ESRS effects on PANSS factors.

If ESRS Parkinsonism scores were related to negative symptoms, patients receiving risperidone 10 or 16 mg/day, which produced more extrapyramidal symptoms than 6 mg/day, would be expected to have less improvement on negative symptoms than patients receiving risperidone 6 mg/day. On the contrary there were significantly greater improvements with 6 mg than 10 or 16 mg/day on factors less potentially related to EPS (Factor 4 hostility/excitement, Factor 5 anxiety/depression, and total PANSS), but not on the factors more likely related to EPS (Factor 1 negative symptoms, Factor 2 positive symptoms, and Factor 3 disorganized thought) (Marder et al., 1997).

After investigating ESRS specificity through two different approaches, path analyses (Moller et al., 1995), and ANCOVA PANSS factors changes (Marder et al., 1997), we conclude that the ESRS measurement of drug-induced EPS is a valid one and has little influence on drug changes in psychopathology as measured by the PANSS total and factors.

7. Discussion

One widely used rating scale for drug-induced Parkinsonism is the Simpson–Angus Scale (Simpson and Angus, 1970). In comparison to the ESRS, this scale does not include an EPS questionnaire, which is included in the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn and Elton, 1987) the most widely used scale in IPD. The Simpson–Angus Scale rates bradykinesia indirectly through gait and arm dropping, and emphasizes rigidity (four out of ten items and even 5 items in some versions of the scale). An inconvenience is to have the patient go through the glabellar tap procedure, especially during the acute phase of the illness. This last procedure is obsolete in the evaluation of Parkinsonian symptoms and is not included in the UPDRS and was removed early from the ESRS. In the evaluation of tremors, the five-point tremor item of the Simpson–Angus does not capture the fact that one or more regions of the body may be involved, which is taken into account by the ESRS and the UPDRS (Fahn and Elton, 1987). The Simpson–Angus akathisia item (which has been added in some versions of the scale) measures objective akathisia and is analyzed separately from Parkinsonism. Seven items are left to evaluate drug-induced Parkinsonism compared to 16 items with the ESRS examination and 19 items for the UPDRS examination. In contrast to the Simpson–Angus, which focuses on rigidity, the ESRS measures all features of drug-induced Parkinsonism (reduced facial expression/speech, tremor, rigidity, impaired gait/posture, postural instability and body bradykinesia/hypokinesia) and is comparable to the UPDRS. Since its introduction, the validity of the ESRS has been well established through its concurrent use with the other gold standard in IPD, stage of Parkinsonism (Hoehn and Yahr, 1967, 2001), which is not the case for the Simpson–Angus. The first requisite of a rating scale is its validity to measure a disorder, and in the case of drug-induced Parkinsonism, it needs to be comparable to the well-established scales in IPD.

The two most widely used rating scales for tardive dyskinesia are the Abnormal Involuntary Movement Scale (AIMS) (Guy, 1976; Munetz and Benjamin, 1988) and the ESRS (Chouinard et al., 1979a). Correll et al. (2004) systematically reviewed the 1-year incidence of TD with atypicals and pooled the data from 11 studies, 6 used the AIMS and 5 the ESRS, demonstrating the importance of investigating the reliability between the two scales. A recent AIMS and ESRS inter-scale reliability and cross-scale comparison found a significant relationship between AIMS and ESRS dyskinesia scores, including a high level of agreement (96.5%) for identifying TD (Gharabawi et al., in press) The ESRS CGI-S dyskinesia ≥ 4 (95% CI: 3.61,4.76) was found to be the best predictor of the AIMS-defined TD with a $\geq 95\%$ probability of AIMS-defined TD.

