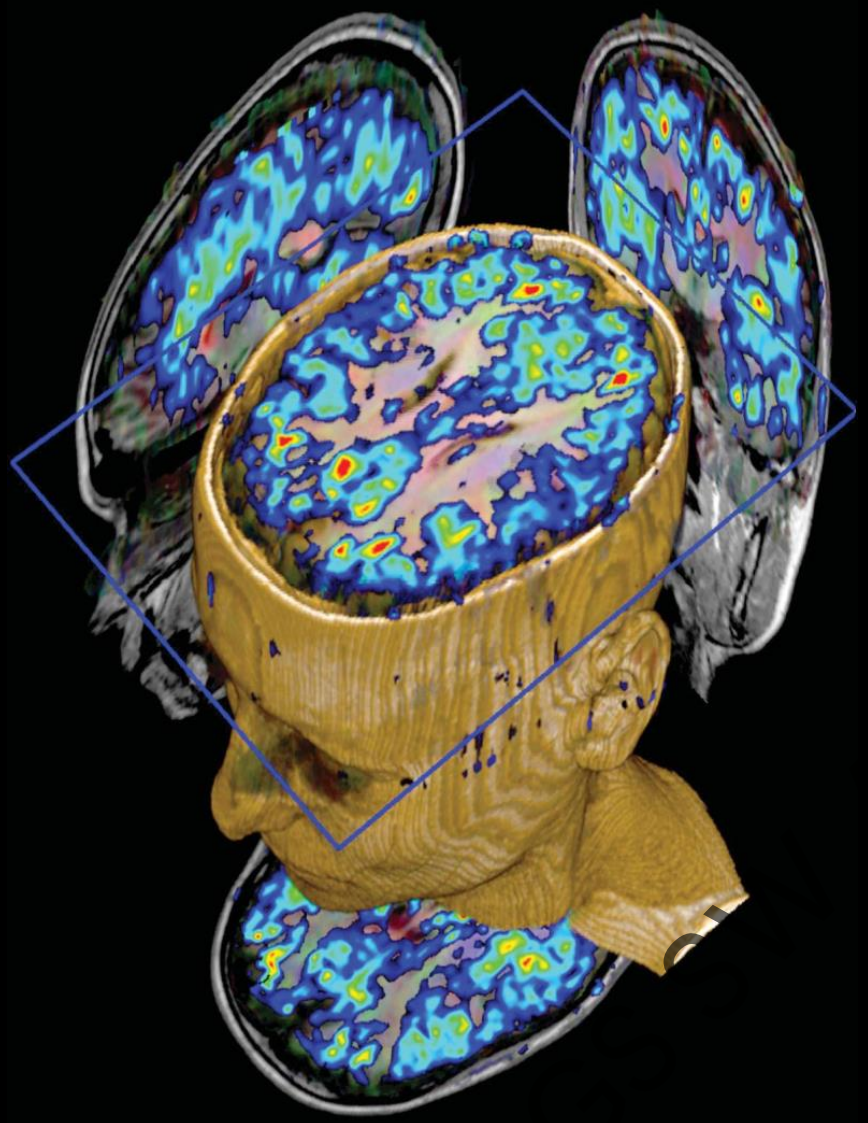
Management of Sialhorrhea (Drooling)

Timothy Harrower



Disclosures

I have received support to attend meetings, provide advice for adboards, delivering lectures etc from:

Merck Serrono, Biogen, UCB, Eisai, Brittania, Ipsen, MERZ, Allergan, Medtronic, GSK, GWP Pharma, Solvay Health Care

I am/have been CI/PI on the following

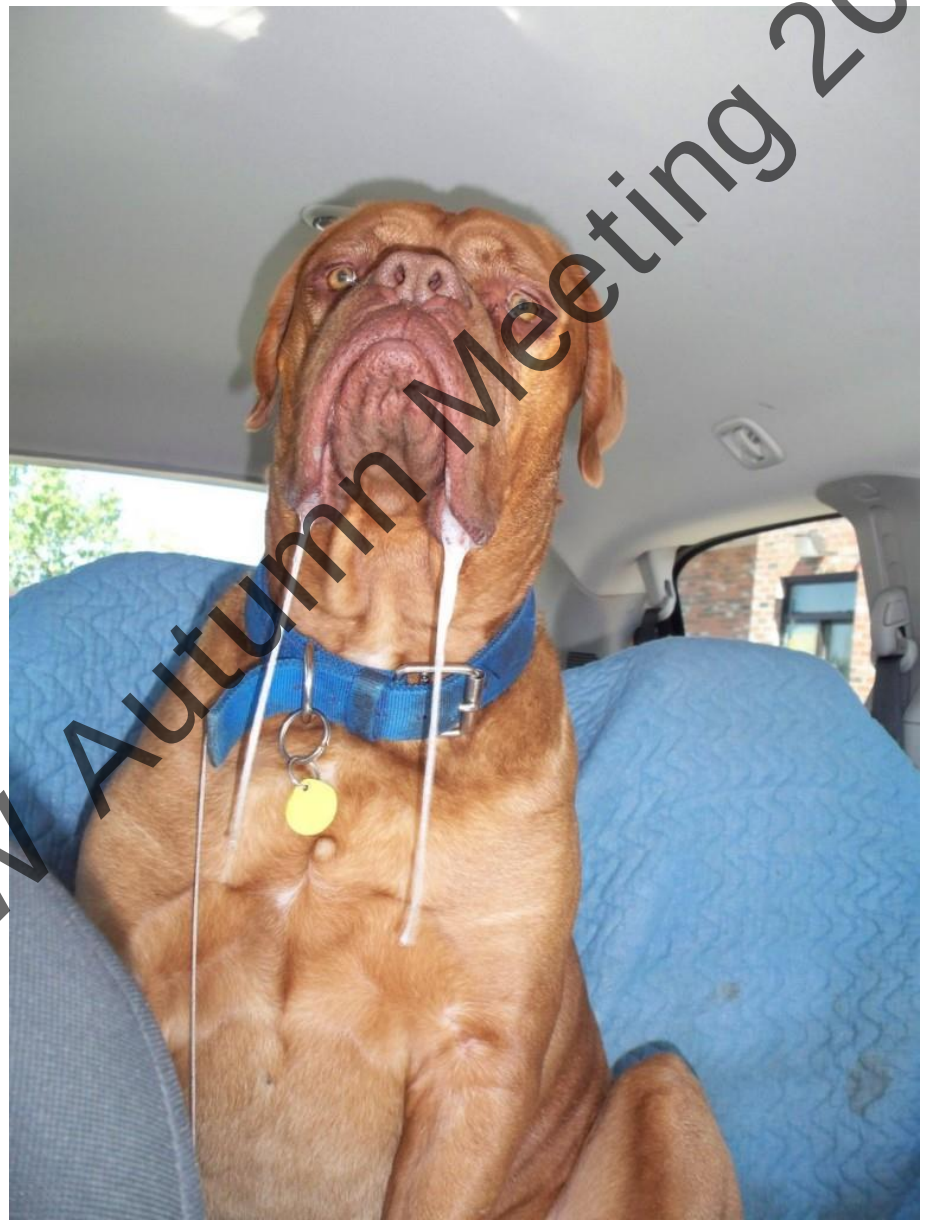
MS studies:
OPERA, ASCEND, TOP, JEMS, GAMES, PASSAGE, Arpeggio, Esteem, Enhance, Assure, TONIC, MS STAT2, Opera, Casting, Esteem, Lem PASS, LEM QOL,

Dystonia Studies:
Interest in CD1, CD2, ASPEN

Huntington's Disease studies:
EuroHD Registry , Enroll HD, HD Clarity, Precision WAVE 1 and 2.

Encephalitis studies:
SINAPPS-2, Dexenceph

Drooling, Sialorrhea, ptyalis



Embarrassment
Isolation
Aspiration
Skin breakdown
Bad odour
Infection

Conditions

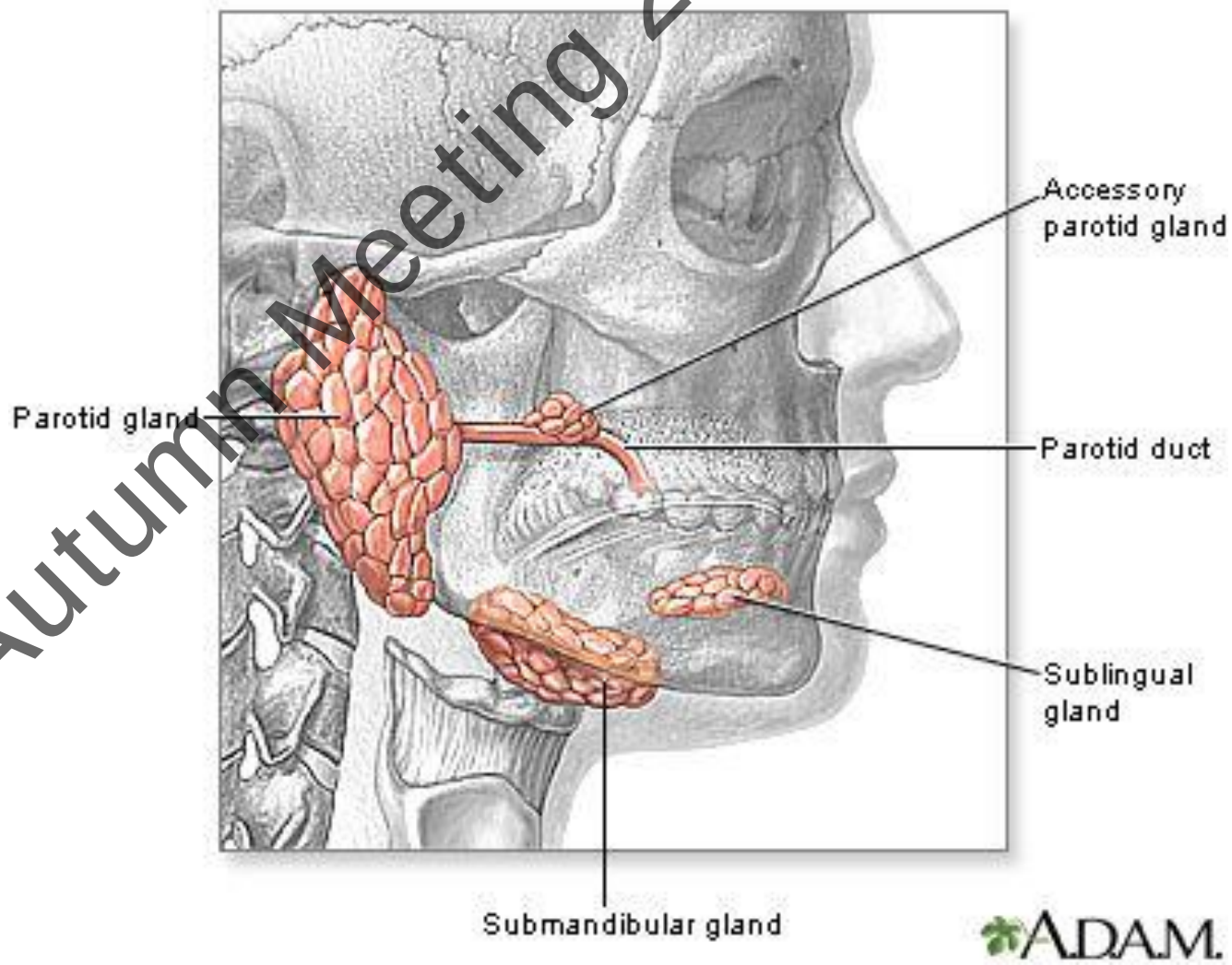
- Motor Neuron Disease
- Parkinson's Disease
- Head injury

- Cerebral Palsy

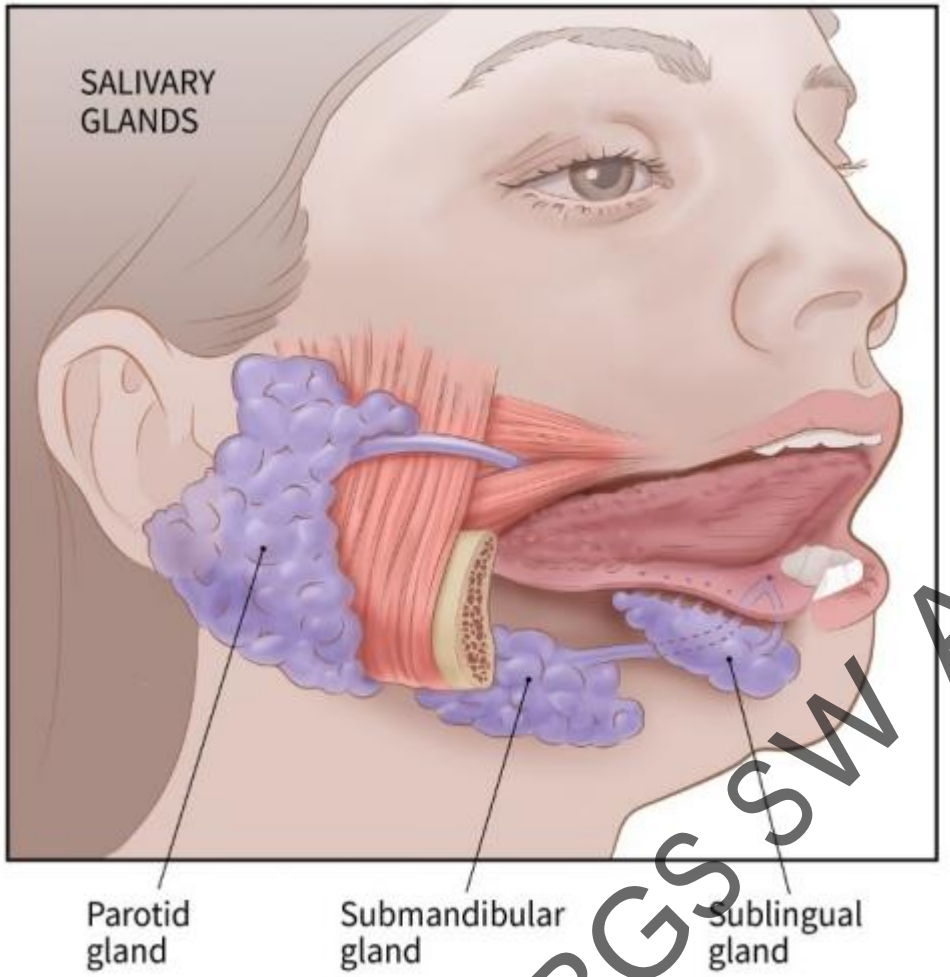
- Schizophrenia (Clozapine)
- Wilson's Disease

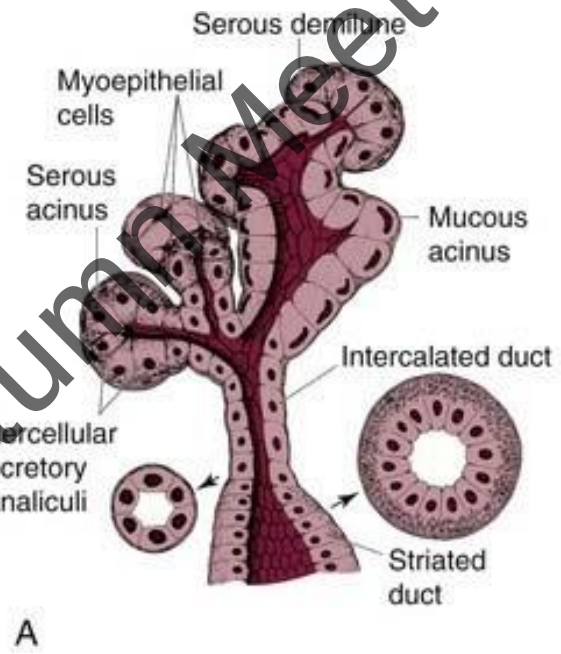
Outline

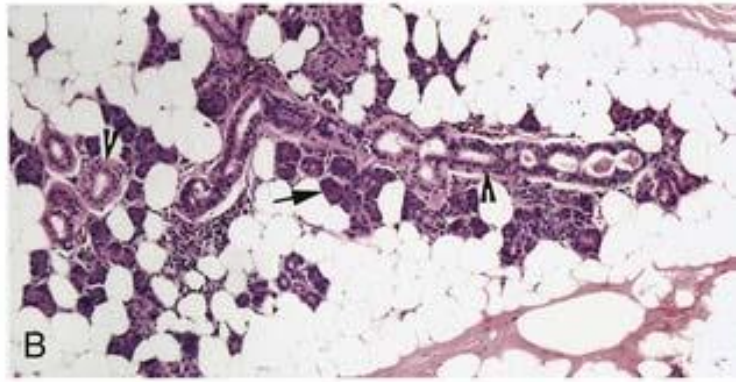
- Saliva physiology
- Saliva anatomy
- Pharmacology
- Bont A

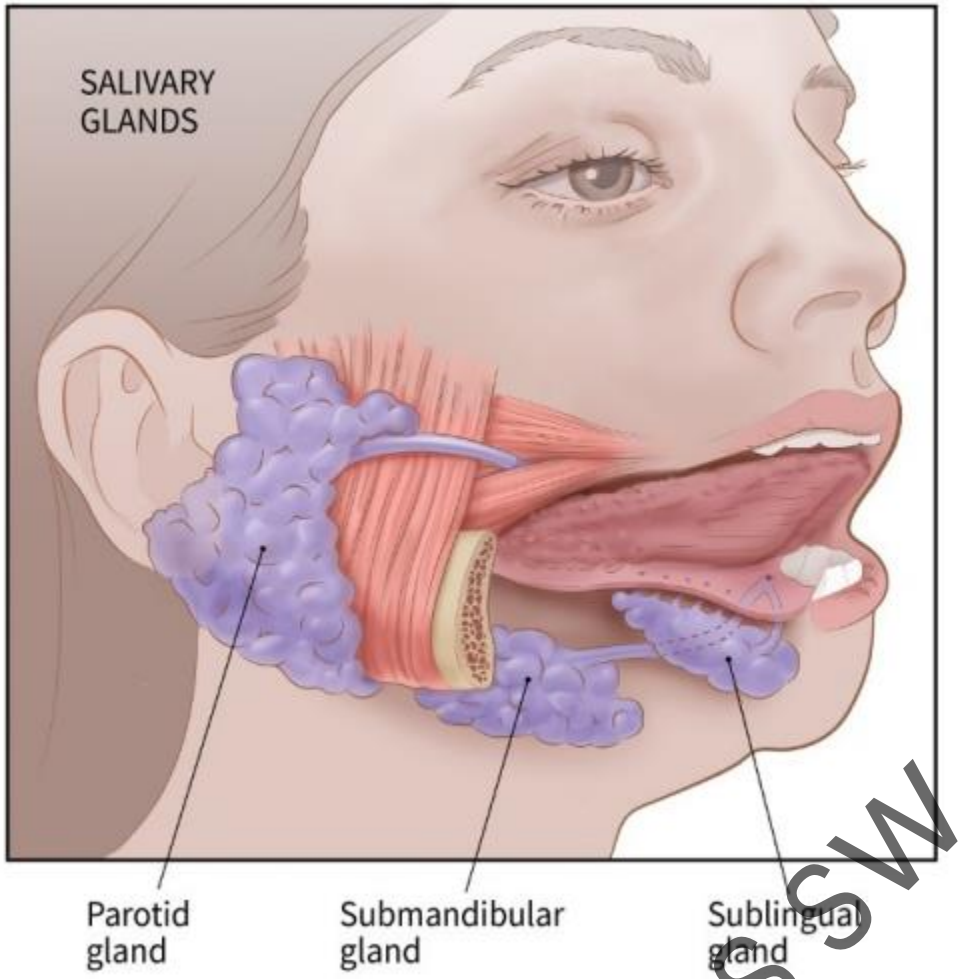


Anatomy and Physiology









Major Glands (92-95%) (6)

Parotid
- Watery serous – rich in Amylase, proline rich proteins
  - Stenson's Duct

Submandibular
- More mucinous
  - Wharton's Duct

Sub Lingual
- Viscous Saliva
  - Ducts of Rivinus
  - Duct of Bartholin

Minor Glands (5-8%) – (600-1000)

Found in Gingiva anterior part of hard palate
Serous glands – von Ebner glands (below circumvallate papillae on tongue)
Glands of Blandin- Nuhn – ventral tonue
Palatine, glossopalatine glands (mucinous)
Weber Glands

These glands secrete saliva which has a major role in:

Lubrication,
Digestion,
Immunity,
Maintenance of homeostasis in the human body

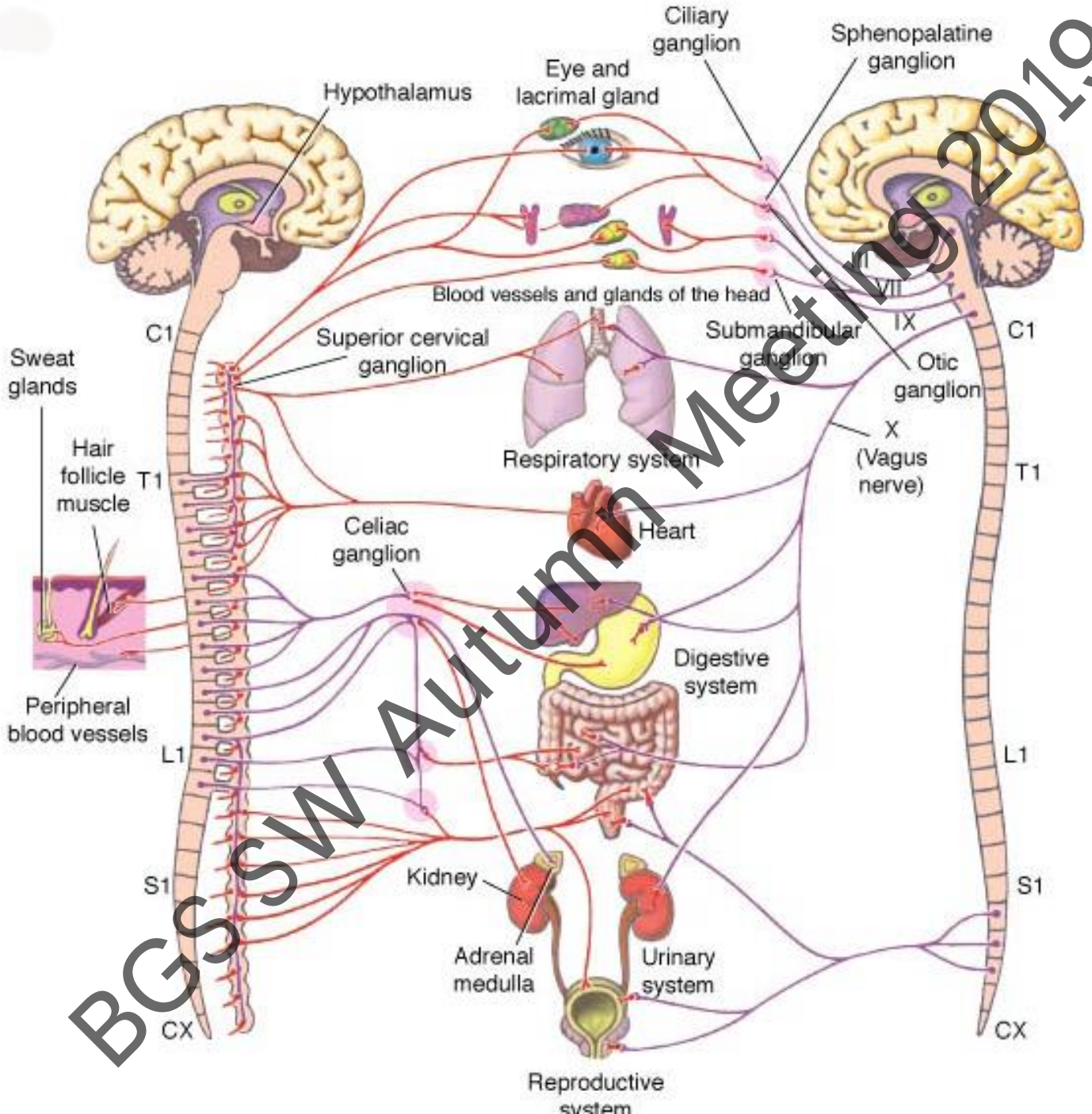
1000 – 1500 ml per day!

