Anatomical Distribution of Involuntary Movements and Clinician-Reported Impact of Tardive Dyskinesia: A Real-World Analysis of the IMPACT-TD Registry

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Craig Chepke,[1,2] Stacy Finkbeiner,[3] Martijn Konings,[3] Mark Henegar,[3] Diana Klakotskaia,[3] Winona Tse[4]

[1]Excel Psychiatric Associates, Huntersville, NC, United States; [2]Atrium Health, Charlotte, NC, United States; [3]Teva Branded Pharmaceutical Products R&D LLC, Parsippany, NJ, United States; [4]Icahn School of Medicine at Mount Sinai, NY, United States

Objective: To examine the relationship between the multidimensional impact of tardive dyskinesia on daily functioning and the anatomical distribution and severity of tardive dyskinesia-associated movements

Background

- Tardive dyskinesia (TD) is a hyperkinetic movement disorder associated with exposure to dopamine receptor-blocking agents, including antipsychotic drugs[1]
- TD is characterized by involuntary, repetitive movements in the face, trunk, and extremities[2]
- Abnormal TD-associated movements may have a negative impact on multiple areas of functioning[3,4] and have been associated with worse quality of life[5]
- Understanding the relationship between the anatomical location of involuntary movements and the impact of TD on daily functioning may enhance clinical awareness of the burden of TD

Methods

- The IMPACT-TD Registry is an ongoing, phase 4, 3-year longitudinal study
  - Individuals aged ≥18 years with a score of ≥2 on at least 1 item of the Abnormal Involuntary Movement Scale (AIMS) and with probable TD were included
  - Individuals with vesicular monoamine transporter type 2 (VMAT2) inhibitor treatment at enrollment were excluded from the current analysis
- Clinicians rated TD impact in 4 life domains (social, psychological/psychiatric, physical, and vocational/educational/recreational) using the IMPACT-TD clinician-reported outcome (ClinRO) scale (4-point Likert scale, highest domain score = global score)[6]
- Individual AIMS item scores (muscles of facial expression, jaw, lips/perioral area, tongue, upper extremities, lower extremities, and trunk) and their relationship with moderate/severe ClinRO domain scores were evaluated
  - Each AIMS item was scored from 0–4 for abnormal movements (0 = none, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe) (**Table 1**)

Table 1. AIMS Scoring Definitions for Body Regions

0	1	2	3	4
None = No abnormal movements observed	Minimal = Barely noticeable movement; could be within normal limits	Mild = Definite but not pronounced abnormal movement	Moderate = Clearly abnormal movement	Severe = Markedly abnormal movement (very noticeable)

- Participants who experienced moderate/severe impact of TD in any life domain (per the IMPACT-TD ClinRO scale) had median AIMS item scores of 2 (mild) for muscles of facial expression and upper extremities, 1 (minimal) for the tongue and lower extremities, and 0 (none) for the trunk (**Table 2**)
  - When examining individual life domains, AIMS item scores varied for the lips/perioral area and in the jaw, with a median of 2 among participants experiencing social and physical impacts and a median score of 1 among those experiencing psychological/psychiatric and vocational impacts

Table 2. Median AIMS Body Region Score in Patients With Moderate/Severe Impact of TD per IMPACT-TD ClinRO Domains

	AIMS body region items						
IMPACT-TD ClinRO domains	Muscles of facial expression	Lips and perioral region	Jaw	Tongue	Upper extremities	Lower extremities	Trunk
Global, n	327	327	326	326	326	325	326
AIMS, median	**2**	**1**	**1**	**1**	**2**	**1**	**0**
Social, n	225	225	224	224	224	223	224
AIMS, median	**2**	**2**	**2**	**1**	**2**	**1**	**0**
Psychological, n	264	264	263	263	263	262	263
AIMS, median	**2**	**1**	**1**	**1**	**2**	**1**	**0**
Physical, n	216	216	215	215	215	215	215
AIMS, median	**2**	**2**	**2**	**1**	**2**	**1**	**0**
Vocational, n	217	217	216	216	216	216	216
AIMS, median	**2**	**1**	**1**	**1**	**2**	**1**	**0**

- Among participants with an individual AIMS item score of 1 or 2 in any body region, 71% to 81% experienced moderate/severe global TD impact, with the highest rate seen in the psychological domain, particularly among those with tongue movements (**Table 3**)

Table 3. Percentage of Patients With Moderate/Severe Impact per Baseline Body Region AIMS (Score of 1 or 2)