If one considers the examination procedure and the first seven items of the AIMS, both scales can be easily compared since the examination procedure is comparable and the same seven body regions are evaluated (this permitted the cross-scale comparison and mapping that we described earlier). This is not surprising since the two scales were developed at the same time. Thus, when using the Schooler and Kane (1982) or DSM-IV-TR criteria (American Psychiatric Association, 2000) to define the presence of TD, both scales (ESRS and AIMS) can be used since the examination procedure is nearly identical and the 7 body areas rated are the same. Compared to the AIMS, the ESRS rating system for dyskinesia is a two-axis rating based on the frequency and amplitude of symptoms. The ESRS scale permits a rating through a description of the abnormal movements with anchor points on a 7-point rating system versus AIMS 5-point rating without anchor points. AIMS Global judgments and dental status are overemphasized with 3 items each. Dental status is one of many methods that act to uncover dyskinesia and is not included in the total AIMS score, while the 3 items of Global judgment that include patient's awareness, when most patients are unaware of their movements, are included in the total AIMS score. Despite these differences, the two scales, AIMS and ESRS, which are the most often used for TD, were found to have a 96.5% (366/374) agreement between TD-defined cases, thus a comparison of their results is possible by using the criteria mentioned (see Section 6.4: Inter-scale reliability and cross-scale comparison: AIMS). With regards to the AIMS, similarities and differences between the two scales have been discussed and we note the fact that the AIMS is over inclusive for tardive dystonia, which cannot be rated separately from tardive dyskinesia (Gharabawi et al., in press). In addition, compared to the AIMS, the ESRS, with well-defined anchor points, helps to understand better clinical manifestations of dyskinesia. Furthermore, there is a lack of consensus for the AIMS whether to rate positively an abnormal movement if it is observed only when activated.

Analyses of the baseline EPS data from two major international multi-center trials, Intersept (Meltzer et al., 2003) and Risperidone Consta (Bhanji et al., 2004) were conducted to investigate the clinical relevance of the ESRS in the era of atypicals using the ESRS procedure described in this paper. In the first study (Chouinard et al., 2002), the international multi-center Intersept study (Meltzer et al., 2003), we analyzed baseline ESRS data of 958 patients that were included from March 19, 1998 (first patient), to February 14, 1999 (last patient). We found EPS in 551 (57.5%) and tardive dyskinesia in 115 (12%) patients at baseline. Patients taking an atypical antipsychotic alone (25.6% of the sample) or an atypical antipsychotic and a conventional antipsychotic together (42.9% of the sample) had fewer EPS than patients taking a conventional antipsychotic alone (31.5% of the sample). In the second study (Chouinard et al., 2003), we analyzed the ESRS baseline data from 3 multi-center studies {Ris USA-121 (Kane et al., 2003), Ris Int-57 (Fleischhacker et al., 2003), and Ris Int-61 (Chue et al., 2001)} that included their first patient October 21, 1999 and their last December 1, 2000, and found that 970 (47.4%) of the 2048 patients had EPS and that tardive dyskinesia was present in 209 (10.2%) at baseline. These 2 ESRS studies conducted in the era of classicals and atypicals, which included over 3000 patients worldwide, showed decreasing incidence of EPS at baseline, which varied from 57.5% (1998–1999) to 47.4% (1999–2000) and TD from 12% (1998–1999) to 10.2% (1999–2000). We conclude that the ESRS remains sensitive over time and that it is still necessary to measure EPS in the era of atypicals even though the incidence of EPS is decreasing as classical antipsychotics are prescribed less. The review by Correll et al. (2004) on the 1-year incidence of new cases of TD with atypicals is in agreement with the findings of reduced risks of TD with atypicals.

In conclusion, compared to the Simpson–Angus and AIMS, the ESRS measures all drug-induced movement disorders, thus permitting the evaluation of mixed EPS syndromes that should be recognized in diagnostic and rating procedures. This has been a critique of several studies on tardive dyskinesia, which neglected the rating of drug-induced Parkinsonism and chronic dystonia (Chouinard, 2004). In addition, the ESRS has been found to specifically measure drug-induced EPS, independently of changes in psychopathology as measured by the PANSS.

Appendix A. ESRS Manual and scoring sheet

Extrapyramidal symptom rating scale (ESRS) (Chouinard) © 1979

In case of doubt score the lesser severity.