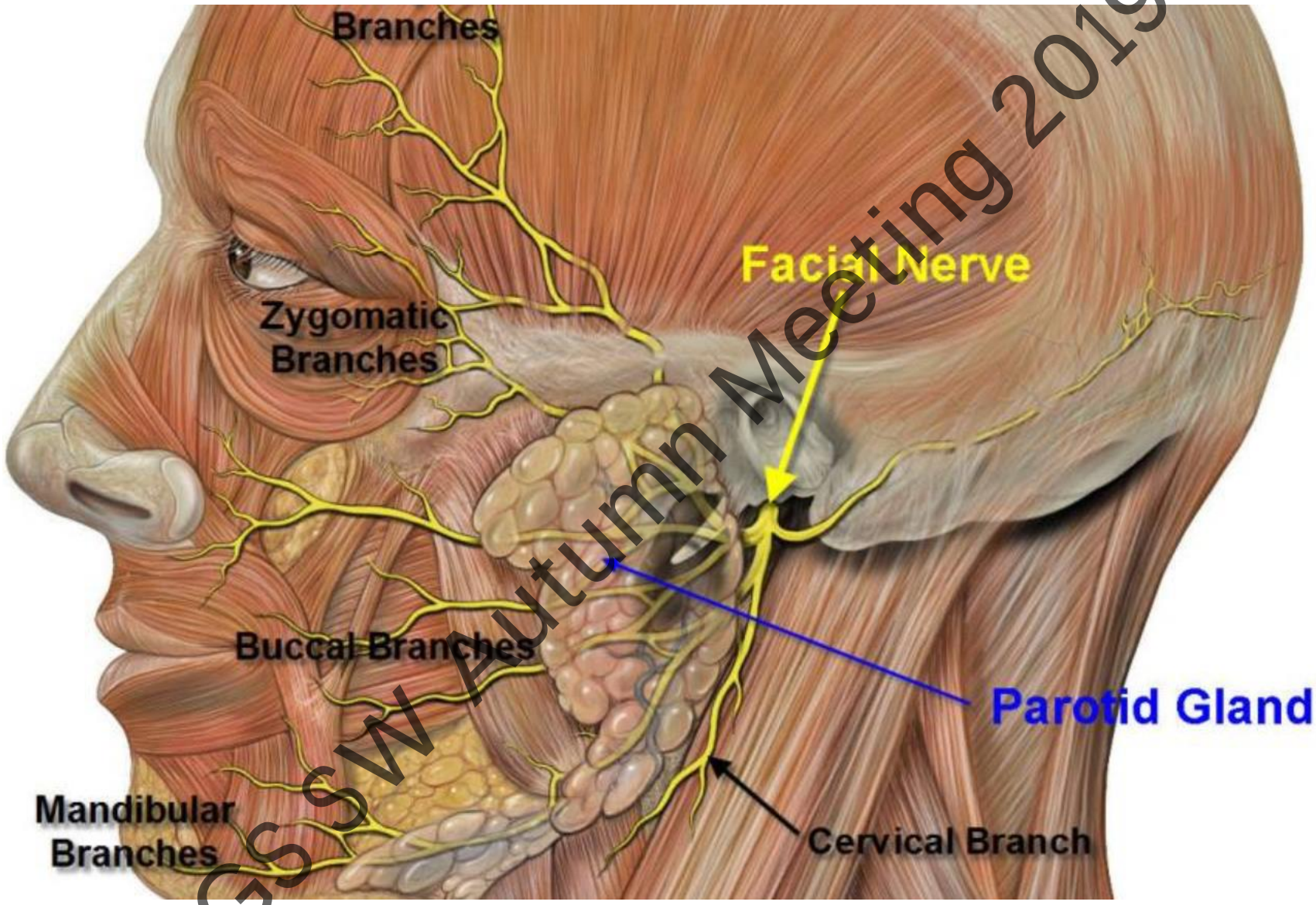
In the unstimulated state, 70% of saliva is secreted by submandibular and sublingual glands.

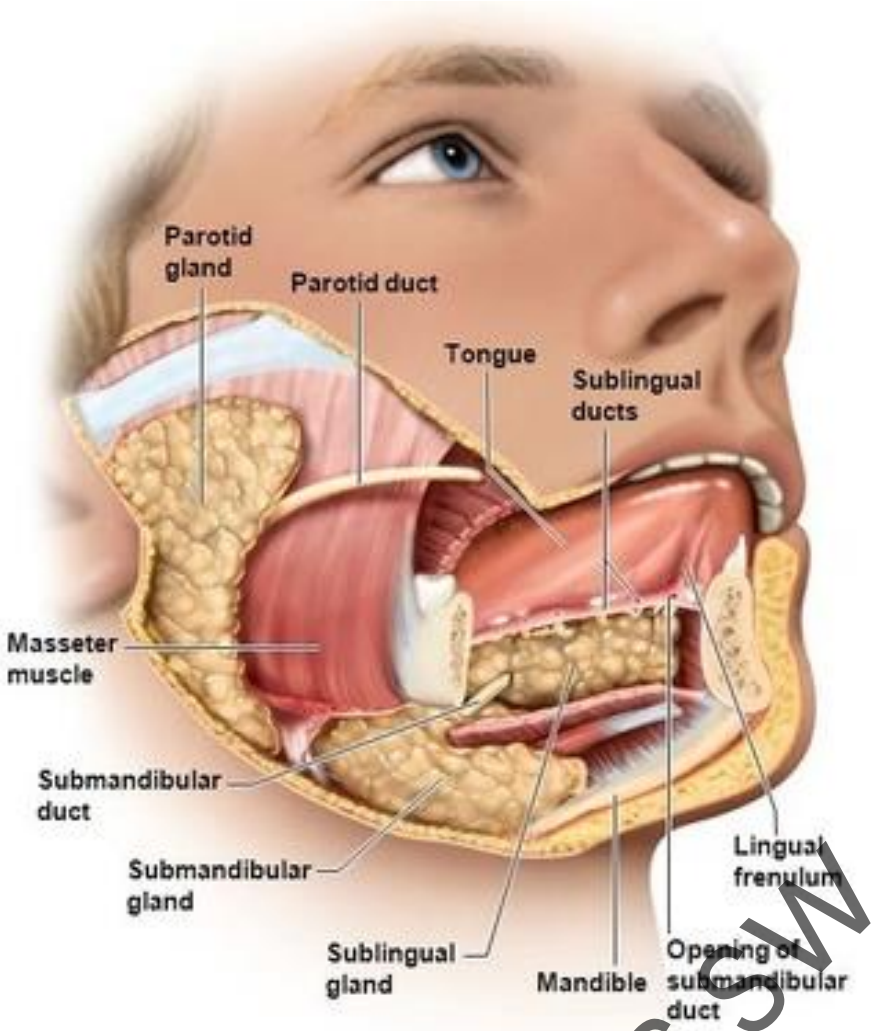
Conversely, in the stimulated state the parotids glands provide most of the saliva.

The flow of saliva is five times greater in the stimulated state than in the resting state.

An example of an exogenous source causing stimulation is chewing.







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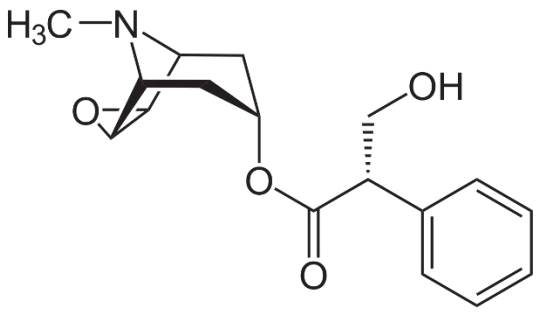
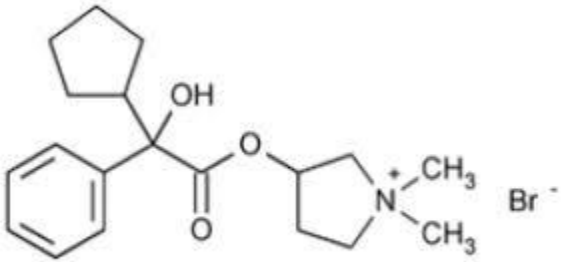
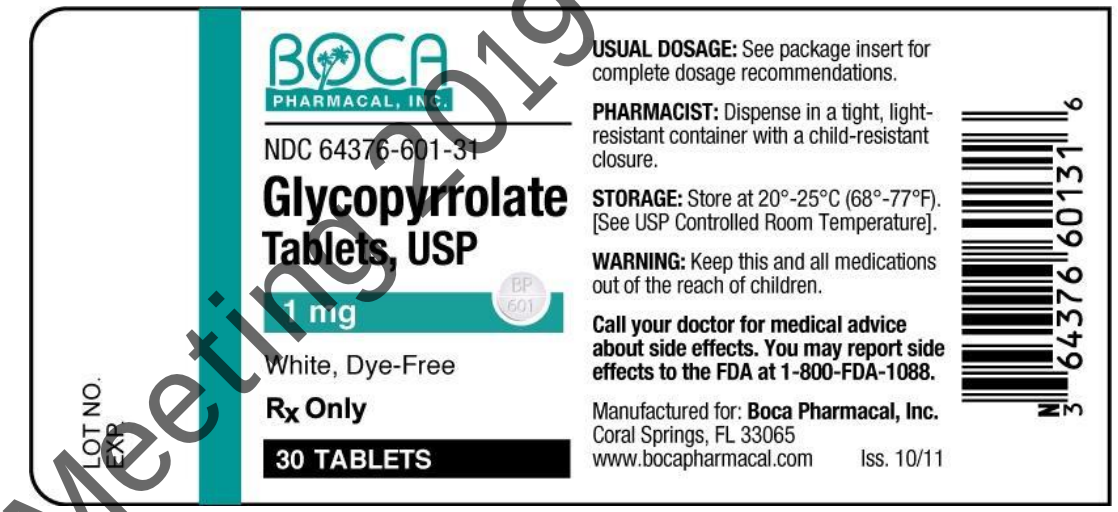
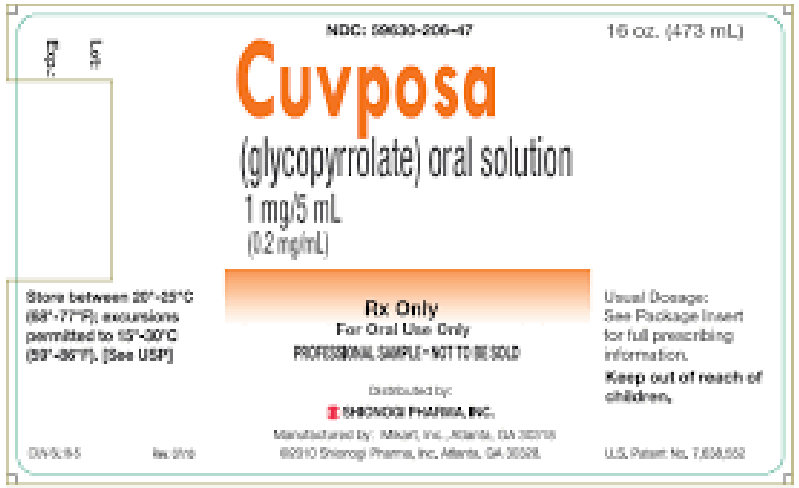


Hyoscine Patches



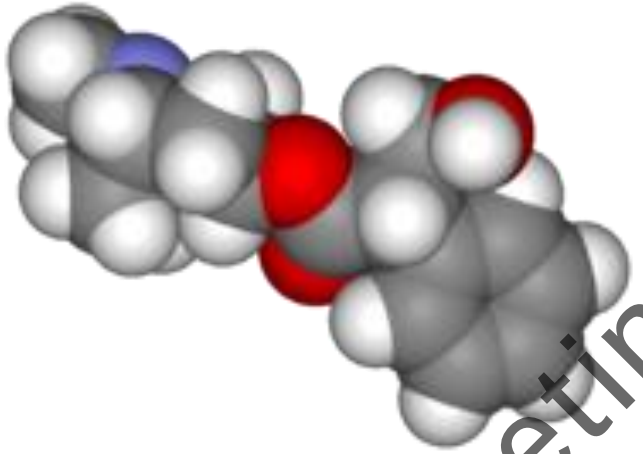
C19H28BrNO3 MW: 398.33

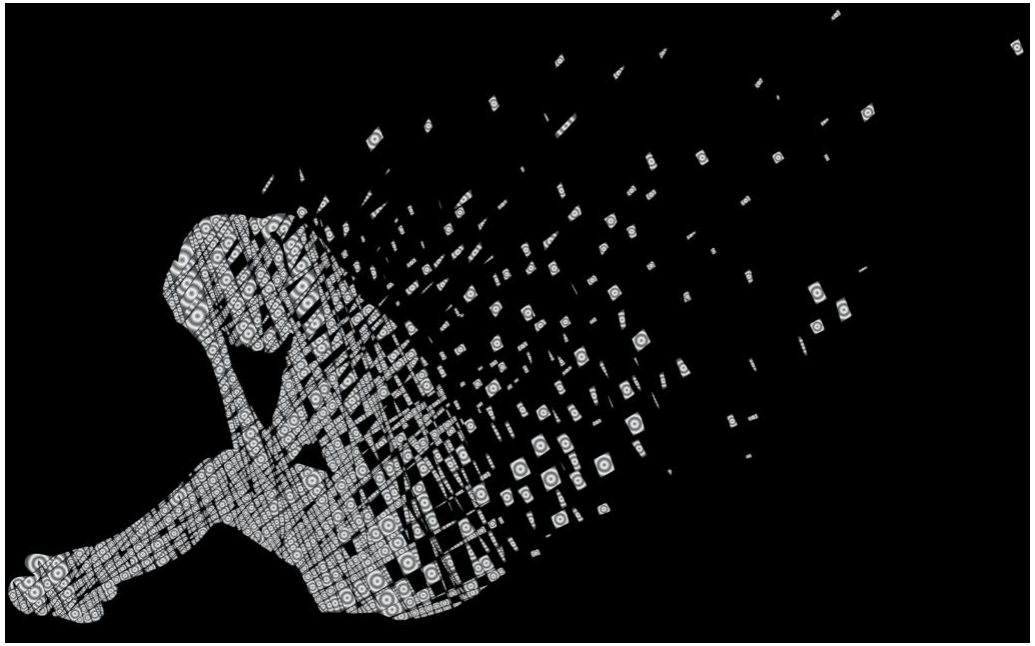




Parenteral: 0.1 mg (0.5 mL) IV or IM every 4 hours, 3 to 4 times daily. If a more profound effect is required the dose may be increased to 0.2 mg (1 mL).

1 mg oral tablet:
Initial dose: 1 mg orally 3 times daily or 1 mg in the morning, 1 mg in the early afternoon, and 2 mg at bedtime.
Maintenance dose: 1 mg orally twice daily to a maximum of 8 mg per day.



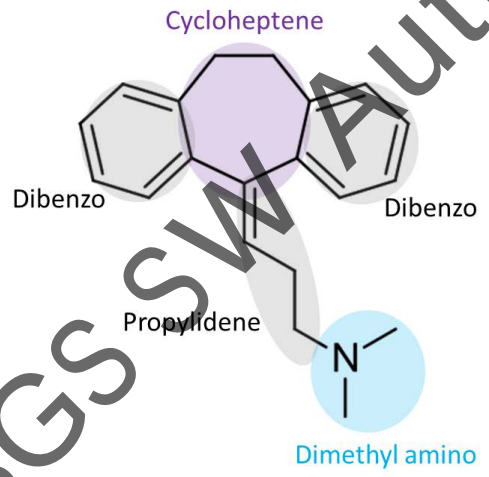


How to memorize drug structures

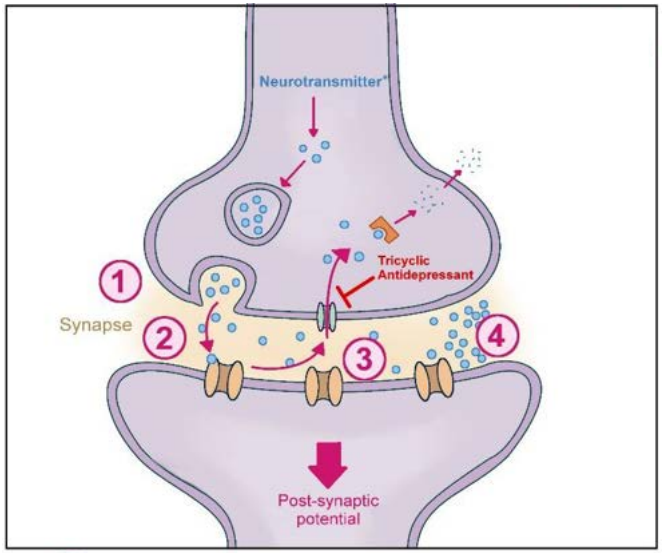
Tricicilc antidepressant (TCA)

Amitriptyline

10,11-dihydro-5-(gamma-Dimethylamino**propylidene**)-5H-dibenzo(a,D)**cycloheptene**



Pharmwar ©Silvi Hoxha



1. Neurotransmitter released in the synapse
2. Neurotransmitter activates post-synaptic receptor
3. Neurotransmitter reuptake is blocked by TA
4. Increased synaptic concentration of Neurotransmitter available to bind to the post-synaptic receptors

==> increased post-synaptic nerve transmission

* Neurotransmitter = serotonine or norepinephrine

Table 2: Summary of the dose variation of the treatments prescribed for the management of oral secretions

	Number of different doses	Dose range	Most common dose
Anticholinergic medications			
Hyoscine Patch (n=69)	8	¼ of 1mg patch per 72 hours – 1 ½ 1mg patch per 24 hours	1mg patch per 72 hours
Oral Hyoscine (n=8)	4	0.15mg TDS – 0.3mg TDS	0.3mg TDS
Amitriptyline (n=25)	13	10mg ON – 175mg	10mg ON
Sublingual Atropine Drops (n=24)	15	1% solution 2 drops ON – 1% solution 2 drops QDS	1-2 drops TDS
Glycopyrronium	13	02.mg BD – 3mg TDS	1mg TDS
Dysport	12	60U – 400U	100U
Neurobloc	6	1000U – 3000U	2500U
BOTOX A	2	14U – 100U	Each used once

Scopalamine?