	IMPACT-TD ClinRO domains				
Body region AIMS score, 1 or 2	Social	Psychological	Physical	Vocational	Global
Muscles of facial expression (n=260)	49	58	45	47	71
Lips and perioral region (n=225)	52	59	48	49	72
Jaw (n=201)	53	57	51	50	74
Tongue (n=238)	52	67	52	58	81
Upper extremities (n=236)	50	62	45	53	77
Lower extremities (n=174)	49	55	52	46	74
Trunk (n=108)	58	61	56	47	75

The percentages of patients shown in the table cells are coded from green (0%) to red (100%)

- Among participants with individual AIMS item scores of 3 or 4 in any body region, 88% to 97% experienced moderate/severe global impact of TD
- Among participants with an AIMS score of 3 or 4 in muscles of facial expression, lower extremities, or trunk, ≥80% experienced moderate/severe impact of TD in each ClinRO domain (**Table 4**)
  - Although the social domain had the highest rates of moderate/severe impact among participants with AIMS scores of 3 or 4 in muscles of facial expression or the tongue, the physical domain was most frequently affected by movements in the remaining body regions

Table 4. Percentage of Patients With Moderate/Severe Impact per Baseline Body Region AIMS (Score of 3 or 4)

	IMPACT-TD ClinRO domains				
Body region AIMS score, 3 or 4	Social	Psychological	Physical	Vocational	Global
Muscles of facial expression (n=69)	86	84	84	80	97
Lips and perioral region (n=84)	73	73	79	61	92
Jaw (n=89)	70	75	83	63	92
Tongue (n=59)	76	73	75	58	88
Upper extremities (n=81)	75	78	81	64	91
Lower extremities (n=60)	82	85	87	80	95
Trunk (n=36)	89	86	94	83	94

The percentages of patients shown in the table cells are coded from green (0%) to red (100%)

Conclusions

- Individuals can experience moderate/severe multidimensional impact of TD even when individual AIMS component scores are mild in severity
- Pronounced movements involving the muscles of facial expression, lower extremities, and trunk are most consistently linked to moderate/severe TD-related impact across multiple functional domains
- These findings underscore the need for clinicians to assess TD functional impact in addition to assessing movement severity

Demographics

- 438 participants in the IMPACT-TD Registry who were not receiving VMAT2i treatment at baseline and had recorded AIMS scores were included in this analysis
  - Included participants had a mean age of 50.5 years; 84.5% were aged <65 years; 51.6% were men, and 59.6% were White (**Table 5**)
  - The most common baseline psychiatric diagnoses were schizophrenia (39.3%) and depression (39.0%), and most participants (59.8%) had received prior treatment with only second-generation or later antipsychotics (**Table 6**)

Table 5. Demographic Characteristics

	No VMAT2 inhibitor with baseline AIMS score (N=438)
Age at index, mean (SD) [range], years	**50.5** (14.5) [18–88]
Age group, years	
18–45	**165** (37.7)
46–65	**205** (46.8)
>65	**68** (15.5)
Sex	
Men	**226** (51.6)
Women	**212** (48.4)
Race	
White	**261** (59.6)
Black/African American	**97** (22.1)
Other[a]	**40** (9.1)
Not reported	**40** (9.1)
Ethnicity	
Not Hispanic or Latino	**312** (71.2)
Hispanic or Latino	**111** (25.3)
Unknown/Not reported	**15** (3.4)

Values shown are n (%) unless otherwise noted

[a]Includes Asian, American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander, and those self-reported as 'Other'

Table 6. Psychiatric History and Prior AP Use

	No VMAT2 inhibitor with baseline AIMS score (N=438)
Previous psychiatric history	**435** (99.3)
Anxiety disorder	**149** (34.0)
Bipolar disorder	**153** (34.9)
Depression	**171** (39.0)
Schizoaffective disorder	**63** (14.4)
Schizophrenia	**172** (39.3)
Other	**134** (30.6)
Known prior AP use	**401** (91.6)
FGAs only	**25** (5.7)
SGAs and beyond only	**262** (59.8)
Both	**112** (25.6)
Years since first AP exposure, median	12.2
Prior or concomitant TD medications	**98** (22.4)
VMAT2 inhibitor[a]	**32** (7.3)
Other	**69** (15.8)
Formal TD diagnosis	
Yes	**177** (40.4)
No	**261** (59.6)
Concomitant TD treatment	**49** (11.2)
Years since first TD movements, median	4.2

Values shown are n (%) unless otherwise noted

[a]Prior treatment only

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Abbreviations

AIMS = Abnormal Involuntary Movement Scale, AP = antipsychotic, ClinRO = clinician-reported outcome, FGA = first-generation antipsychotic, SGA, second-generation antipsychotic, TD = tardive dyskinesia, VMAT2, vesicular monoamine transporter type 2.

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