I. QUESTIONNAIRE : Parkinsonism, Akathisia, Dystonia and Dyskinesia. *In this questionnaire, take into account the verbal report of the patient on the following: 1) the duration of the symptom during the day; 2) the number of days where the symptom was present during the last week; and, 3) the evaluation of the intensity of the symptom by the patient.*

Enquire into the status of each symptom and rate accordingly

	Absent	Mild	Moderate	Severe	
1. Impression of slowness or weakness, difficulty in carrying out routine tasks	0	1	2	3	⌊__⌋
2. Difficulty walking or with balance					
3. Stiffness, stiff posture	0	1	2	3	⌊__⌋
4. Restless, nervous, unable to keep still	0	1	2	3	⌊__⌋
	0	1	2	3	⌊__⌋
5. Tremors, shaking					
6. Oculogyric crisis, abnormal sustained posture	0	1	2	3	⌊__⌋
7. Abnormal involuntary movements (dyskinesia) of tongue, jaw, lips, face, extremities or trunk	0	1	2	3	⌊__⌋
	0	1	2	3	⌊__⌋

II. EXAMINATION: PARKINSONISM AND AKATHISIA

Items based on physical examinations for Parkinsonism.

	Occasional	Frequent	Constant or almost so				
1. Tremor							
None:	0			Right upper limb			⌊__⌋
Borderline:	1			Left upper limb			⌊__⌋
Small amplitude:	2	3	4	Right lower limb			⌊__⌋
Moderate amplitude:	3	4	5	Left lower limb			⌊__⌋
Large amplitude:	4	5	6	Head	⌊__⌋	Jaw/Chin	⌊__⌋
				Tongue	⌊__⌋	Lips	⌊__⌋
2. Bradykinesia	0:	normal					
	1:	global impression of slowness in movements					
	2:	definite slowness in movements					
	3:	very mild difficulty in initiating movements					⌊__⌋
	4:	mild to moderate difficulty in initiating movements					
	5:	difficulty in starting or stopping any movement, or freezing on initiating voluntary act					
	6:	rare voluntary movement, almost completely immobile					
3. Gait & posture	0:	normal					
	1:	mild decrease of pendular arm movement					
	2:	moderate decrease of pendular arm movement, normal steps					
	3:	no pendular arm movement, head flexed, steps more or less normal					⌊__⌋

	4:	stiff posture (neck, back) small step (shuffling gait)		
	5:	more marked, festination or freezing on turning		
	6:	triple flexion, barely able to walk		
4. Postural stability	0:	normal		
	1:	hesitation when pushed but no retropulsion		
	2:	retropulsion but recovers unaided		
	3:	exaggerated retropulsion without falling		⌊⌋
	4:	absence of postural response would fall if not caught by examiner		
	5:	unstable while standing, even without pushing		
	6:	unable to stand without assistance		⌊⌋
5. Rigidity	0:	normal muscle tone	Right upper limb	⌊⌋
	1:	very mild, barely perceptible	Left upper limb	⌊⌋
	2:	mild (some resistance to passive movements)	Right lower limb	⌊⌋
	3:	moderate (definite difficulty to move the limb)	Left lower limb	⌊⌋
	4:	moderately severe (moderate resistance but still easy to move limb)		
	5:	severe (marked resistance with definite difficulty to move the limb)		
	6:	extremely severe (limb nearly frozen)		

Items based on overall observation during examination for Parkinsonism.

6 . Expressive automatic movements (Facial mask / speech)	0:	normal		
	1:	very mild decrease in facial expressiveness		
	2:	mild decrease in facial expressiveness		
	3:	rare spontaneous smile, decrease blinking, voice slightly monotonous		⌊⌋
	4:	no spontaneous smile, staring gaze, low monotonous speech, mumbling		
	5:	marked facial mask, unable to frown, slurred speech		
	6:	extremely severe facial mask with unintelligible speech		
7 . Akathisia	0:	absent		
	1:	looks restless, nervous, impatient, uncomfortable		
	2:	needs to move at least one extremity		
	3:	often needs to move one extremity or to change position		⌊⌋

4:	moves one extremity almost constantly if sitting, or stamps feet while standing
5:	unable to sit down for more than a short period of time
6:	moves or walks constantly

