**ASK THE DOCTOR**

**AUTISM AND SEVERE/PROFOUND INTELLECTUAL DISABILITY: THINGS THAT DO GO BUMP IN THE NIGHT**

**Q.** Dr. Barnhill, what clinical problems complicate the differential diagnosis of abnormal movements?

**A.** It is obvious that we should exercise extra caution and avoid prematurely dismissing abnormal movements as just a part of the autism spectrum and severe/profound intellectual disability (ID). The prevalence of stereotypies, ritualistic behaviors, and mannerisms vary inversely with the level of ID. These individuals are also at greater risk for co-occurring genetic and neurodevelopmental brain disorders. Severe/profound ID and autism both adversely affect adaptive skills and indirectly, threshold and sensitivity to a wide range of environmental challenges. There is an increased vulnerability to stressors that influences the frequency and intensity of challenging behaviors as well as risk/vulnerability factors for mental disorders. In addition, it complicates the diagnosis in patients with evolving neurodegenerative disorders such as Huntington’s disease. It becomes very difficult to recognize neurodegenerative changes amid these clinical variables.

There is a higher prevalence rate of abnormal movements among patients with comorbid obsessive-compulsive, psychotic, stereotypic movement, mood and anxiety disorders. Psychiatric illness, especially depression, can also affect frequency, intensity and function of repetitive movements (baseline exaggeration). Finally, medication side effects (akathisia), pain, and hormonal changes (e.g., hypothyroidism) can also influence abnormal movements. It is apparent that the process of differential diagnosis is not a simple straightforward one.

Movement disorders pose special problems for clinicians assessing and treating patients with movement disorders and ID. It is not uncommon for clinicians to not recognize abnormal movements as symptoms of underlying neurological disorders. In order to minimize such errors, we need to pay careful attention to differential diagnosis. For example, patients with autism and severe/profound ID have movement disorders associated with genetic, neurological and metabolic syndromes. It is often critical that we differentiate subtypes of neurodegenerative movement disorders. An added complication relates to their high rates of many subtypes of “benign” repetitive behaviors. Unfortunately, busy clinicians can misattribute serious abnormal movements with co-occurring neurocognitive and behavioral symptoms as primary psychiatric disorder, “nervous” habits, stereotypies, mannerisms, focal seizures, or tardive dyskinesia (TD). It is important to recognize this form of diagnostic overshadowing, especially when working with with nonverbal patients with autism and/or severe/profound ID.

**Q.** How would a busy clinician approach such patients?

**A.** First, know your own limitations. Most of us are not familiar with or trained to recognize the many conditions that contribute to movement disorders. With this caveat, the clinician can screen cases for symptoms that suggest involuntary movements rather than stereotypies or mannerisms. It is helpful to document your observations and provide data on co-occurring behaviors or psychiatric symptoms. A very helpful
technique is videotaping the movements in as many environmental conditions as possible. For example, most movements are exacerbated by distraction, novel learning or stressful task demands but generally decrease in intensity or disappear altogether during familiar tasks or sleep. Many patients with tic and some chorea can partially suppress their movements making recognition difficult. On the other hand patients with severe/profound ID may be unable suppress abnormal movements.\textsuperscript{1,6}

If taping in multiple settings is not possible, then videotape the standard AIMS or discuss for review.\textsuperscript{??don’t understand } Such videos help preserve valuable pieces of information for assessment, rating change over time and eventual review by consultants. It is often easier to categorize and rate abnormal movements on replay than during real time. From replay the clinician can review typology, setting, variability and intensity of movements. For example, the clinician can assess the relationship between environmental factors and the intensity or frequency of movements; changes in level of awareness or consciousness that might suggest seizures and capture information regarding mood, cognition, or other behavioral changes associated with the movements.