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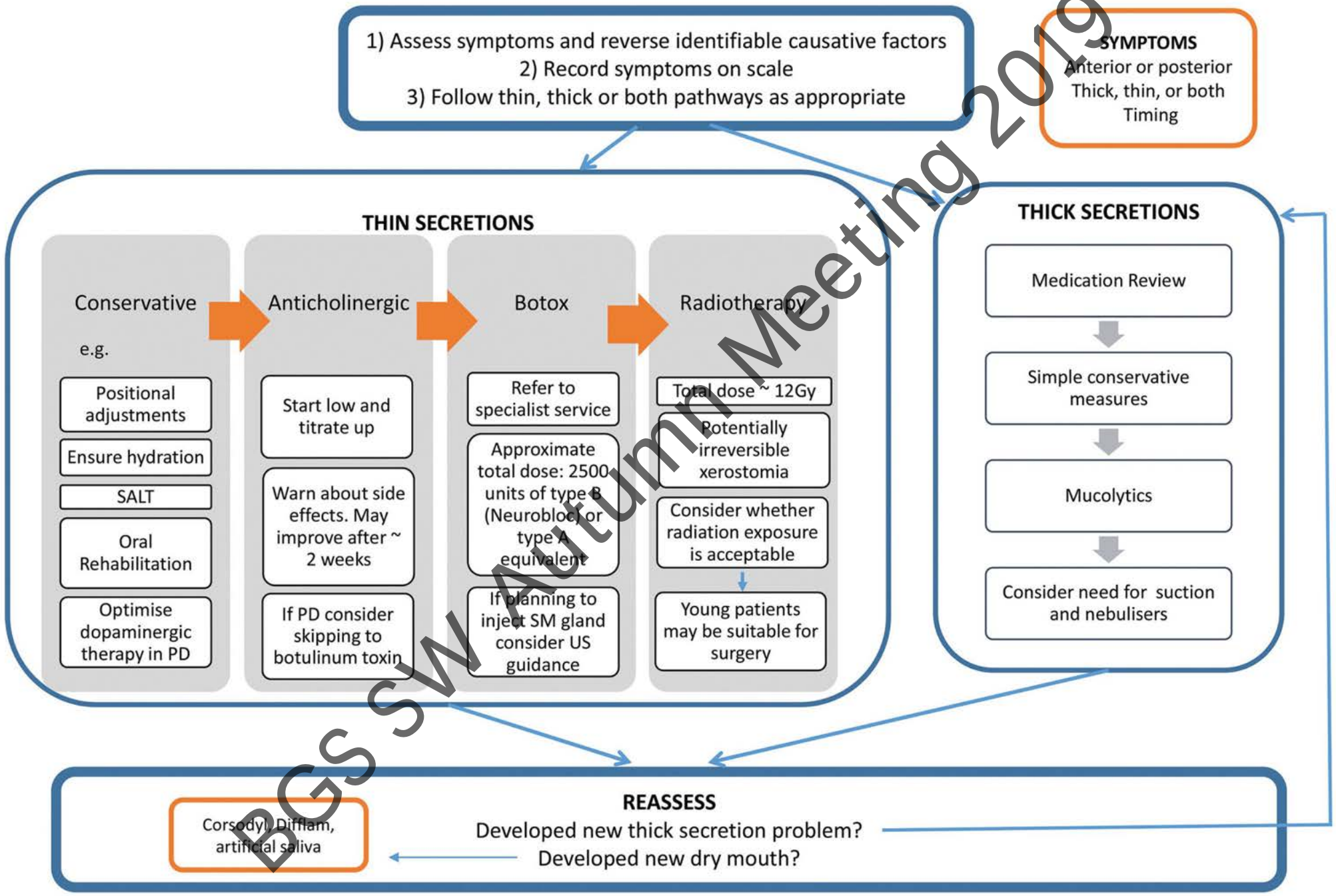
Table 1 Summary of treatment options

Type of therapy	Benefits of this approach	Side effects	Additional information
Conservative measures	Largely cheap Simple Minimal side effects	Few	Consider these in all patients
Anticholinergics	Easy to prescribe Cheap	Urinary retention, blurred vision, confusion	Caution in myasthenia gravis-related drooling
Botulinum toxin	Targeted therapy	Excessively dry mouth	Concerns over effects on bulbar function
Radiotherapy	Targeted therapy	Excessively dry mouth Risk of malignancy	Effects (including adverse effects) last from months to years
Surgery	Long-term symptom relief if effective	Generic surgical and anaesthetic risks Retention cysts	Irreversible Patients may be too frail to tolerate



SIAXI: Efficacy and safety of incobotulinumtoxinA for the treatment of sialorrhea in Parkinson's disease (PD) and other neurological conditions: Results of a Phase III, placebo-controlled, randomized, double-blind study

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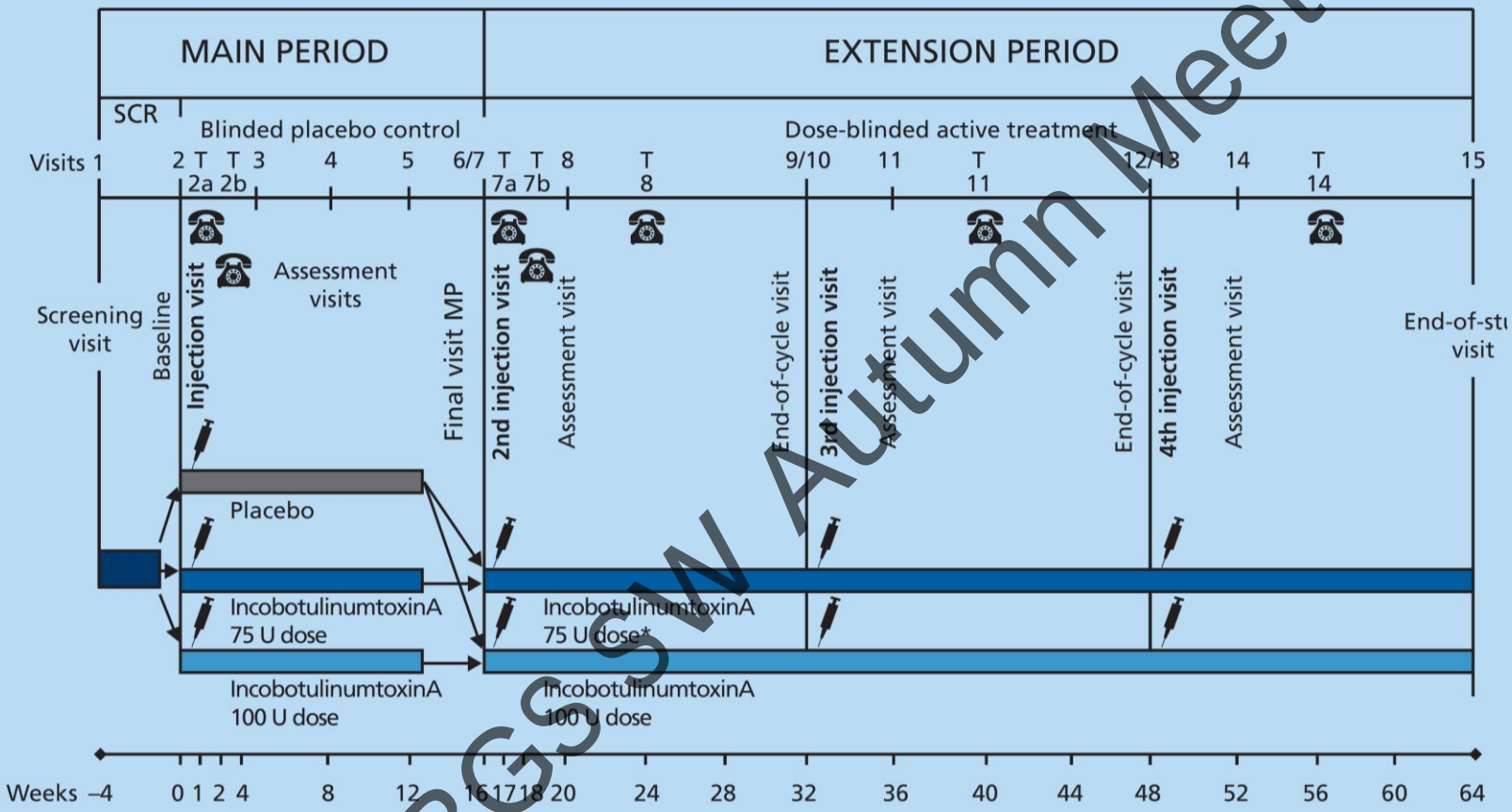
[3]Otorhinolaryngology University Hospital Brussels, Brussels, Belgium; [4]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany; [5]Parkinson-Klinik Ortenau, Wolfach, Germany



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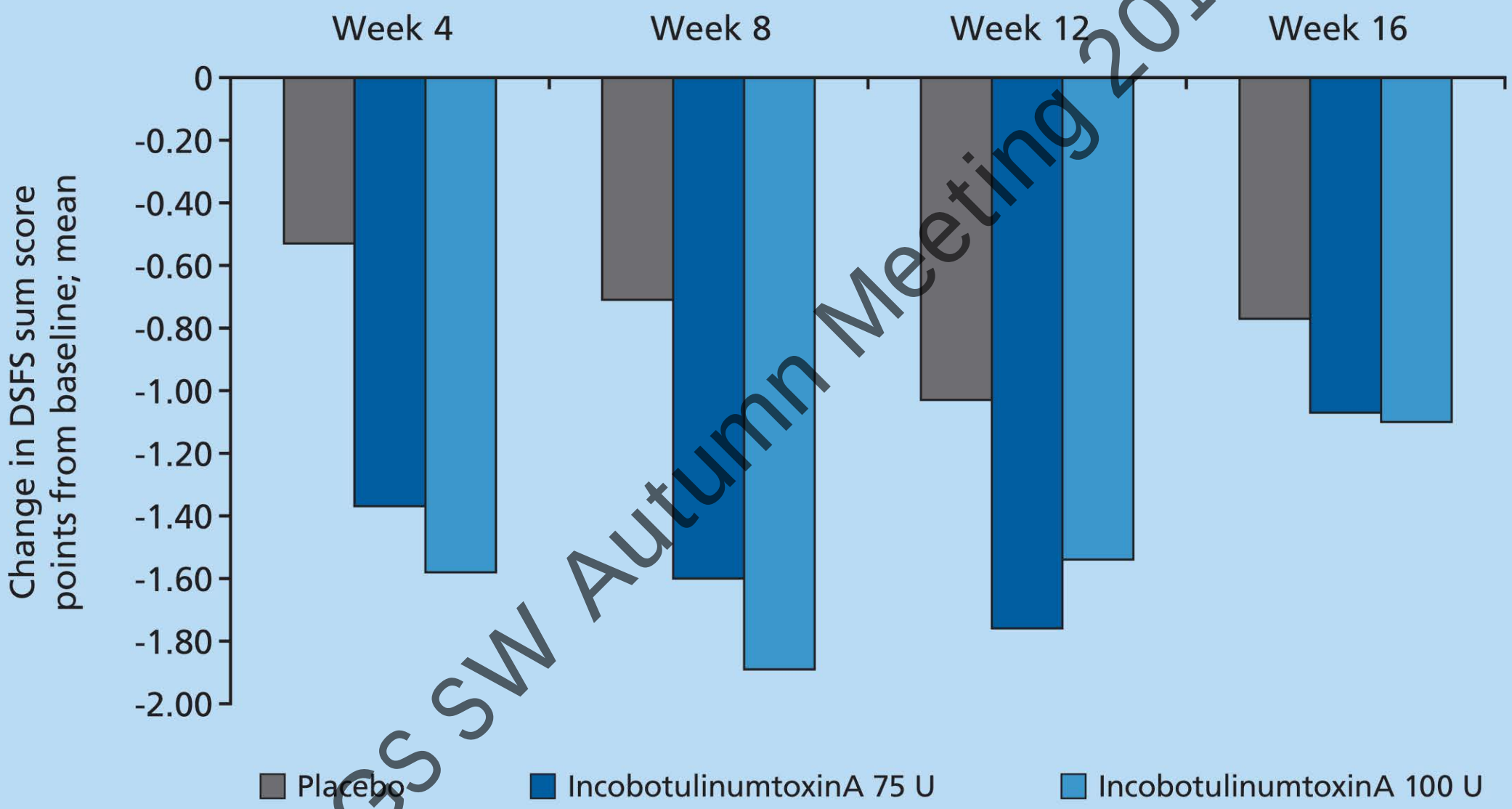

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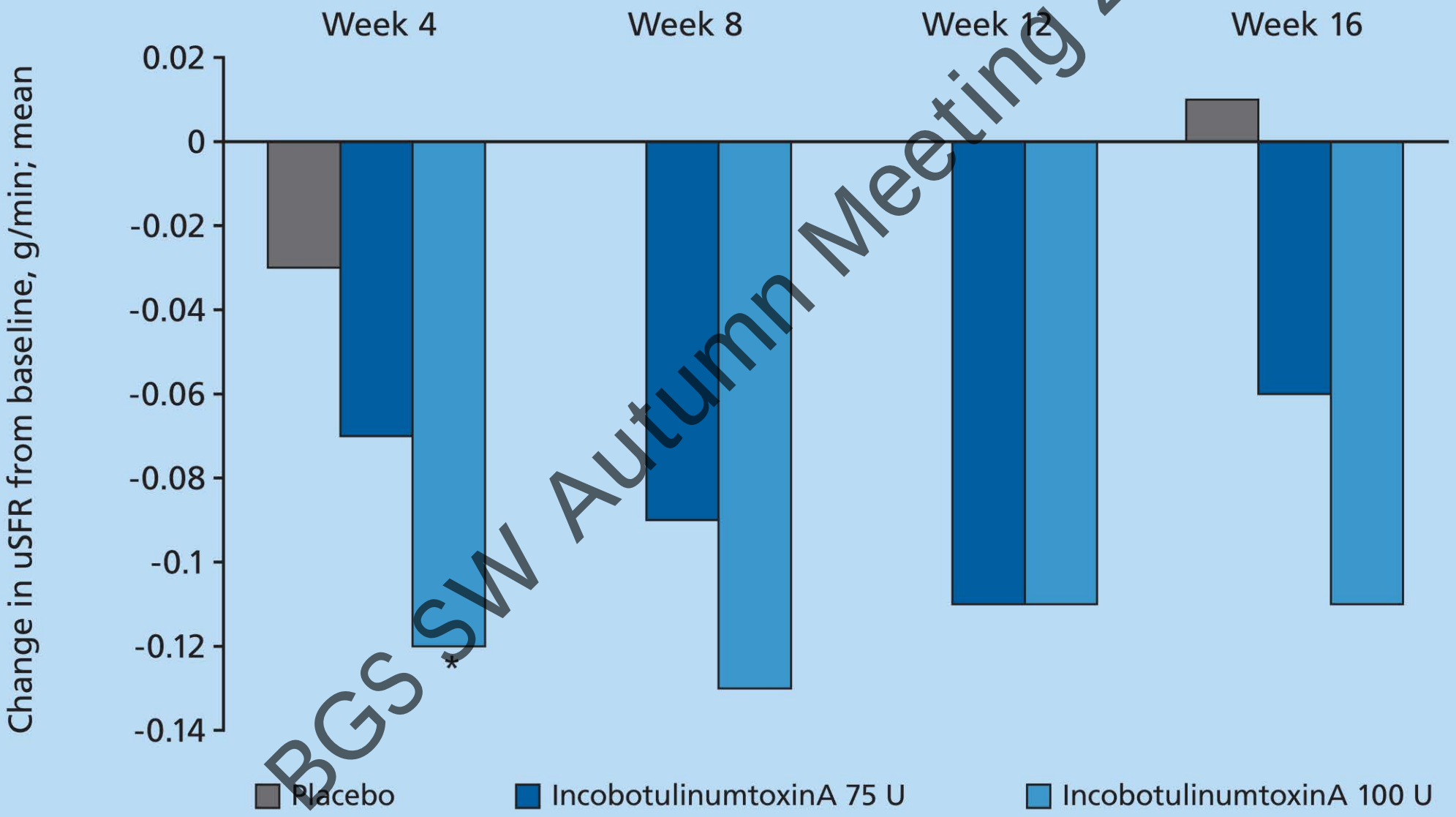
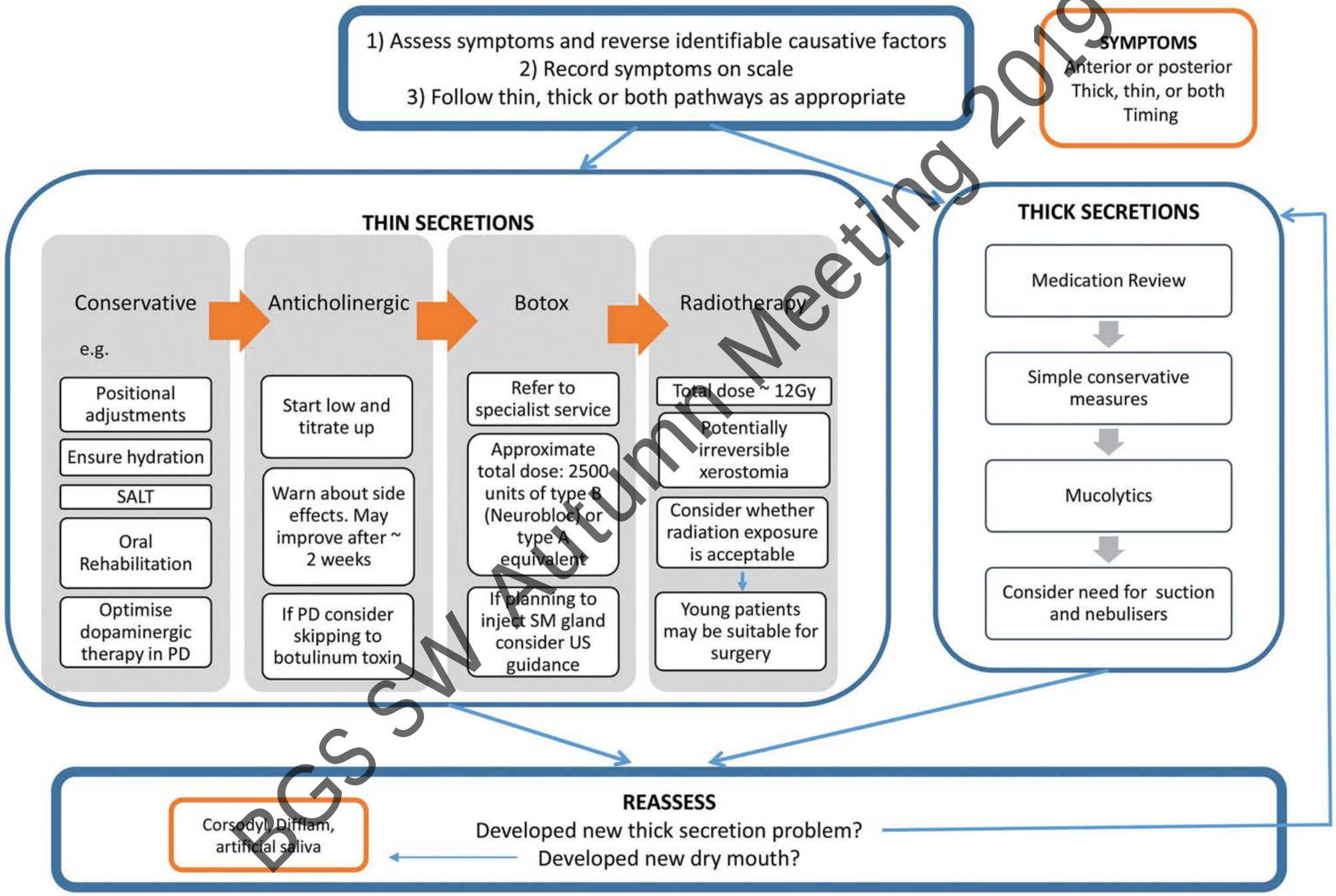
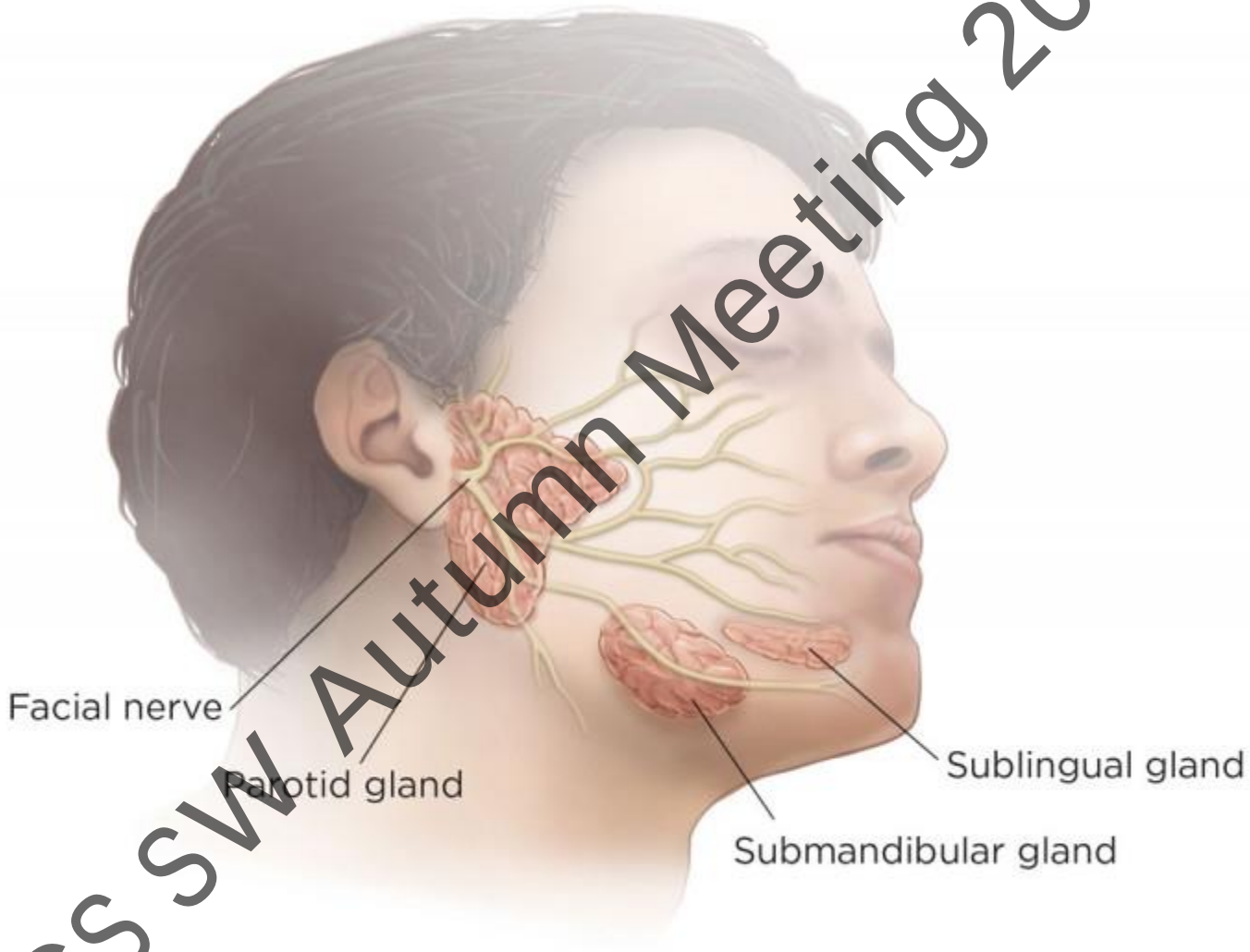
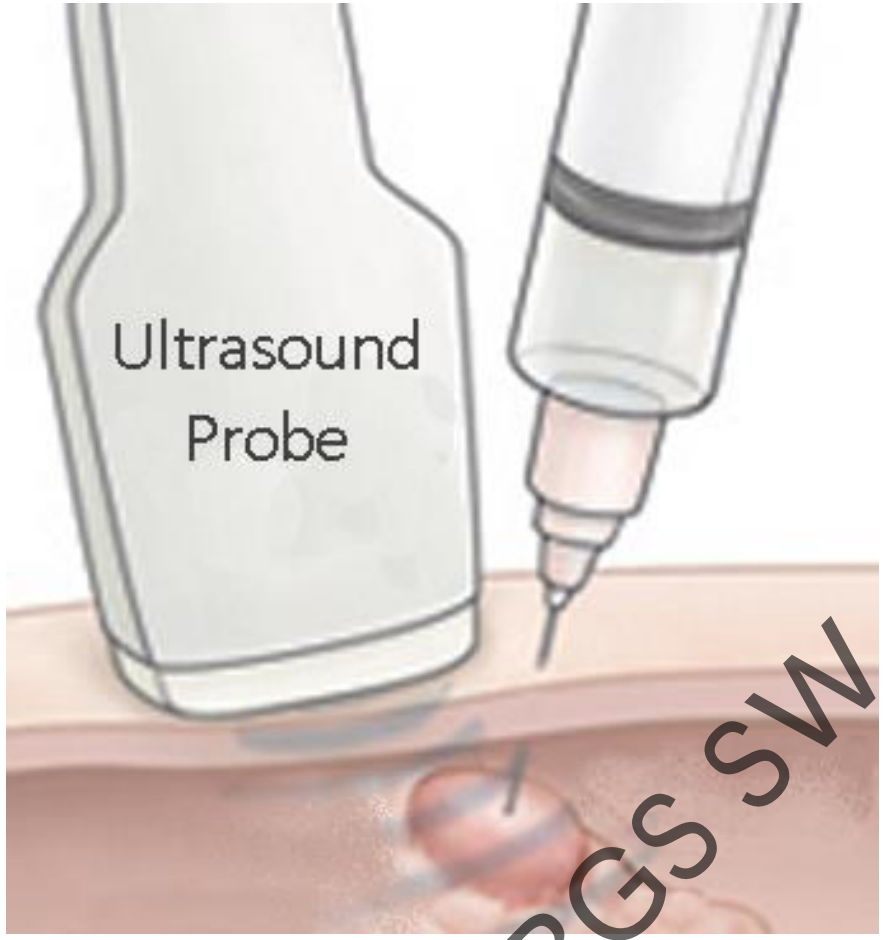
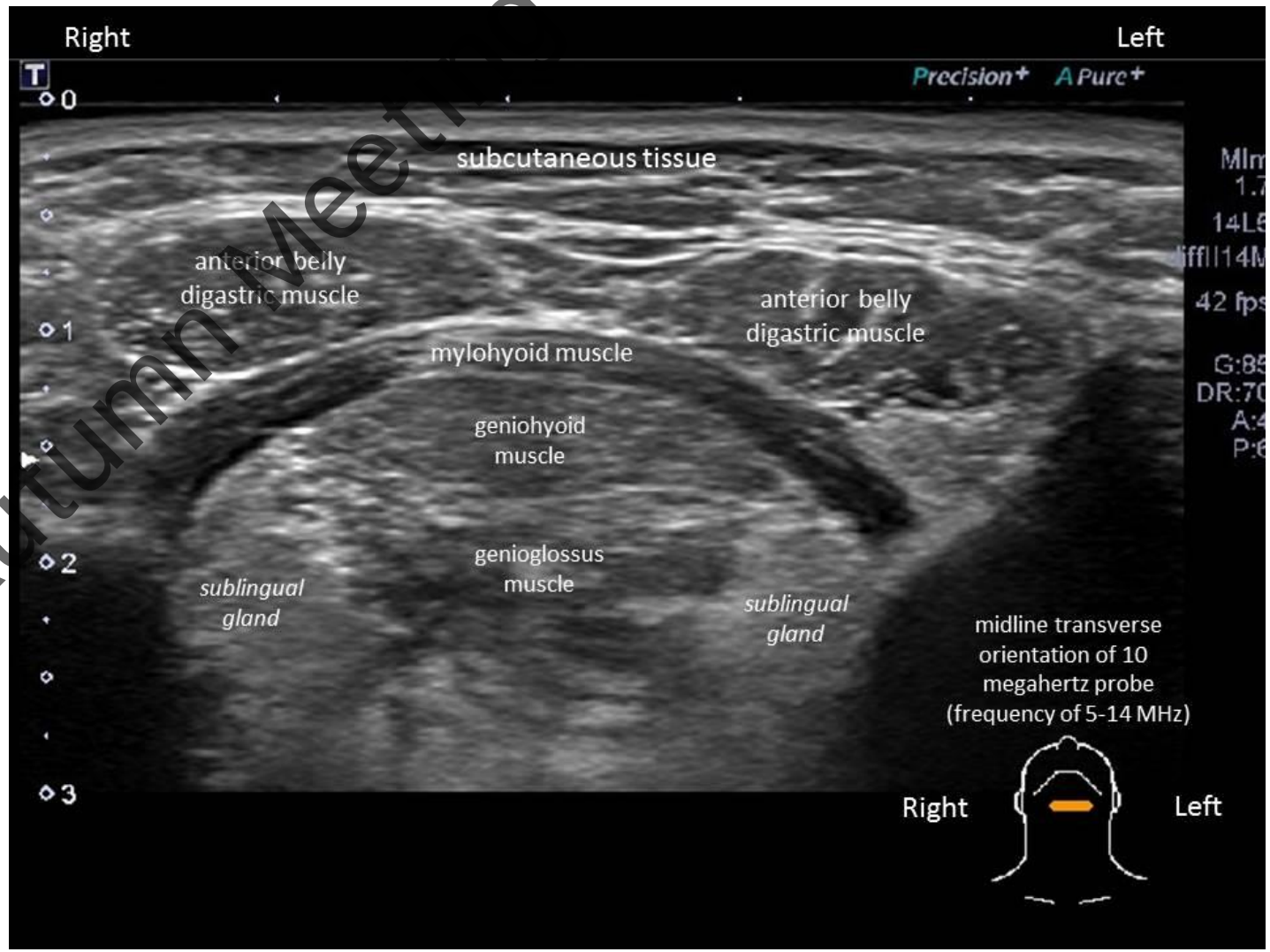