III. EXAMINATION: DYSTONIA

Based on examination and observation

Acute torsion, and non acute or chronic or tardive dystonia

0:	absent	Right upper limb			⌊⌋
1:	very mild	Left upper limb			⌊⌋
2:	mild	Right lower limb			⌊⌋
3:	moderate	Left lower limb			⌊⌋
4:	moderately severe	Head	⌊⌋	Jaw/Chin	⌊⌋
5:	severe	Tongue	⌊⌋	Lips	⌊⌋
6:	extremely severe	Eyes	⌊⌋	Trunk	⌊⌋

IV. EXAMINATION: DYSKINETIC MOVEMENT

Based on examination and observation

		Occasional*	Frequent**	Constant or almost so	
1. Lingual movements (slow lateral or torsion movement of tongue)					
none:	0				
borderline:	1				
clearly present, within oral cavity:		2	3	4	
with occasional partial protrusion:		3	4	5	
with complete protusion:		4	5	6	⌊⌋
2. Jaw movements (lateral movement, chewing, biting clenching)					
none:	0				
borderline:	1				
clearly present, small amplitude:		2	3	4	
moderate amplitude: but without mouth opening:		3	4	5	
large amplitude: with mouth opening:		4	5	6	⌊⌋
3. Bucco-labial movements (puckering, pouting, smacking, etc.)					
none:	0				
borderline:	1				
clearly present, small amplitude:		3	3	4	
moderate amplitude, forward movement of lips:		4	4	5	
large amplitude; marked, noisy smacking of lips:		5	5	6	⌊⌋

4. Truncal movements (involuntary rocking, twisting, pelvic gyrations)					
none:	0				
borderline:	1				
clearly present, small amplitude:		2	3	4	
moderate amplitude:		3	4	5	
greater amplitude:		4			⌊⌋
5. Upper extremities (choreoathetoid movements only: arms, wrists, hands, fingers)			5	6	
none:	0				
borderline:	1				
clearly present, small amplitude, movement of one limb:		2	3	4	
moderate amplitude, movement of one limb or movement of small amplitude involving two limbs:		3	4	5	
greater amplitude, movement involving two limbs:		4	5	6	⌊⌋
6. Lower extremities (choreoathetoid movements only: legs, knees, ankles, toes)					
none:	0				
borderline:	1				
clearly present, small amplitude, movement of one limb:		2	3	4	
moderate amplitude, movement of one limb or movement of small amplitude involving two limbs:		3	4	5	
greater amplitude, movement involving two limbs:		4	5	6	⌊⌋
7. Other involuntary movements (swallowing, irregular respiration, frowning, blinking, grimacing, sighing, etc.)					
none:	0				
borderline:	1				
clearly present, small amplitude:		2	3	4	
moderate amplitude:		4	4	5	
greater amplitude:		5	5	6	⌊⌋

Specify……..…….

* when activated or rarely spontaneous;
** frequently spontaneous and present when activated

V. CLINICAL GLOBAL IMPRESSION OF SEVERITY OF DYSKINESIA		
Considering your clinical experience, how severe is the dyskinesia at this time?		
0: absent	3: mild	6: marked
1: borderline	4: moderate	7: severe
2: very mild	5: moderately sever	8: extremely severe
VI. CLINICAL GLOBAL IMPRESSION OF SEVERITY OF PARKINSONISM		
Considering your clinical experience, how severe is the parkinsonism at this time?		
0: absent	3: mild	6: marked
1: borderline	4: moderate	7: severe
2: very mild	5: moderately sever	8: extremely severe
VII. CLINICAL GLOBAL IMPRESSION OF SEVERITY OF DYSTONIA		
Considering your clinical experience, how severe is the dystonia at this time?		
0: absent	3: mild	6: marked
1: borderline	4: moderate	7: severe
2: very mild	5: moderately sever	8: extremely severe
VIII. CLINICAL GLOBAL IMPRESSION OF SEVERITY OF AKATHISIA		
Considering your clinical experience, how severe is the akathisia at this time?		
0: absent	3: mild	6: marked
1: borderline	4: moderate	7: severe
2: very mild	5: moderately sever	8: extremely severe

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