In addition to video data, it is also helpful to obtain a family history of movement disorders, dementias, severe mental disorders and known degenerative disorders. This data may help define risk factors. The second step is establish a time line that includes age of onset; precipitating factors; clinical course, especially changes in symptoms over time; relationship to medical conditions and medication history. If possible some data on the effects of various treatments on the movements can be quite helpful. Finally, laboratory tests including basic CBC with Diff, clinical chemistries, urine heavy metal screens, neuro-imaging studies or EEGs can assist the consultant in his/her differential diagnosis.\textsuperscript{3}

Q. So once you have this information, how do you go about diagnosing a movement disorder?

A. Movement disorders are generally classified based on the typology of abnormal involuntary movements. This approach relies on categorizing movements as dystonic, tic-like, choreiform, athetoid, myoclonic or tremor-related. This approach is still used by clinicians in the field but accurate diagnosis is hampered by the considerable overlap between these various categories of movements. Even if you feel reasonably certain about the type of movements, there are still major differences in etiology. These subtypes may result from a number of genetic syndromes or specific topographies and are associated with other comorbid neurological disorders. For example, myoclonic movements can arise from the cortex, brainstem and peripheral nervous system and differ in terms of distribution, EEG and CNS changes. Chorea, tremor and dystonias have complicated differential diagnoses that frequently care a detailed neurological and genetic workup that is best supervised by a specialist in the field.\textsuperscript{1,3,6}

Q. Since there are so many exceptions in this diagnostic scheme, are there others that are simpler or more usable for the average non-specialist in the field?

A. Not exactly. A more recent descriptive approach classifies movement disorders in terms of rate or speed of movements, muscle tone, motivation or capacity for spontaneous movement. For example, Parkinson’s disease (PD) is a neurodegenerative disorder classified by progressive motor slowness or bradykinesia (hypokinesia or slowing down), increased rigidity and a form of motor inertia or decreased urge to move (akinesia). Several types of tremor are also observed in individuals with classic PD. Generally in PD the tremor is characterized as a 4-6 cps, often asymmetric tremor seen mainly in a “position of repose” or at rest. But there are other hypertonic/hypokinetic movement disorders that lack tremor, or have significant blood pressure, gait instability, or co-ordination problems. Since many individuals with ID, challenging behaviors and dual diagnoses are still treated with antipsychotic drugs, differentiating EPS from PD can be complicated in older patients.\textsuperscript{5}

Chorea and TD present a different picture. The movement disorders are classified in terms of hyperkinetic-hypotonic disorders—excessive movements with decreased muscle tone. There are many immunological, endocrine, genetic and pharmacologically induced hyperkinetic movement disorders. For example, Huntington’s Disease is an autosomal dominant movement disorder associated with not only progressive movements but also cognitive and psychiatric symptoms. It can be confused with TD, especially if prodromal psychotic or disruptive behaviors
Tic disorders present another set of problems. Although nonprogressive, tics wax and wane and change their topography over time. Many complex tics appear volitional or overlap both compulsions and stereotypies. There can be a mixture of tics, including dystonic tics (hyperkinetic-hypertonic movements) as well as obsessive-compulsive disorder, ADHD and explosive-aggressive behaviors and SIB. Patients with ID and tic disorders are frequently treated with APDs and are at risk for rebound worsening of tics, due to waxing-waning or a tardive form of tics. For individuals with ID, many challenging behaviors display periodic worsening of both tics and behavioral symptoms, and all too often are mislabeled with bipolar disorder. 1,3,6

Q. It appears that clinical diagnosis can be complicated. Do other approaches such as genetic or neuropharmacological findings help?

A. Both can be helpful. Perhaps the most useful approach involves a pharmacological dissection of the movement disorder. This involves using the patient’s response to various medications to develop a list of possible neurochemical subtypes. For example, extrapyramidal side effects (EPS) may improve with either reducing the antipsychotic agent or adding anti-cholinergic medications like Cogentin. It is useful to think of the emergence of TD in terms of an “opposites” model—decreasing antipsychotic or increasing anticholinergics will worsen abnormal movements. These “opposite” findings provide two useful pieces of information about the role of dopamine and acetylcholine in TD and EPS.