Ultra sound guidance





Questions?

Ruben Hayward – OPAL enterprises

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Management of sialorrhoea in motor neuron disease: a survey of current UK practice.

Hobson EV[1], McGeachan A, Al-Chalabi A, Chandran S, Crawley F, Dick D, Donaghy C, Ealing J, Ellis CM, Gorrie G, Hanemann CO, Harrower T, Jung A, Majeed T, Malaspina A, Morrison K, Orrell RW, Pall H, Pinto A, Talbot K, Turner MR, Williams TL, Young CA, Shaw PJ, McDermott CJ.

McGeachan AJ, McDermott CJ. *Pract Neurol* 2017;**17**:96–103. doi:10.1136/practneurol-2016-001515

Management of oral secretions in neurological disease

Alexander J McGeachan, Christopher J McDermott

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Journal of Clinical Neuroscience 51 (2018) 12–17

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Review article

Pharmacological interventions for treating sialorrhea associated with neurological disorders: A mixed treatment network meta-analysis of randomized controlled trials

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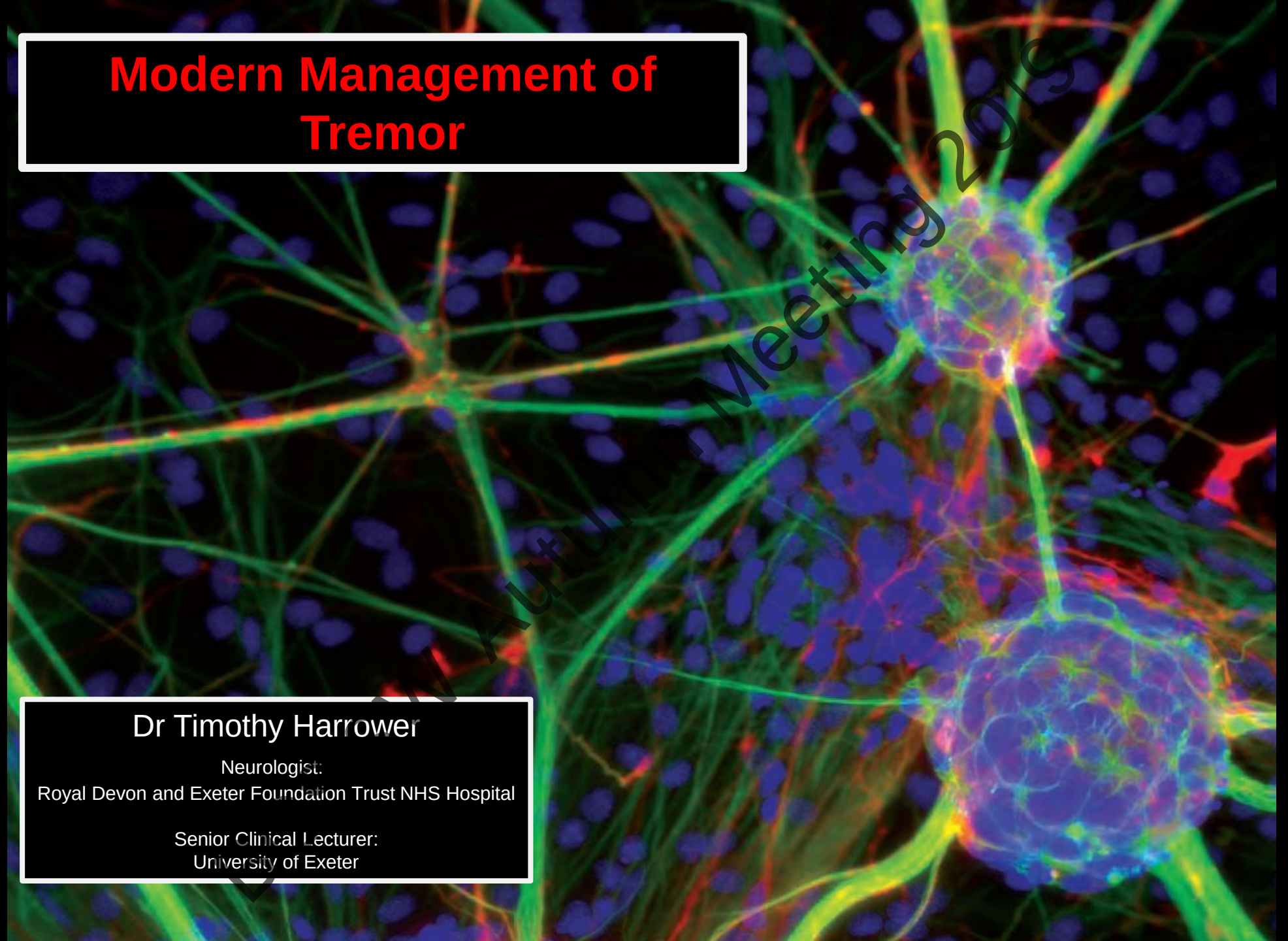
[a] Department of Pharmacology and Therapeutics, College of Medicine and Medical Sciences, Arabian Gulf University, Manama, Bahrain
[b] School of Oral Health, College of Medicine, Nursing and Health Sciences, Fiji National University, Suva, Fiji

ABSTRACT

Sialorrhea is a common distress associated with certain neurological disorders. The aim of this study is to compare the pharmacological agents used for treating sialorrhea by network meta-analysis. Electronic databases were searched for randomized clinical trials comparing active drugs with either placebo or other active drugs. Total drooling scores was the primary outcome measure. Inverse variance heterogeneity model was used for both direct and mixed treatment comparison analysis. Twenty one studies were included in the systematic review and 15 in the meta-analysis. Compared to placebo, benztropine, botulinum toxins A and B are associated with a significant reduction in the frequency and severity of drooling both in the overall neurological disorders as well as for children with cerebral palsy. Only botulinum toxin A and B were associated with significant therapeutic effects in Parkinson's disease. Benztropine and botulinum toxins A and B were observed to be effective in reducing sialorrhea associated with neurological disorders.

Modern Management of Tremor



Dr Timothy Harrower

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REVIEW

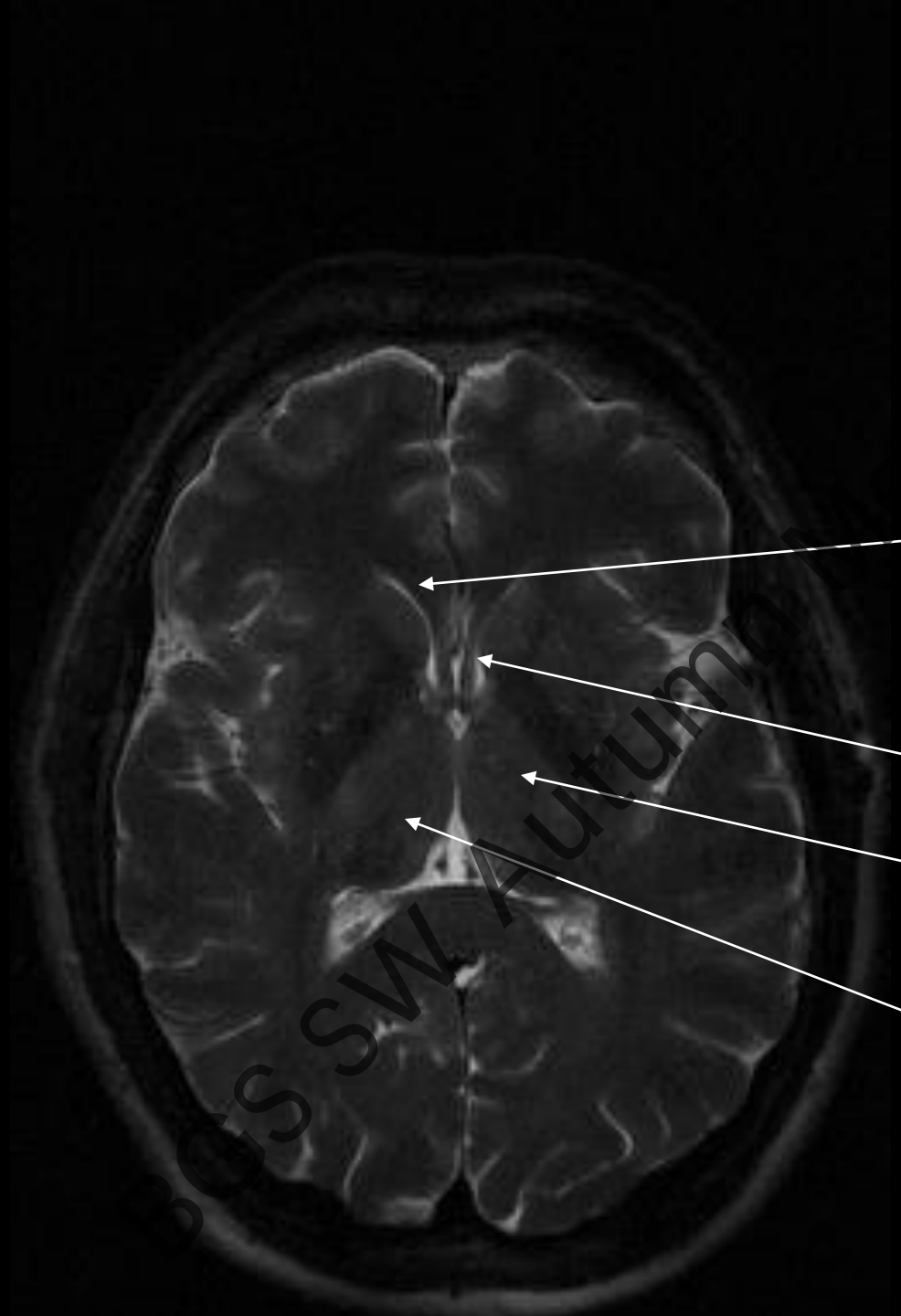
Movement Disorders, Vol. 30, No. 11, 2015

Therapeutic Advances in Tremor

Alfonso Fasano, MD, PhD[1] and Günther Deuschl, MD[2]*

TABLE 2. Selection of active trials enrolling tremor patients, as submitted to the US NIH database (https://clinicaltrials.gov)

NCT Number	Study Title	Condition(s)
Medication		
02277106	Evaluate SAGE-547 in Patients With Essential Tremor	ET
02197104	Citocoline for Treatment of FXTAS	FXTAS
01961297	Voice Tremor in Spasmodic Dysphonia: Central Mechanisms and Treatment Response	Dystonia
01958177	Clinical Study to Evaluate the Safety and Efficacy BMMNC in Cerebellar Ataxia	Cerebellar Ataxia
01864525	Effects of Octanoic Acid for Treatment of Essential Voice Tremor	ET
Botulinum neurotoxin		
02427646	Use of Kinematic Assessment of Hand Tremor Pre- and Post- Treatment With Botulinum Toxin Type A in Essential Tremor and Parkinson Disease	ET and PD
02334683	Compare Two Guidance Techniques for Botulinum Toxin Injections for the Treatment of Limb Spasticity and Focal Dystonia	Spasticity and dystonia
02207946	Botulinum Toxin A to Treat Arm Tremor	ET
02419313	Investigation of the Efficacy and Safety of IncobotulinumtoxinA (Xeomin) in Parkinson's Tremor: A Customized Approach	PD
Transcranial magnetic stimulation		
02441985	rTMS Therapy for Primary Orthostatic Tremor	Primary Orthostatic Tremor
02443181	Demand-driven Management of Essential Tremor	ET
02387346	The Cerebellum as a Potential Treatment Site for PD Motor Symptoms	PD
02370108	The Study of Rest Tremor Suppression by Using Electrical Muscle Stimulation	PD
01792336	Transcranial Magnetic Stimulation for Focal Hand Dystonia	Dystonia
Deep brain stimulation		
02418858	Functional Outcomes of Awake vs Asleep Deep Brain Stimulation (DBS) for Essential Tremor	ET
02384421	Adaptive Closed Loop Neuromodulation and Neural Signatures of Parkinson's Disease	PD
02288468	One Pass thalamic aNd subthalamic stimulatiON	PD
02264925	Thalamic LFPs and VIM DBS in Essential Tremor: Correlation, Evolution, and Therapeutic Perspectives	ET
02119611	Deep Brain Stimulation Therapy in Movement Disorders	ET and PD
02087046	Deep Brain Stimulation (DBS) for the Suppression of Tremor	ET
02071446	Local Fields Potentials Recorded From Deep Brain Stimulating Electrodes	ET, PD and dystonia
01945567	Randomised Crossover Trial of Deep Brain Stimulation of Differential Posterior Subthalamic Area Regions in Parkinson's Disease and Tremor	PD
01934881	Voltage Adjustment Only Versus Combined Parameters Adjustment in PD Patients Treated With Bilateral STN DBS	PD
01909531	Deep Brain Stimulation (DBS) Data Base Study	ET and PD
01809613	Functional Magnetic Resonance Imaging (fMRI) During Deep Brain Stimulation (DBS) to Treat Parkinson's Disease	ET, PD and dystonia
01681641	Managing Changes in Life After Deep Brain Stimulation for Parkinson's Disease	PD
01581580	Deep Brain Stimulation Surgery for Movement Disorders	ET, PD and dystonia
Gamma knife radiosurgery		
02406105	An Effectiveness and Toxicity of CyberKnife Based Radiosurgery for Parkinson Disease	PD
02255929	Gamma Knife Radiosurgery for Treatment of Essential Tremor	ET
02095600	Radiosurgery for Drug Resistant Invalidating Tremor	Tremor
01734122	Stereotactic Radiosurgery for Essential Tremor and Parkinsonian Tremor	ET and PD
MRI-Guided Focused Ultrasound		
02289560	Continued Access Protocol: ExAblate Transcranial MR Guided Focused Ultrasound for the Treatment of Essential Tremors	ET
02252380	ExAblate Transcranial MRgFUS for the Management of Treatment-Refractory Movement Disorders	ET, Holmes Tremor, PD, dystonia
02037217	ExAblate Transcranial MR Guided Focused Ultrasound in the Treatment of Essential Tremor	ET
01827904	ExAblate Transcranial MR Guided Focused Ultrasound for the Treatment of Essential Tremors	ET
01772693	ExAblate Transcranial MR Guided Focused Ultrasound for the Treatment of Parkinson's Disease	PD
Others		
02370134	Development of Parkinson's Glove for Detection and Suppression of Hand Tremor	PD
02067702	Limb Cooling in Essential Tremor	ET
01989013	Effect on Parkinson's Disease After Therapeutic Induction of CranioSacral Integrated Therapy	PD
01940406	The Essential Tremor (ET) and Parkinson Disease (PD) Tremor Acute Stimulation Study	ET and PD
01860794	Evaluation of Safety and Tolerability of Fetal Mesencephalic Dopamine Neuronal Precursor Cells for Parkinson's Disease	PD


Head of Caudate
Lentiform nucleus
- Putamen
- Globus Pallidus
Internal Capsule
Thalamus

Clinically…..pragmatically

Diagnostically

Parkinson's Disease or Essential Tremor

Drugs responsible/ Hyperthyroidism (secondary tremor)

Dystonic Tremor?

Odd tremor - Functional Tremor, orthostatic?

Treatment

Reassurance if possible

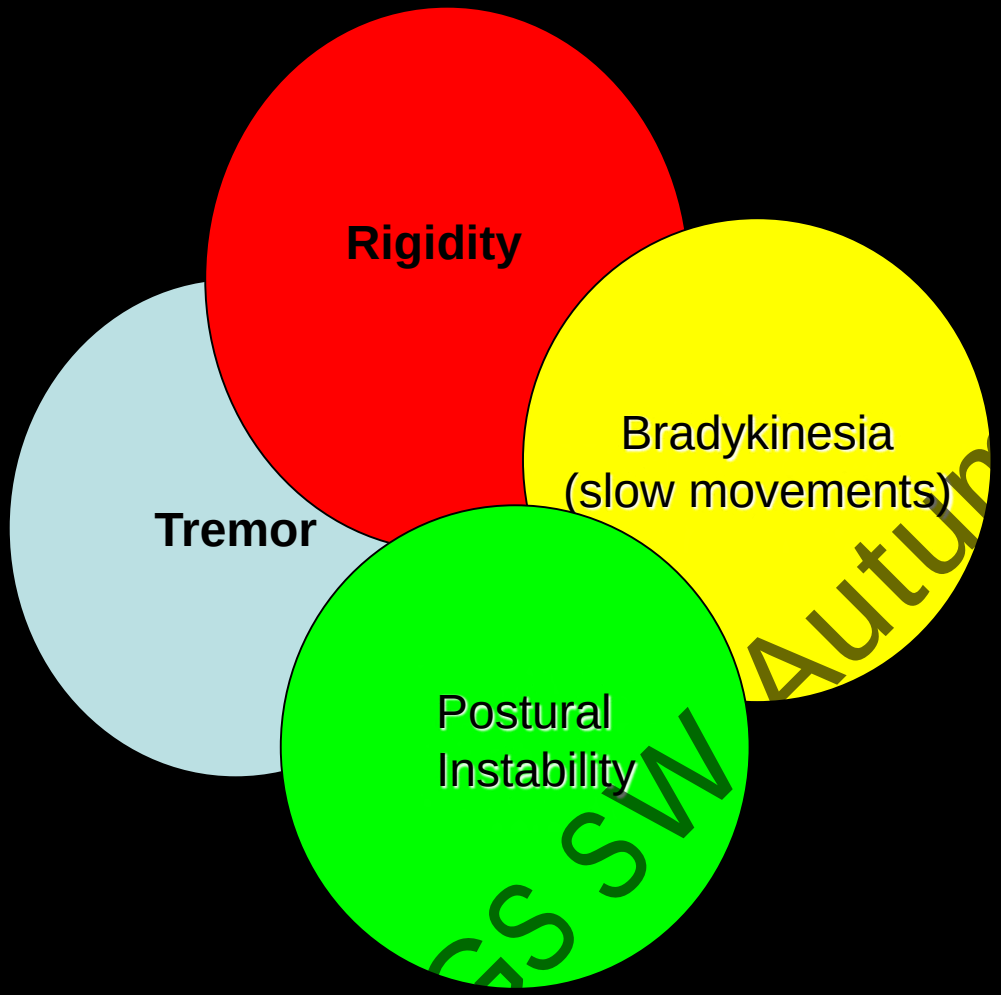
Limited number of effective drugs (Propanolol, Primadone, Topiramate

Alternatives – Devices, New drugs, DBS, New procedures

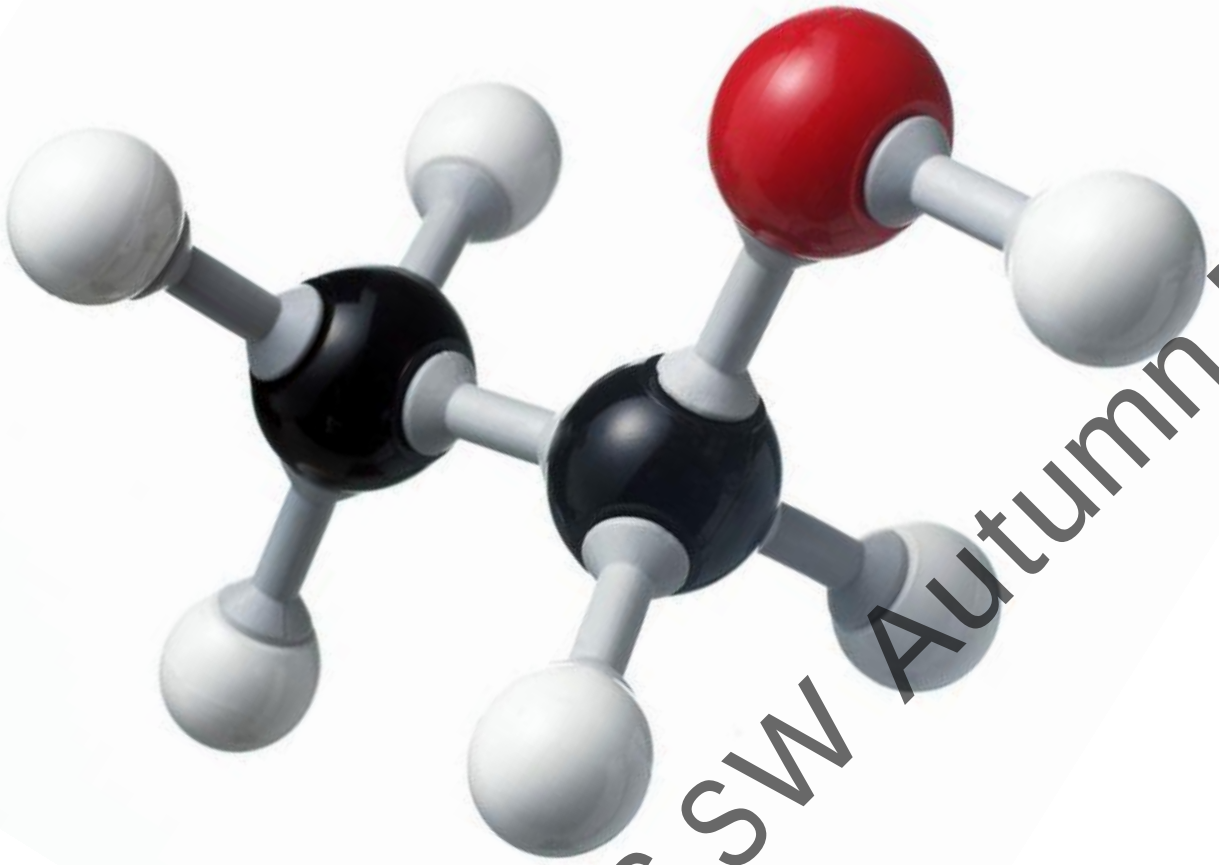
TABLE 2. Etiological causes of tremor (selection)

- Neurodegenerative disease
  - PD
  - Multiple system atrophy
  - Corticobasal degeneration
  - PSP
  - Genetic disorders: genes causing predominantly parkinsonism
  - Genes causing frontotemporal dementia with parkinsonism
  - Genes causing predominantly dystonia
  - Neuroferritinopathy
  - Spinocerebellar ataxias
  - Genes causing Fahr's disease
  - Genes causing peripheral neuropathies that produce tremor
  - Wilson's disease
  - X-linked dystonia parkinsonism/Lubag
  - Lesch-Nyhan's syndrome
  - Fragile X–associated tremor/ataxia syndrome
  - Spinal muscular atrophy
- Chromosomal aneuploidy
  - XYY, XXY (Klinefelter's syndrome), and XXYY syndromes
- Mitochondrial genetic disorders
  - Leigh's syndrome
  - Mitochondrial polymerase gamma mutations
- Infectious and other inflammatory diseases
  - Demyelinating diseases such as multiple sclerosis
  - Encephalitis lethargica, subacute sclerosing panencephalitis,
  - HIV
  - Tuberculosis, syphilis, measles, typhus, neuroborreliosis
  - Bacterial or viral encephalitis
  - Antineuronal antibody disease
- Endocrine and metabolic disorders
  - Nephrotic or liver failure
  - Hyperthyroidism
- Neuropathies and spinal muscular atrophies
  - Kennedy's syndrome
  - Guillain-Barre's syndrome
  - Gammopathy-induced neuropathies
- Toxins
  - Mercury
  - Lead
  - Manganese
  - Arsenic
  - Cyanide, DDT, CO
  - Naphthalene
  - Toluene
  - Lindane
- Drugs
  - Anticonvulsants: valproate, carbamazepine, phenytoin
  - Tetrabenazine, antidepressants, sympathomimetics, bronchodilators, beta-2 agonists
  - Lithium
  - Neuroleptics, metoclopramide
  - Amiodarone
  - Thyroid hormone replacement
  - Anticancer drugs: vincristine, cisplatin, paclitaxel, doxorubicin, cytosine arabinoside, ifosfamide, tacrolimus, 5-fluorouracil, m
  - Drug and alcohol withdrawal
- Others
  - Brain neoplasms
  - Brain injury: head trauma, brain surgery, and electrical injury
  - Vascular: ischemia, hemorrhage, and arteriovenous malformations
  - Anxiety and stress
  - Fatigue
  - Cooling
  - Trauma of peripheral tissues
  - HIV, human immunodeficiency virus.

Parkinson’s disease



Dopa responsiveness



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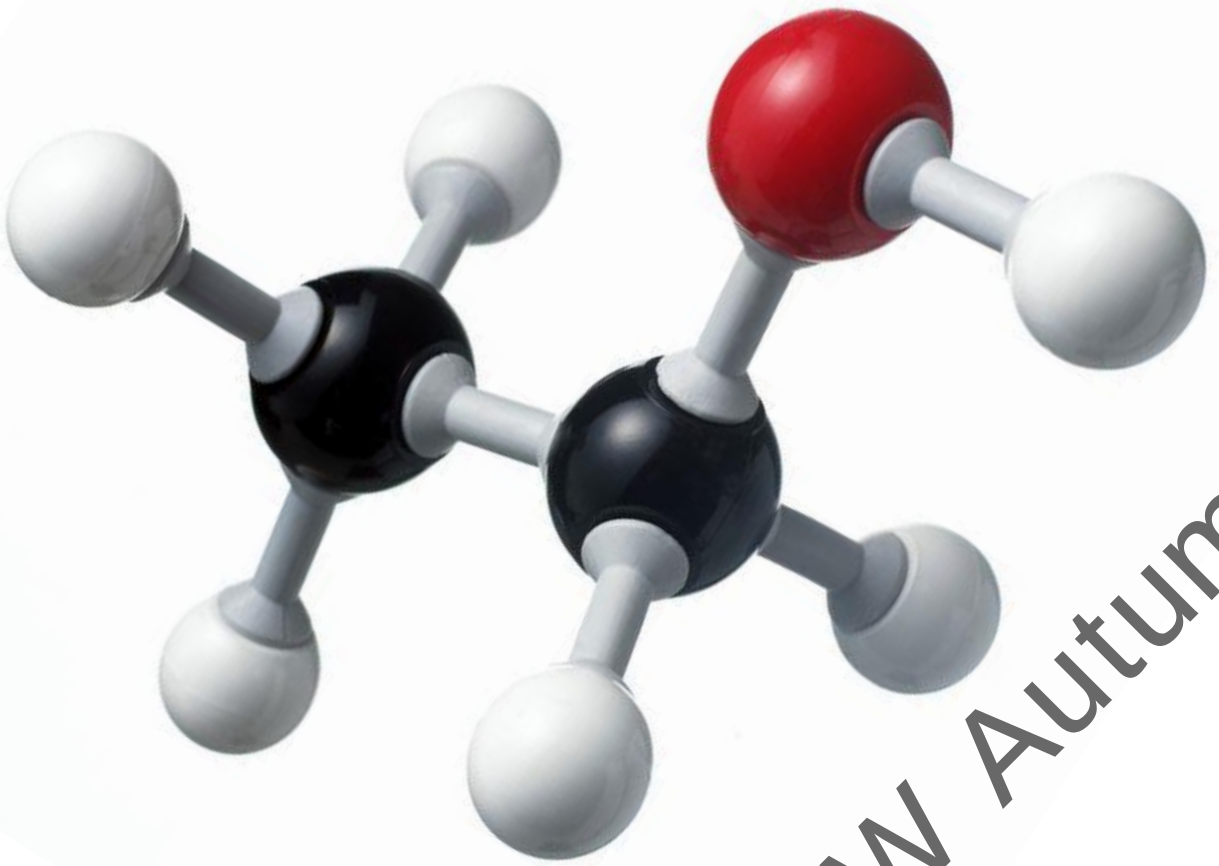

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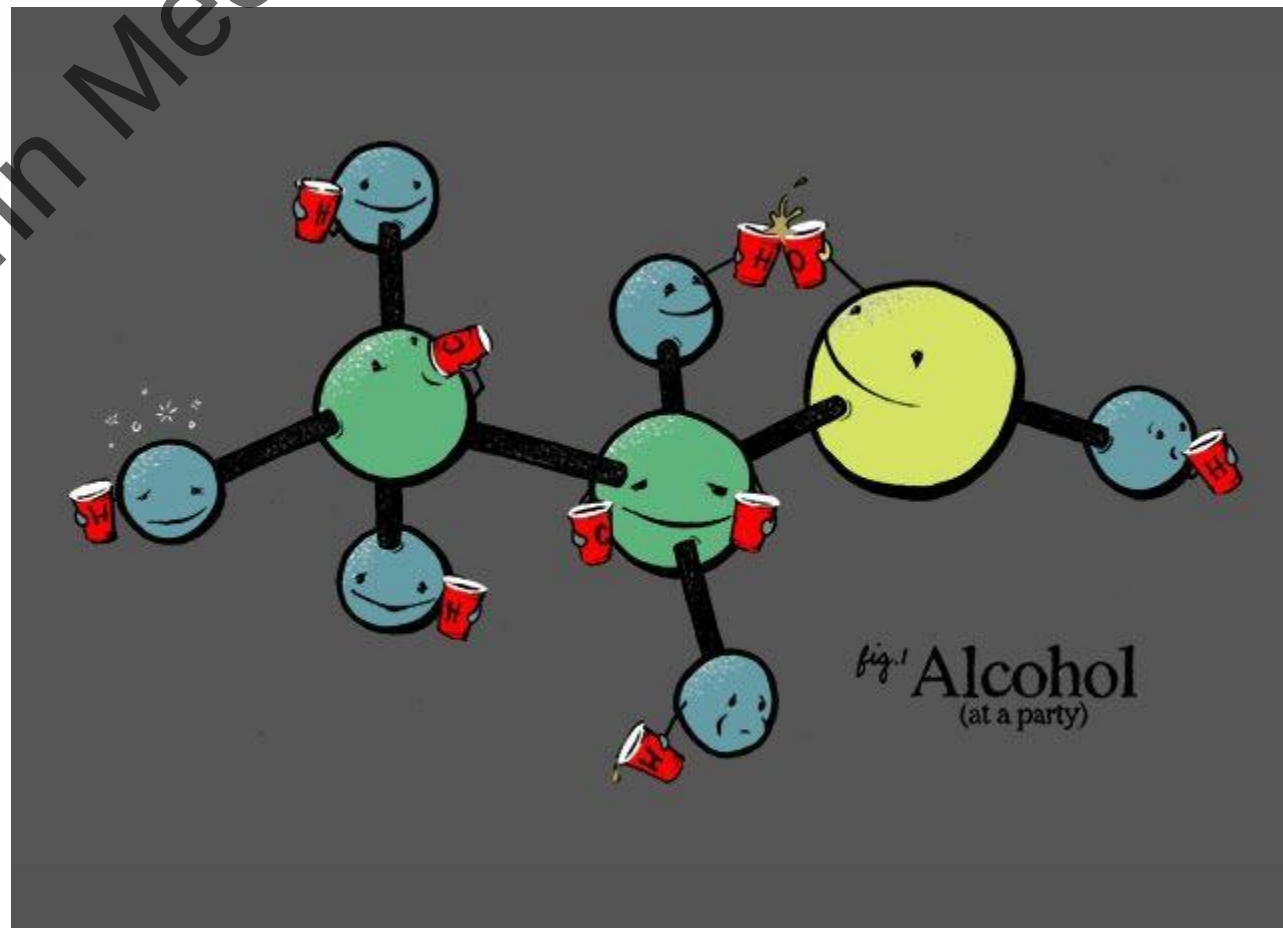

TABLE 2. Etiological causes of tremor (selection)

Toxins
- Mercury
- Lead
- Manganese
- Arsenic
- Cyanide, DDT, CO
- Naphthalene
- Toluene
- Lindane

Drugs
- Anticonvulsants: valproate, carbamazepine, phenytoin
- Tetrabenazine, antidepressants, sympathomimetics, bronchodilators, beta-2 agonists
- Lithium
- Neuroleptics, metoclopramide
- Amiodarone
- Thyroid hormone replacement
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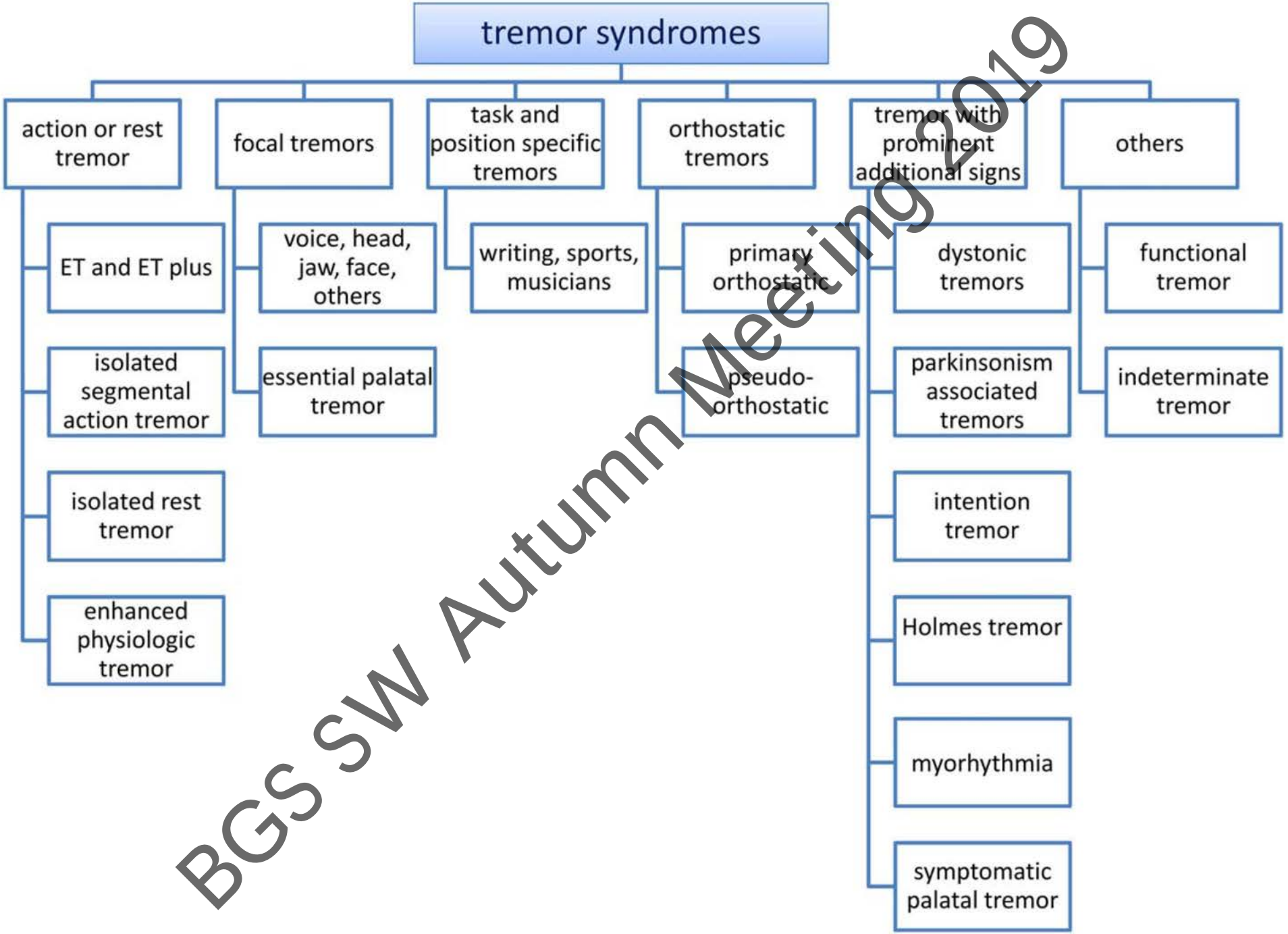
- Drug and alcohol withdrawal

Others
- Brain neoplasms
- Brain injury: head trauma, brain surgery, and electrical injury
- Vascular: ischemia, hemorrhage, and arteriovenous malformations
- Anxiety and stress
- Fatigue
- Cooling
- Trauma of peripheral tissues
- HIV, human immunodeficiency virus.