The same concept of imbalance DA/Ach ratios is a useful model for explaining primary movement disorders. For example hyperkinetic movement disorders (Huntington’s chorea) are associated with excessive dopaminergic activity and decreased cholinergic tone. Hypokinetic movement disorders like Parkinson’s disease result from the destruction of dopaminergic neurons associated with a relative increase in cholinergic activity. Although woefully oversimplified, this model suggests both causality and potential treatment approaches for other movement disorders.1,3

Q. Tardive dyskinesia is a major concern for clinicians treating individuals with severe challenging behaviors and major mental disorders. What advise would you give to physicians about prescribing antipsychotics medications to patients with severe/profound ID?

A. As you know TD is ......................... First of all think of TD as more than one disorder. Secondly, prevention is the best treatment. Thirdly, learn as much as you can about various risk factors. TD is a hyperkinetic disorder with considerable variability in typology, topography, subtype of psychiatric disorder, level of EPS/akathisia, 2 co-occurring neurological disorders, and duration of neuroleptic treatment. For example, older patients are at greater risk for oro-lingual-mandibular movements that display a relatively consistent relationship to total cumulative dose (dose times duration of treatment). This is especially true if there are cognitive and memory changes associated with most dementias. Because aging affects DA neurons, the threshold for EPS may be lower; this factor influences risk for persistent TD. On the other hand, young people may show relatively higher rates of withdrawal or reversible dyskinesia that is likely due to their youth. But some young patients develop severe holokinetic or dystonic forms of TD very early in the course of treatment.

There is a degree of increased risk associated with the use of APDs in nonschizophrenic psychiatric patients. This applies to mood and anxiety disorders (including obsessive-compulsive) as well as many challenging behaviors. The risk for TD is elevated for patients placed on long term APDs for SIB, aggression, or extreme irritability. Pre-existing movement disorders, brain disorders including CNS trauma, and neurodevelopmental disorders may be a problem for patients with SPID. Perhaps the one advantage of the new second and third generation APDs is the diminished rates of EPS and use of relatively low doses commonly used for severe challenging behaviors.

Preventive measures are the best treatment. These include minimizing exposure to non-psychotic individuals; caution among patients with psychotic mood disorders, careful monitoring for the emergence of dyskinetic movements, using the least effective dose, periodic dose reductions, avoidance of anti-cholinergic medications and if possible, tapering and discontinuation of antipsychotic medications when clinically prudent. The old concept of drug holidays from APDs was
a mistake, since repeated stopping and restarting APDs may increase the risk of developing TD.\textsuperscript{3}

Finally, the use of second and third generation APDs is helpful but do not forget these drugs are less likely to but can still cause TD. Metabolic syndrome and Type II diabetes mellitus are reported with the newer APDs. This side effect creates an interesting paradox—a reduced incidence of TD secondary to EPS but a possible increased risk due to insulin resistance and the long term sequelae of Type I diabetes. In short, we should consider the risk benefit ratios for any antipsychotic regardless of generational status.

Once abnormal movements are observed the clinician should still rule out other late-onset hyperkinetic movement disorders. If clinically possible, the neuroleptic should be tapered and discontinued. Many cases of TD are actually reversible or improve over time once the offending agent is removed. Depending on the severity of the movement disorder, treatment of re-emerging psychiatric symptoms with clozapine may allow time for the remission of dyskinetic movements without the resurgence of psychosis.\textsuperscript{3}

Q. What happens if nothing works and you are uncertain about the next step?

A. Of course, this is the easy part. There is a growing body of knowledge from molecular genetics, neurochemistry and functional neuroanatomy of movement disorders that bring neuropeptides, multiple other neurotransmitters, second and third messenger systems and degenerative changes that disconnect complex regulatory pathways in most movement disorders. For most clinicians, if interventions based on the DA/Ach model fail, or if there are other neurological or metabolic findings present, it is definitely time for a referral.

It is prudent to refer when you are no longer comfortable with the differential diagnosis or management strategies. But in some circumstances it may be difficult to find neurologists who are movement disorder specialists. Even if such clinicians are available, some may not be comfortable managing patients with SPID. Searching local medical society or American Neurological Association membership data bases may be helpful. The increasing use of telemedicine hook ups may help resolve this issue since real time observation can occur. The digital videos or home video tapes of the movements are still valuable bit of information.

\section*{References}


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