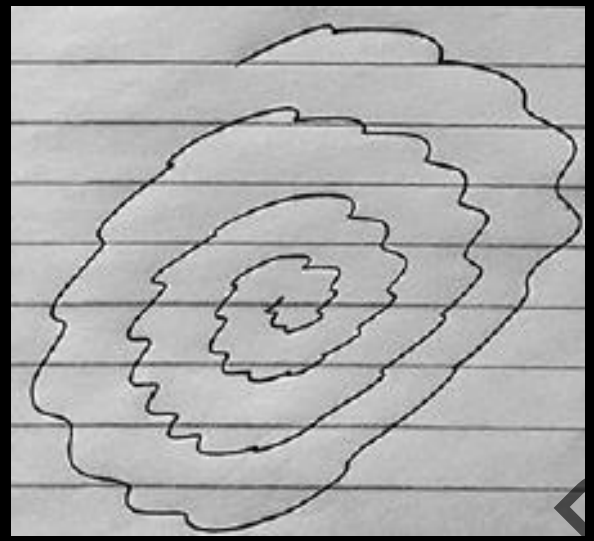
Consensus Statement on the Classification of Tremors. From the Task Force on Tremor of the International Parkinson and Movement Disorder Society

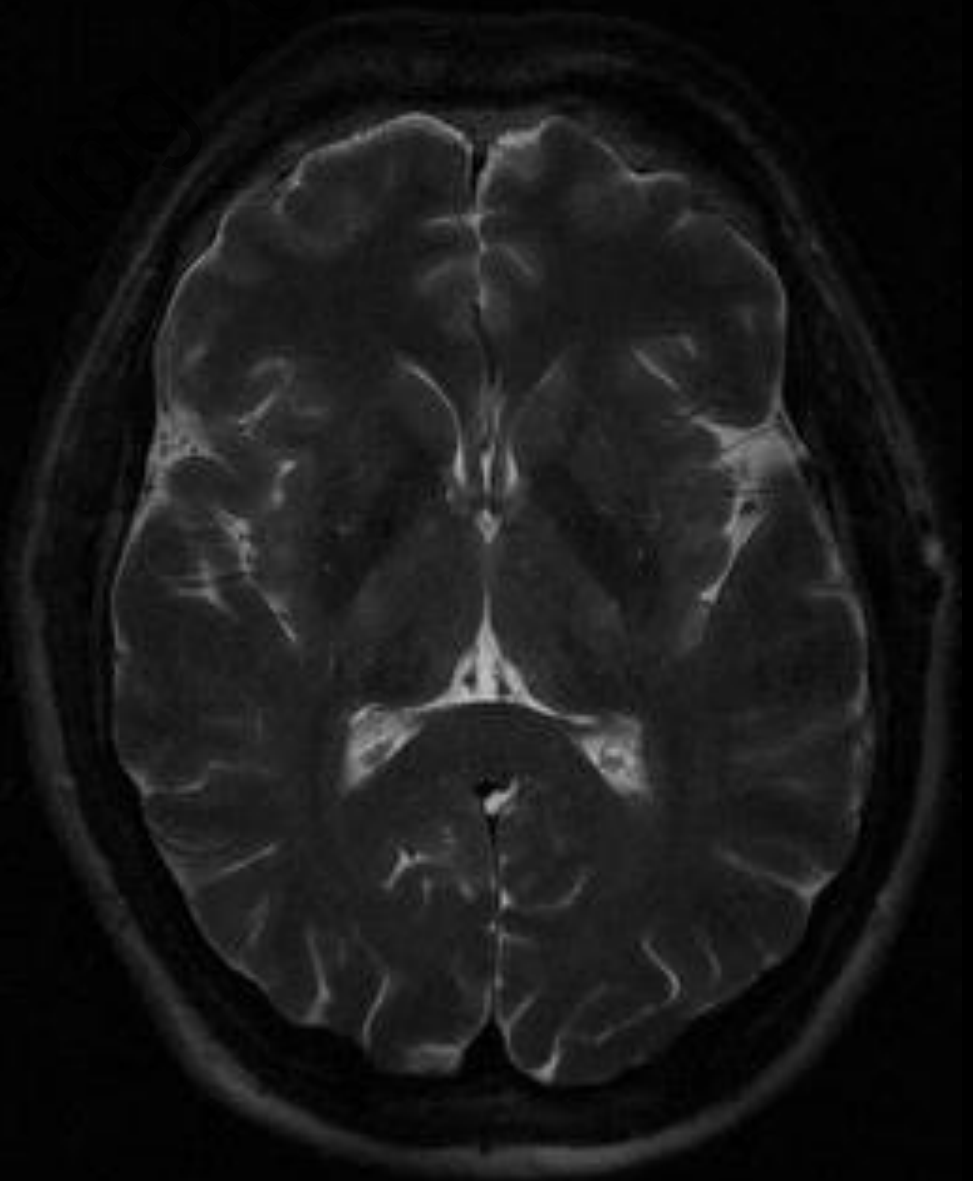
Kailash P. Bhatia, MD, FRCP,[1] Peter Bain, MD, PhD,[2] Nin Bajaj, MD, PhD, FRCP,[3] Rodger J. Elble, MD, PhD,[4] Mark Hallett, MD, PhD,[5] Elan D. Louis, MD,[6] Jan Raethjen, MD, PhD,[7] Maria Stamelou, MD, PhD,[8] Claudia M. Testa, MD, PhD,[9] Guenther Deuschl, MD, PhD,[7*] and the Tremor Task Force of the International Parkinson and Movement Disorder Society[†]

Movement Disorders, Vol. 33, No. 1, 2018



Is the Pen mightier than the MRI scanner?

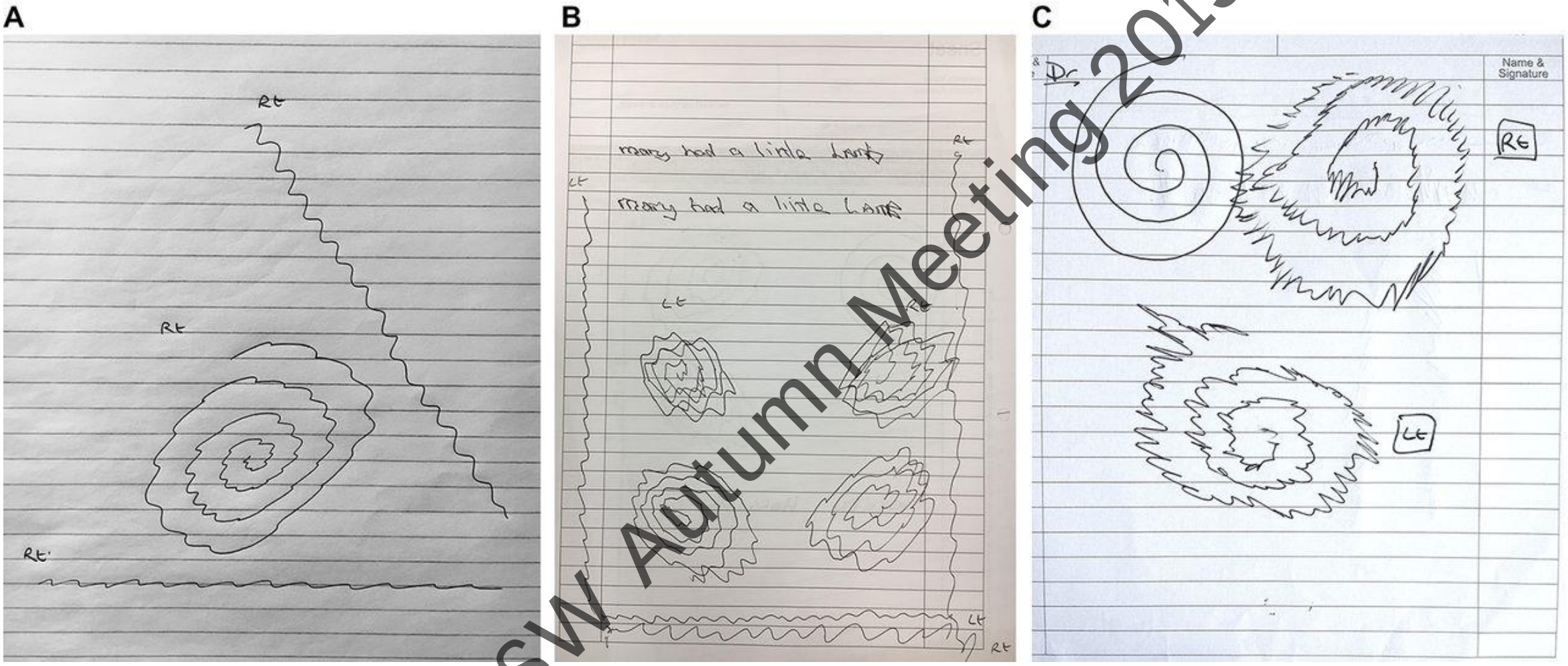




How to use pen and paper tasks to aid tremor diagnosis in the clinic

Alty J, *et al*. *Pract Neurol* 2017;**17**:456–463. doi:10.1136/practneurol-2017-001719

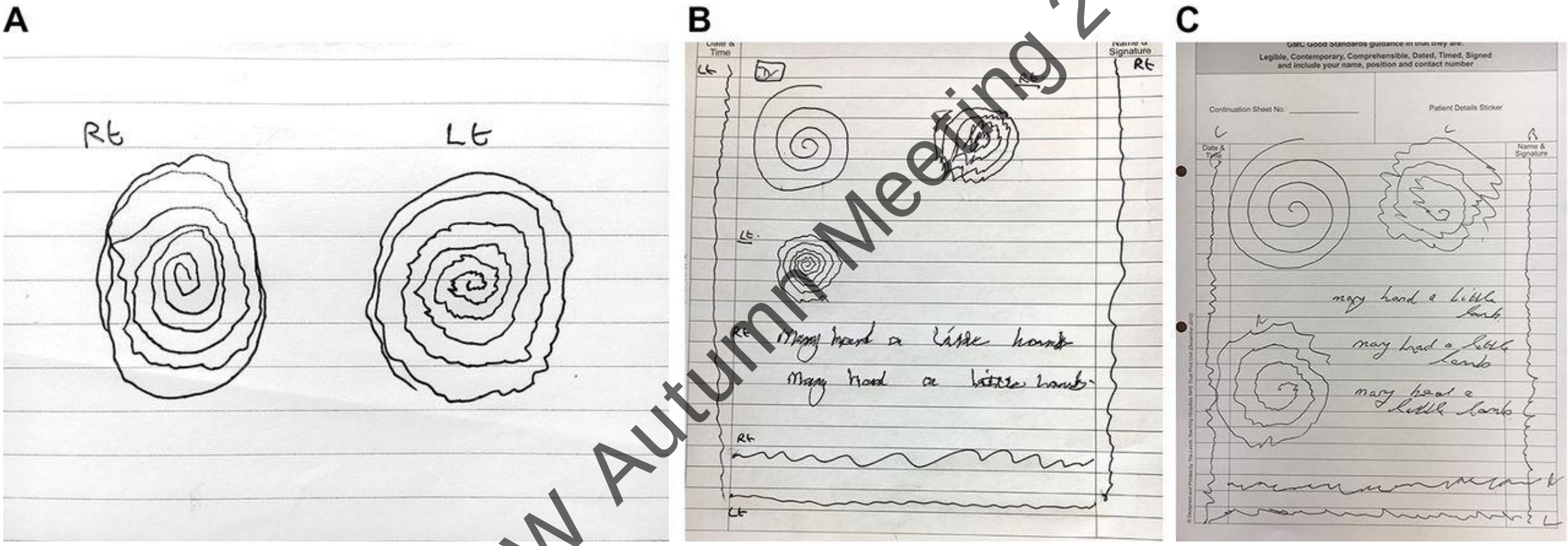
Essential Tremor



Alty J, *et al*. *Pract Neurol* 2017;**17**:456–463. doi:10.1136/practneurol-2017-001719

	Essential tremor	Dystonic tremor	Parkinson's disease	Functional tremor
Handwriting				
Size	Normal or large	Normal	Usually small	Variable
Tremor features	Regular amplitude and frequency	Irregular jerky amplitude and frequency	Regular amplitude and frequency	Variable, often no tremor in writing
Tremor intrusion in letter sections	Vertical letter strokes; unidirectional axis	All sections of letters; multidirectional axis	Vertical letter strokes; unidirectional axis	Variable
Progressive deterioration	No	Yes—shape of letters worsens due to posturing	Sometimes—size of letters may decrement	Not usually
Pen pressure	Normal	Hard pressure	Normal	Normal
Spirals				
Size	Normal	Normal	Small	Variable
Spacing of turns	Normal (maybe wider)	Normal (maybe tighter)	Tighter	Variable
Tremor axis	Unidirectional	Multidirectional	Unidirectional	Variable
Tremor frequency	Regular	Irregular/jerky	Regular	Variable
Progressive deterioration	No	Sometimes—more tremor and pressure	No	Variable tremor frequency, axis and amplitude
Straight lines				
Tremor axis	Unidirectional Right: 8–2 o'clock Left: 10–4 o'clock	Multidirectional	Unidirectional Right: 8–2 o'clock Left: 10–4 o'clock	Variable
Tremor frequency	Regular	Irregular	Usually regular	Variable
Tremor amplitude	Small, regular	Small, irregular	Small, regular	Large, irregular
Symmetry	Symmetrical	Asymmetrical	Asymmetrical	Variable
Other features		Writing may be worse than drawing tasks	Longer duration to compete task (bradykinesia)	Straight lines usually most impaired task

Dystonic tremor.



Alty J, *et al*. *Pract Neurol* 2017;**17**:456–463. doi:10.1136/practneurol-2017-001719

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Other features		Writing may be worse than drawing tasks	Longer duration to compete task (bradykinesia)	Straight lines usually most impaired task

Functional

Figure 8 Functional tremor. (A) The tremor affects both hands but there is variation in amplitude and frequency between the right and left spirals. (B) There is a marked discrepancy when the patient copies the spiral in alternate directions. (C) This patient presented with a right (dominant) hand tremor that was consistently unidirectional (8–2 o'clock direction). Other features were variable and inconsistent, suggesting a functional disorder. The site of tremor intrusion changed within a single spiral and between consecutive spirals; the amplitude changed from small to large within a single spiral but there was a consistent amplitude during straight line

Lift Pulse

Management suggestions for tremor

Avoid precipitants

Drugs

Devices

DBS

New directions

TABLE 1. Pharmacological management of ET (from Schneider and Deuschl[74])

Recommendation for Use	*Drug*	*Total Daily Dosage (mg/d)*	Daily Intakes
Recommended	Propranolol	40–320	2–3 standard 1–2 long-acting
	Primidone	62.5–750	1 (bedtime)-3
	Topiramate	50–300	2–3
Probable or weak efficacy	Atenolol	50–100	1
	Sotalol	80–240	1–2
	Gabapentin	1200–2400	3
	Alprazolam	0.75–3	Intermittent
Level C possibly effective	Clonazepam	0.5–6.0	2–3
	Clozapine	6.25–75	1–2
	Flunarizine	10	1
	Nadolol	120–240	1
	Nimodipine	120	3–6
	Botulinum toxin	OnabotulinumA* doses: vocal muscle: 1.25–3.75 U; cervical muscles: 40–400 U; forearm muscles: 50–100 U; tensor veli palatine: 4–10 U	NA
Recommendations against use	3,4-Diaminopyridine, acetazolamide/methazolamide, amantadine, carisbamate, isoniazid, levetiracetam, pindolol, trazodone, mirtazapine, nifedipine, verapamil		
Inadequate evidence to confirm or exclude efficacy	Olanzapine, pregabalin, tiagabine, sodium oxybate, zonisamide		

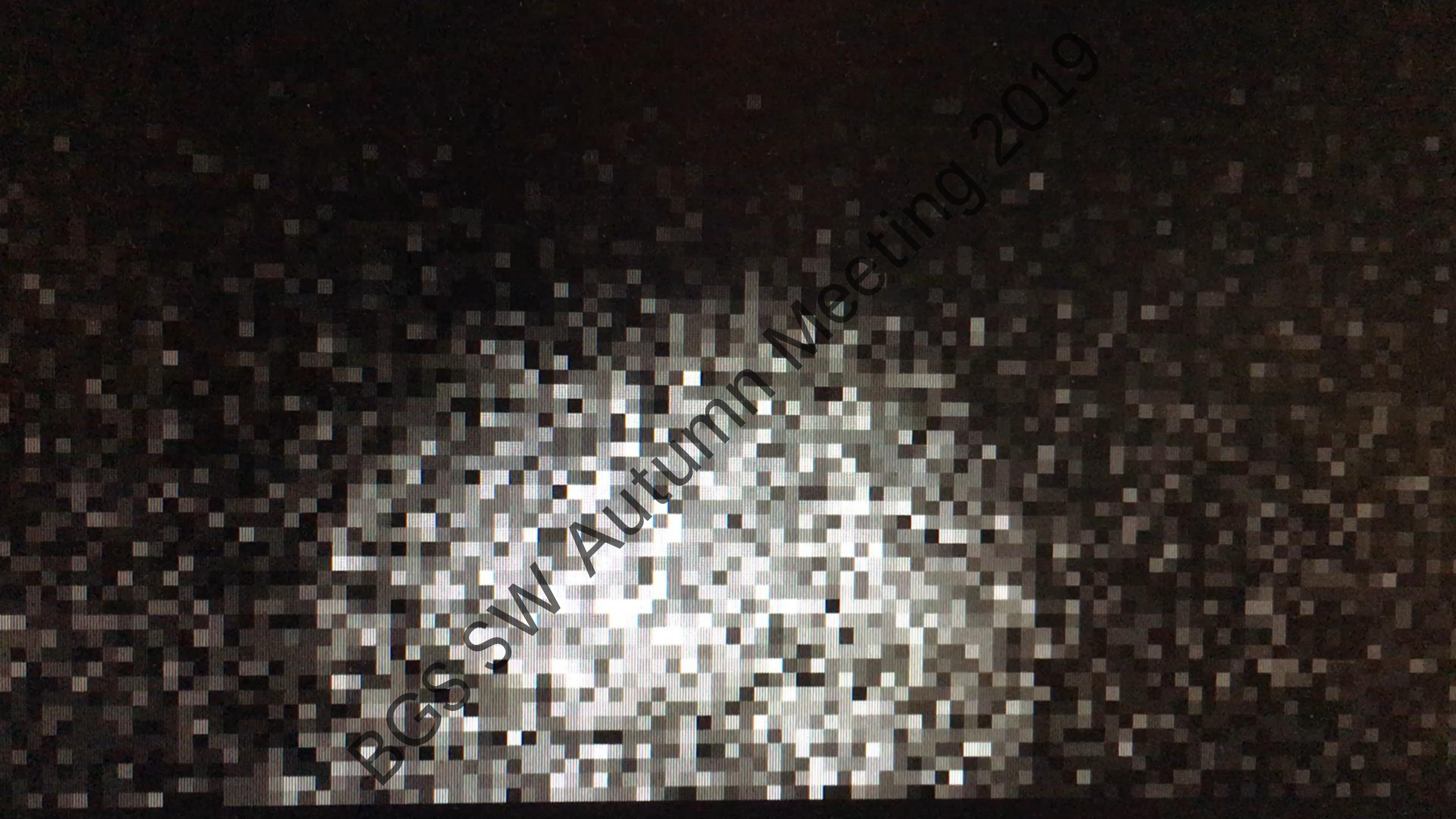
Abbreviations: *Conversion ratio OnabotulinumA: incobotulinumtoxinA = 1:1; conversion ratio OnabotulinumA: abobotulinumtoxinA = 1:3–5; NA, not available.

REVIEW

Movement Disorders, Vol. 30, No. 11, 2015

Therapeutic Advances in Tremor

Alfonso Fasano, MD, PhD[1] and Günther Deuschl, MD[2*]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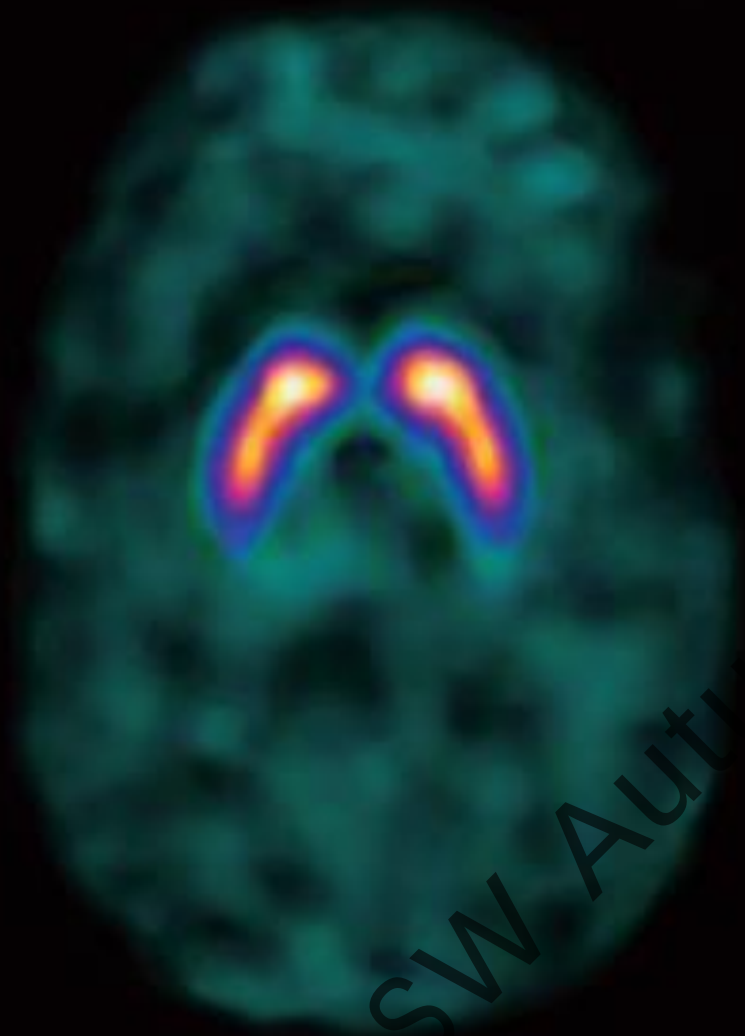
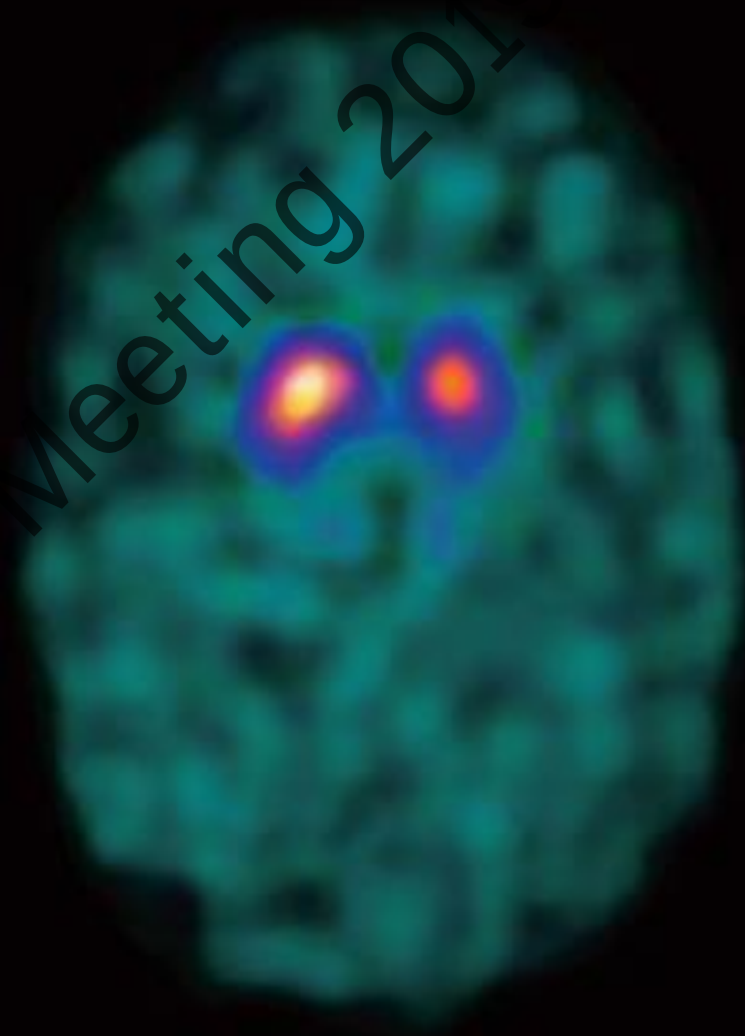


DaTscan of normal patient.



DaTscan of patient with Parkinsonian syndrome.

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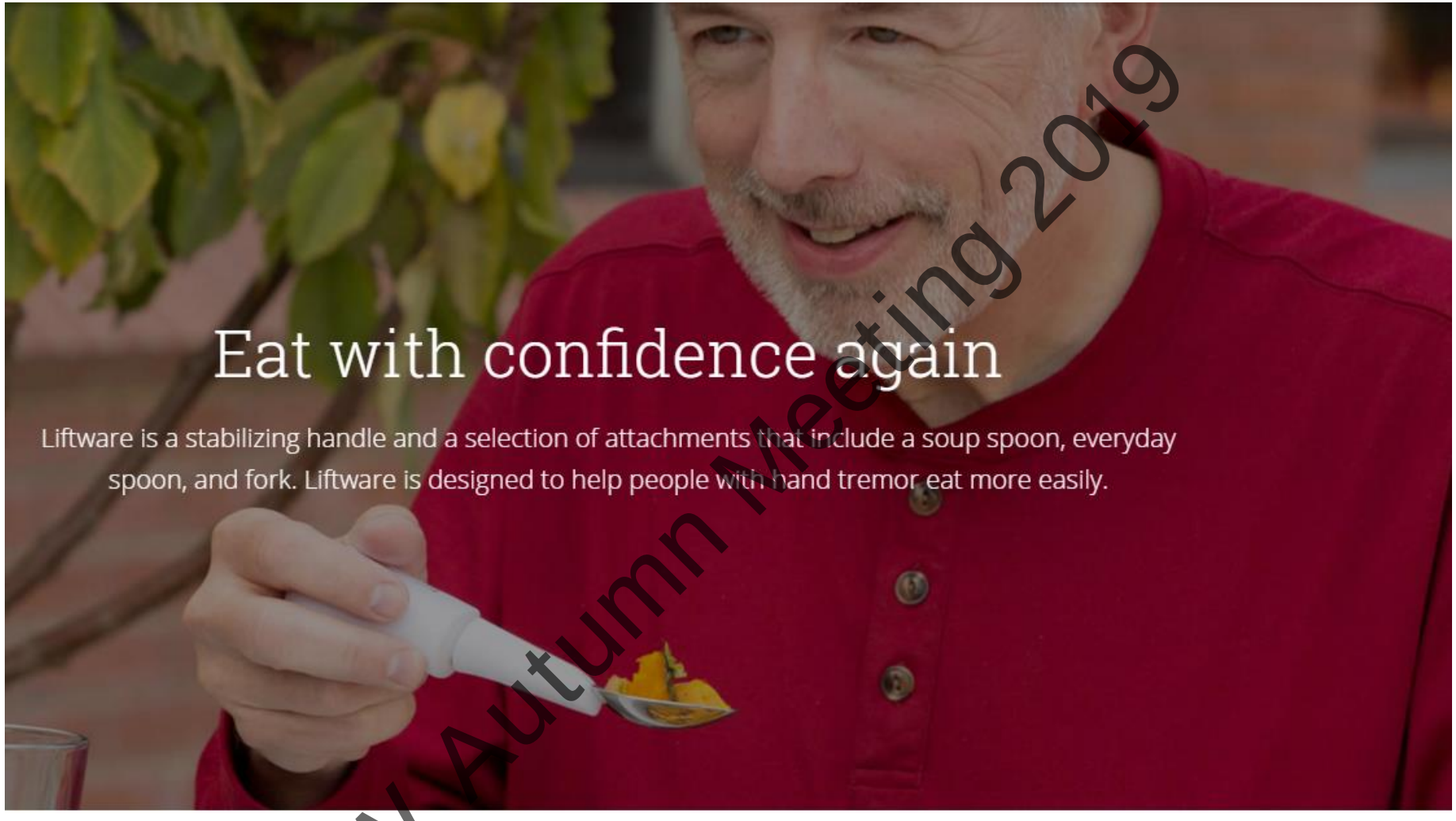
Anupam Pathak, Lift Lab's founder



Adapts to your hand tremor

Liftware automatically stabilizes so the attached utensil shakes 70%* less than your hand. Worry less about spilling and focus on enjoying your meal.

The technology behind Liftware

The Liftware stabilizing handle contains sensors that detect hand motion and a small onboard computer that distinguishes unwanted tremor from the intended movement of the hand. To stabilize the utensil, the computer directs two motors in the handle to move the utensil attachment in the opposite direction of any detected tremor.

Liftware automatically stabilizes and shakes 70%* less than your hand. Worry less about spilling and focus on enjoying your meal.

* As shown in this peer-reviewed and published clinical study.

Multiple attachments
Including a soup spoon, everyday spoon and fork.

Stabilizing technology
Advanced sensors, motors and an onboard computer work to actively detect and counteract your tremor.

Rechargeable battery
Battery will last for several days on a charge.

Tried

Propanolol
Primidone
Clonazepam

Gabapentin

Topiramate
Levodopa
Dopamine Agonist

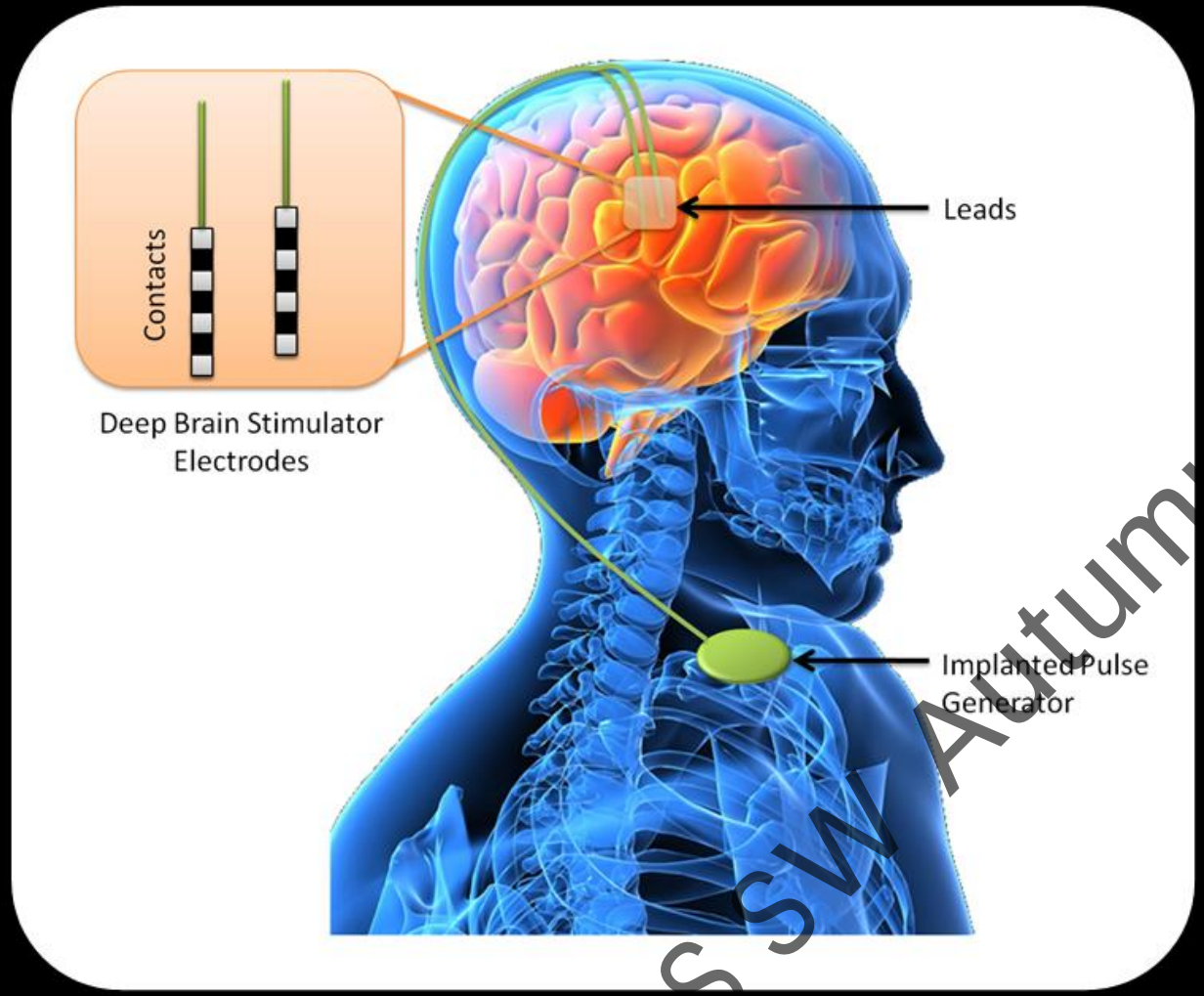
Various devices

DAT scan Normal

Unable to activities of daily living

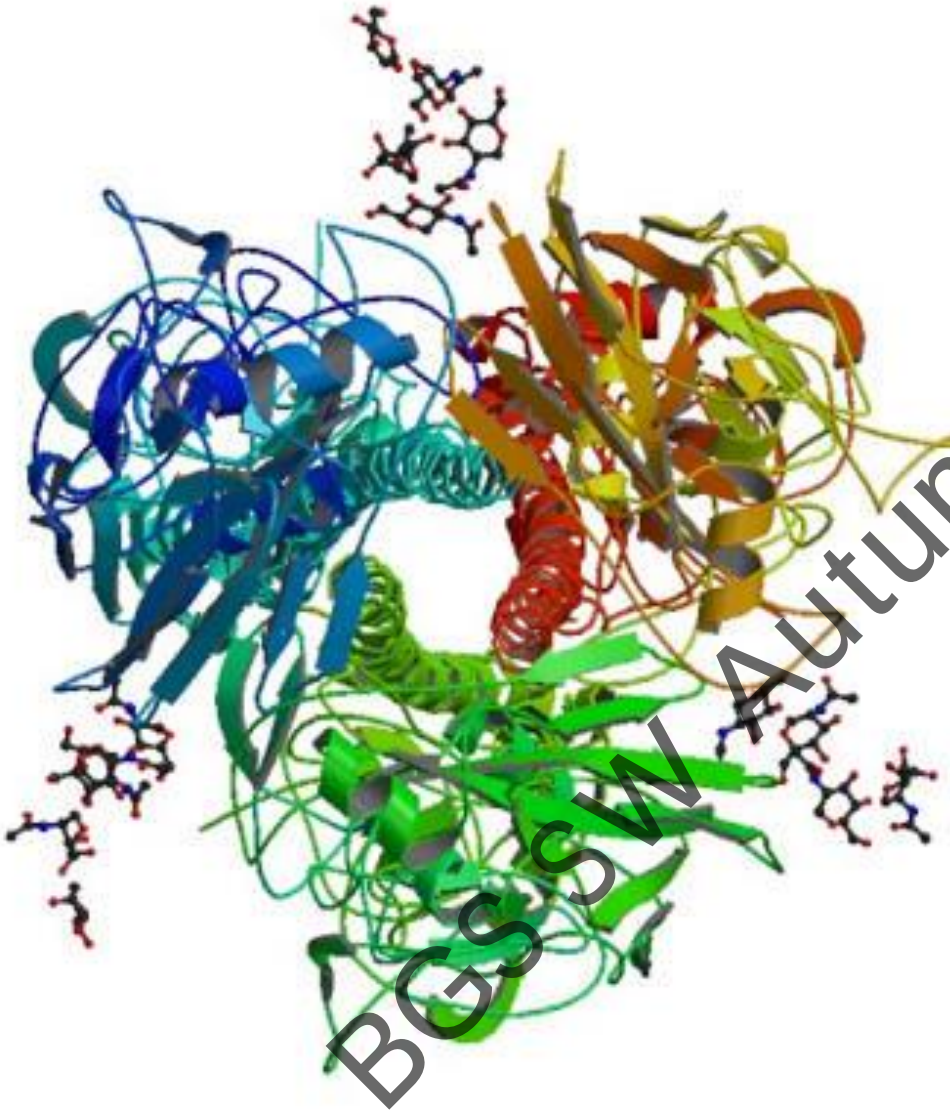
Socially withdrawn

Something of a wreck -

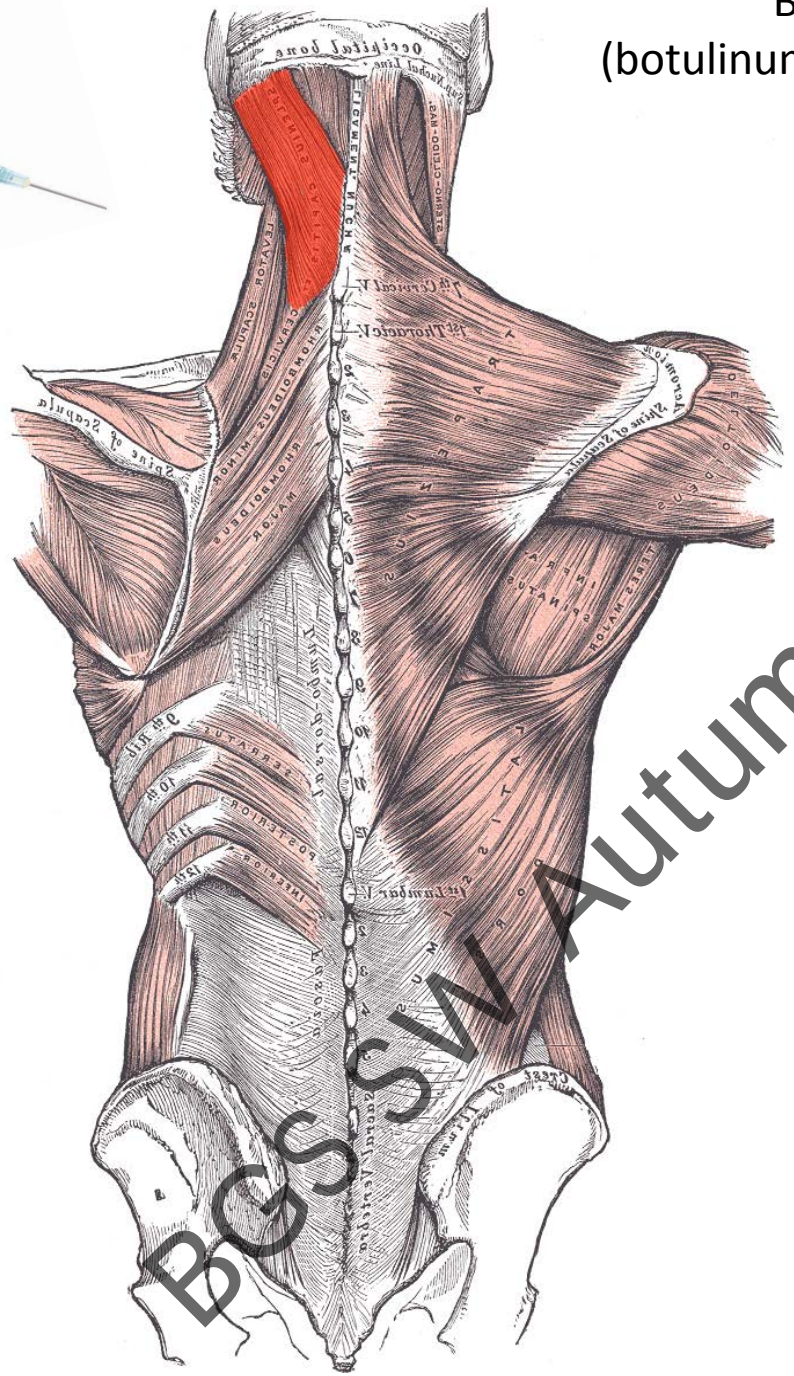


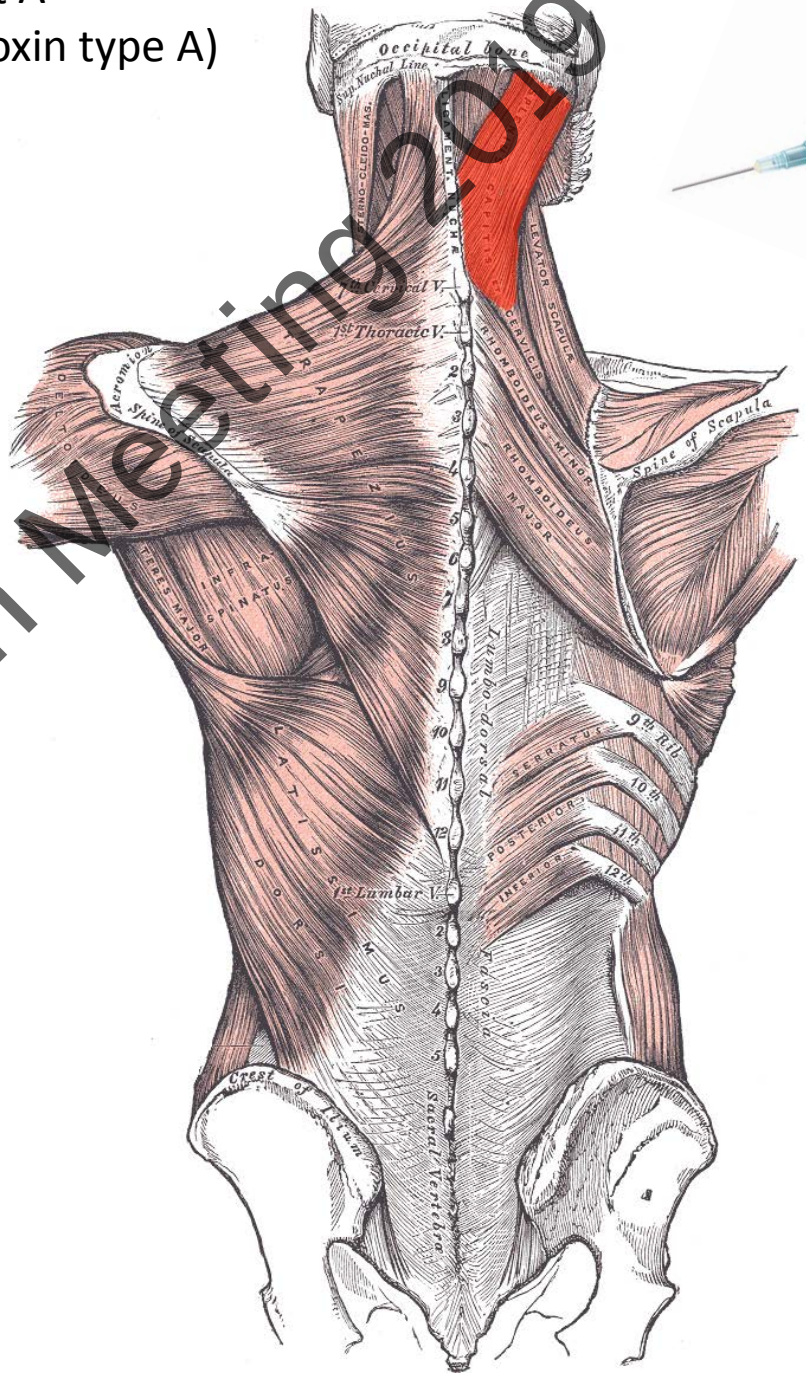
He had bilateral Thalamic stimulators inserted….

And by the way was a part of the ITV program



Bont A
(botulinum toxin type A)





Orthostatic tremor

Direct Questioning

Walking alright – especially in walking faster – never fallen when walking

Standing in ques most noticeably unsteady especially after a few moments

Loss of confidence - more anxious – never goes out now

Present for about 5 years – static after onset

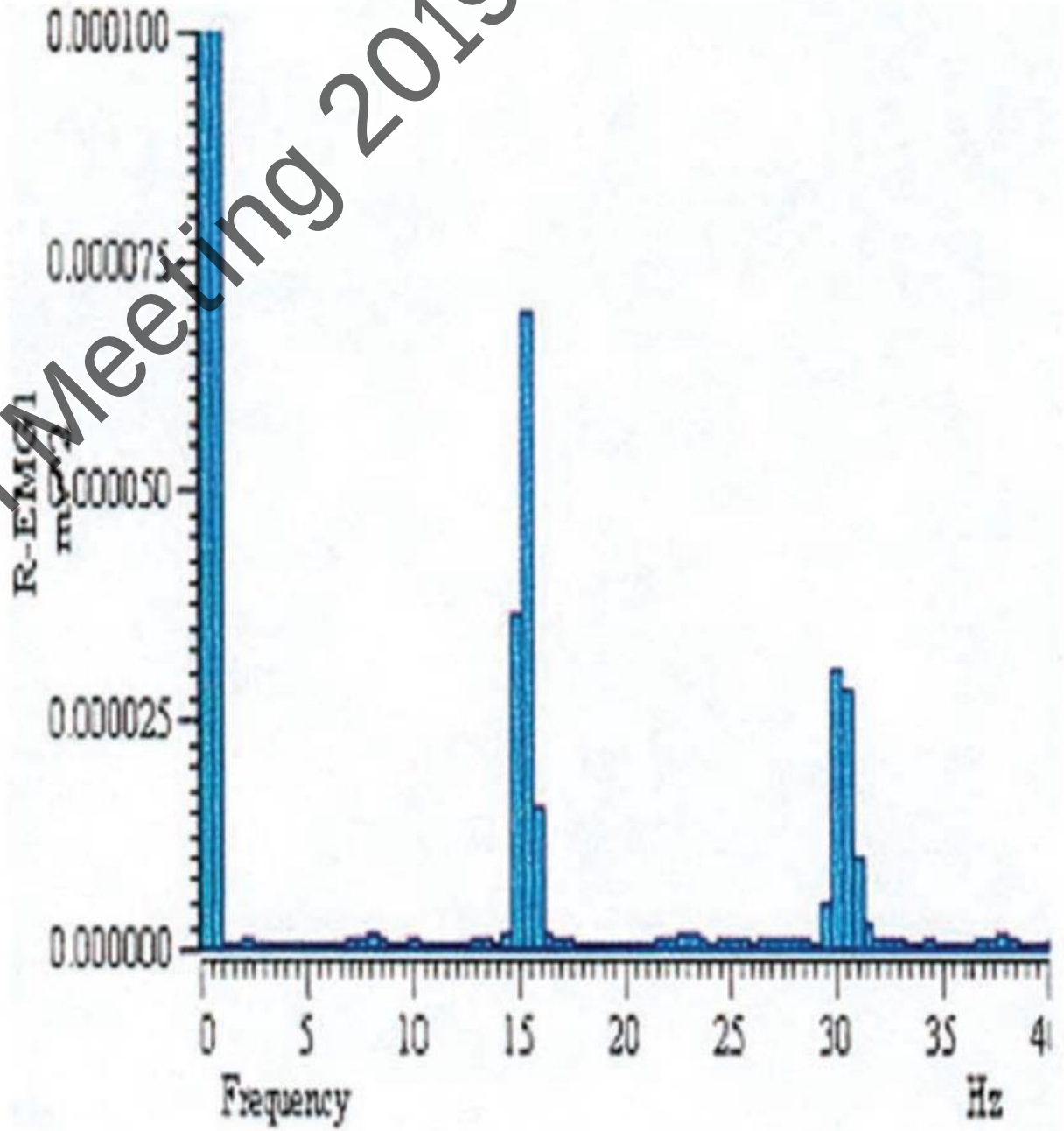
Examination

No features of Parkinson's disease

No arm tremor

No long tract signs

No cerebellar features



NEUROLOGICAL RARITY

Pract Neurol 2011; 11: 240–243

Orthostatic tremor

Leah Jones,[1] Peter G Bain[2]

Table Efficacy of 46 medications trialed in OT cases, separated by medication class

Medication	No. of cases tried	None	Mild	Moderate	Marked	At least mild benefit (%)
Benzodiazepines						
Clonazepam (%)	124	53 (42.7)	30 (24.2)	22 (17.7)	19 (15.3)	71/124 (57.3)
Diazepam	9	4	3	0	2	5/9
Lorazepam	6	3	2	1	0	3/6
Clorazepate	5	2	1	0	2	3/5
Alprazolam	5	3	1	1	0	2/5
Bromazepam	1	0	0	1	0	1/1
Chlordiazepoxide	1	1	0	0	0	0/1
Prazepam	1	1	0	0	0	0/1
All benzodiazepines	152	64	37	25	23	85/152 (55.9)
Anticonvulsants						
Gabapentin	45	29	8	6	1	15/45 (33.2)
Valproate	37	30	0	7	0	7/37 (18.9)
Primidone	31	24	4	3	0	7/31 (22.6)
Topiramate	6	5	1	0	0	1/6
Pregabalin	4	2	1	0	1	2/4
Carbamazepine	5	4	1	0	0	1/5
Levetiracetam	3	2	1	0	0	1/3
Phenytoin	2	2	0	0	0	0/2
Lamotrigine	1	1	0	0	0	0/1
Tiagabine	1	1	0	0	0	0/1
Phenobarbital	1	1	0	0	0	0/1
All anticonvulsants	136	101	16	16	2	34/136 (25.0)
β-Blockers						
Propranolol	38	27	7	3	1	11/38 (28.9)
Nadolol	3	1	2	0	0	2/3
β-Blocker	1	1	0	0	0	0/1
All β-blockers	42	29	9	3	1	13/42 (31.0)

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Levetiracetam	3	2	1	0	0	1/3
Phenytoin	2	2	0	0	0	0/2
Lamotrigine	1	1	0	0	0	0/1
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ings in 184 patients

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Topiramate	6	5	1	0	0	1/6
Pregabalin	4	2	1	0	1	2/4
Carbamazepine	5	4	1	0	0	1/5
Levetiracetam	3	2	1	0	0	1/3
Phenytoin	2	2	0	0	0	0/2
Lamotrigine	1	1	0	0	0	0/1
Tiagabine	1	1	0	0	0	0/1
Phenobarbital	1	1	0	0	0	0/1
All anticonvulsants	136	101	16	16	2	34/136 (25.0)
β-Blockers						
Propranolol	38	27	7	3	1	11/38 (28.9)
Nadolol	3	1	2	0	0	2/3
β-Blocker	1	1	0	0	0	0/1
All β-blockers	42	29	9	3	1	13/42 (31.0)

Table Efficacy of 46 medications trialed in OT cases, separated by medication class

Medication	No. of cases tried	None	Mild	Moderate	Marked	At least mild bene
Benzodiazepines						
Clonazepam (%)	124	53 (42.7)	30 (24.2)	22 (17.7)	19 (15.3)	71/124 (57.3)
Diazepam	9	4	3	0	2	5/9
Lorazepam	6	3	2	1	0	3/6
Clorazepate	5	2	1	0	2	3/5
Alprazolam	5	3	1	1	0	2/5
Bromazepam	1	0	0	1	0	1/1
Chlordiazepoxide	1	1	0	0	0	0/1
Prazepam	1	1	0	0	0	0/1
All benzodiazepines	152	64	37	25	23	85/152 (55.9)
Anticonvulsants						
Gabapentin	45	29	8	6	1	15/45 (33.2)
Valproate	37	30	0	7	0	7/37 (18.9)
Primidone	31	24	4	3	0	7/31 (22.6)
Topiramate	6	5	1	0	0	1/6
Pregabalin	4	2	1	0	1	2/4
Carbamazepine	5	4	1	0	0	1/5
Levetiracetam	3	2	1	0	0	1/3
Phenytoin	2	2	0	0	0	0/2
Lamotrigine	1	1	0	0	0	0/1
Tiagabine	1	1	0	0	0	0/1
Phenobarbital	1	1	0	0	0	0/1
All anticonvulsants	136	101	16	16	2	34/136 (25.0)

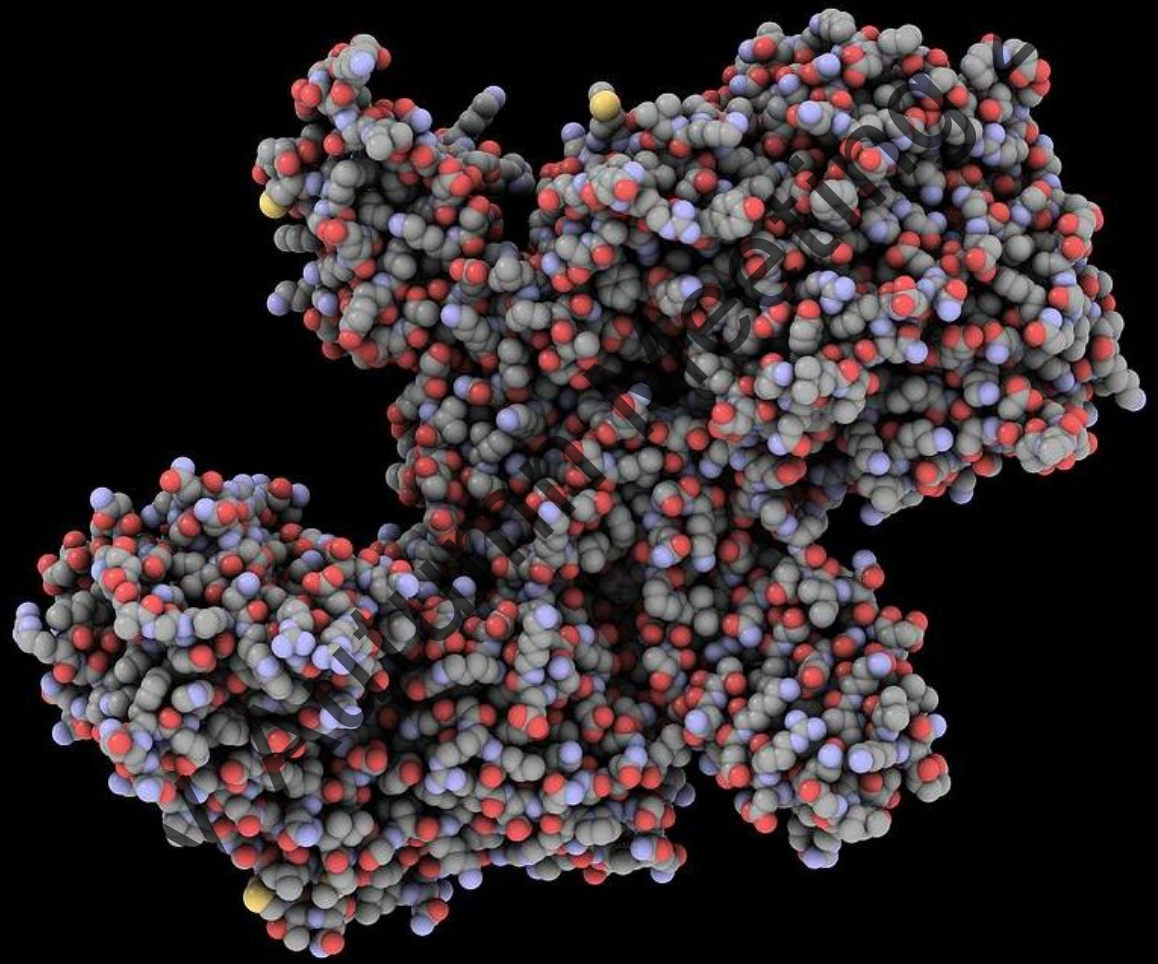
ings in 184 patients

Management of Orthostatic Tremor

- Reassurance

- Clonazepam
- (Gabapentin)
- (Propanolol)

- Tripod seated stick



Botulinum Toxin

The muscles injected were:

teres major (20 units),
teres minor (20 units),
pectoralis major (20 units),
supraspinatus (10 units),
infraspinatus (10 units),
biceps (5 units). and
triceps (5 units; total dose, 90 units).

Treatment of proximal upper limb tremor with botulinum toxin therapy

Samuel D. Kim MB, BS[1], Con Yiannikas MB, BS[2], Neil Mahant PhD[1], Steve Vucic PhD[3,4] and Victor S.C. Fung PhD[1,4,*]

Article first published online: 20 NOV 2013

DOI: 10.1002/mds.25739

Issue

Movement Disorders
Volume 29, Issue 6, pages 835–838, May 2014

Table 2. Injection strategy separated according to injector

	No. of patients/total no.		
Muscle injected	**Injector 1**	**Injector 2**	**Total**
Teres major	9/9	9/10	18/19
Teres minor	8/9	9/10	17/19
Infraspinatus	7/9	2/10	9/19
Supraspinatus	4/9	4/10	8/19
Deltoid	0/9	6/10	6/19
Pectoralis major	9/9	1/10	10/19
Biceps	3/9	5/10	8/19
Triceps	0/9	4/10	4/19

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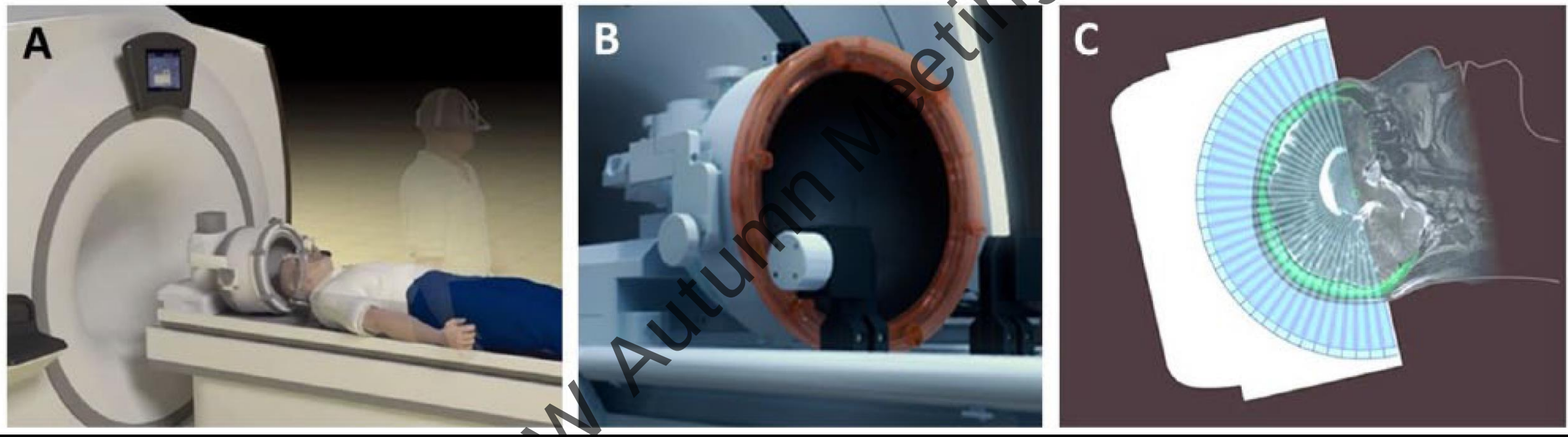
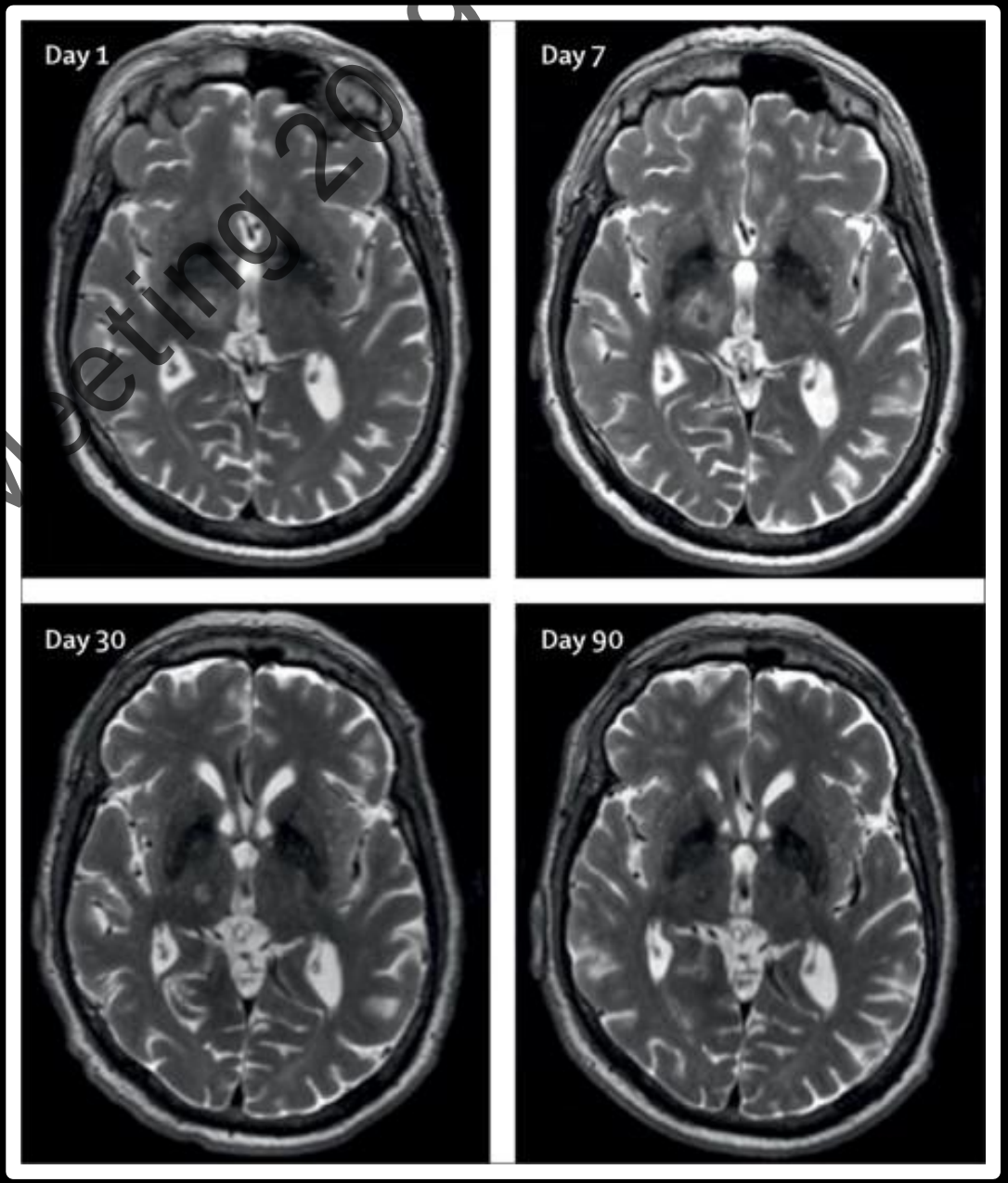
Coming soon …. To a Movement Disorder unit nearby:

MRI Guided focused Ultrasound Thalamotomy


A
B
C



MR-guided focused ultrasound thalamotomy for essential tremor: a proof-of-concept study

Nir Lipsman, Michael L Schwartz, Yuexi Huang, Liesly Lee, Tejas Sankar, Martin Chapman, Kullervo Hynynen, Andres M Lozano

Lancet Neurol 2013; 12: 462–68
Published Online
March 21, 2013
http://dx.doi.org/10.1016/S1474-4422(13)70048-6

Division of Neurosurgery, Department of Surgery, Krembil Neuroscience Centre, Toronto Western Hospital, University of Toronto, Canada

	Sex	Treated hand	Age (years)	Illness duration (years)	Medication at surgery	Number of sonications	Maximum temperature achieved (°C)
Patient 1	M	R	71	6	Propranolol Primidone Gabapentin	27	56
Patient 2	M	L	77	25	Primidone Propranolol	22	63
Patient 3	M	R	77	20	Primidone	12	59
Patient 4	M	R	58	20	Propranolol	29	59
Mean			70·8	17·8		22·5	59·3

Table 1: **Patient demographics and clinical characteristics**

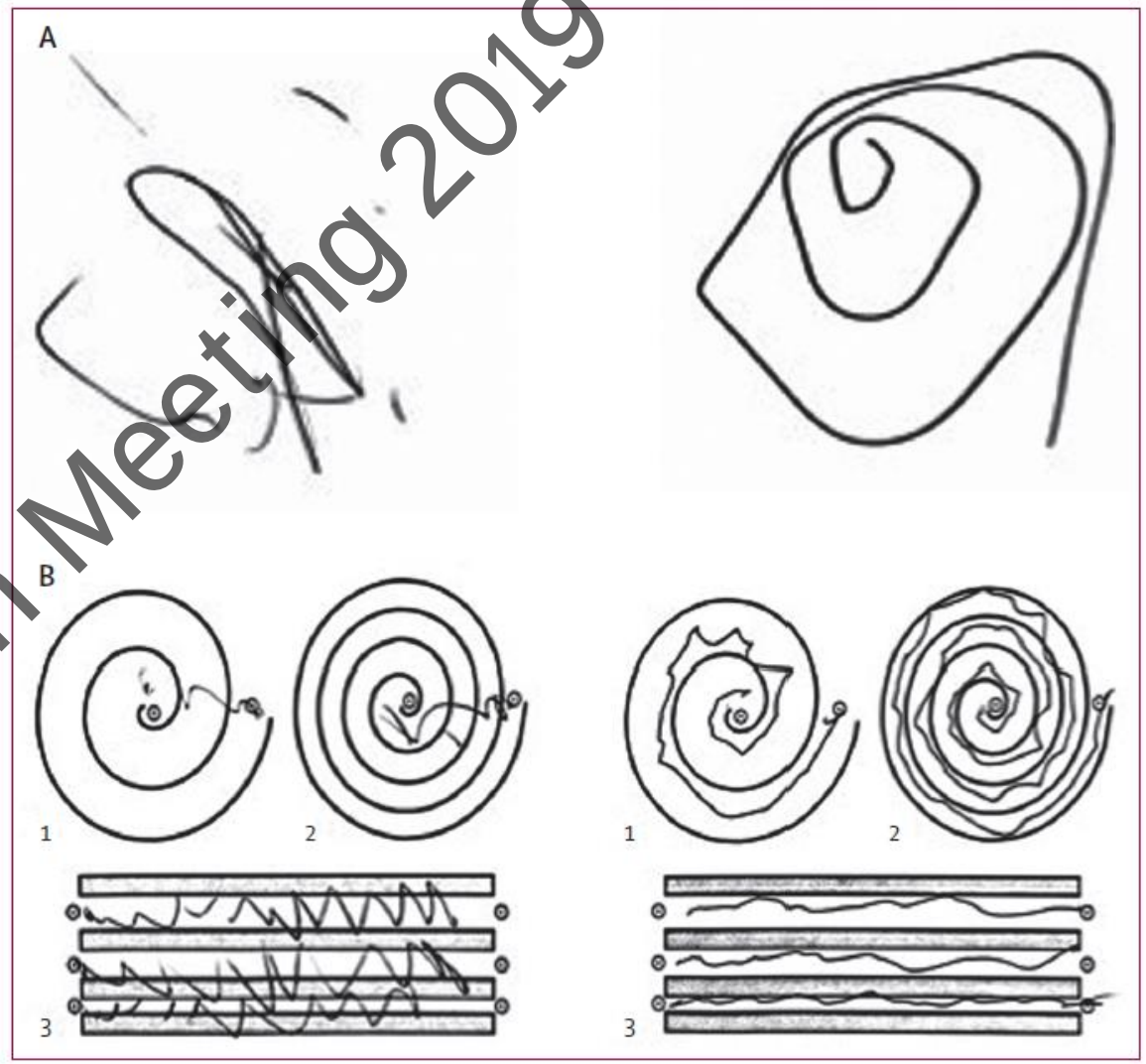


Figure 1: **Drawings by patient 2 (left handed) before and after he underwent right-sided MR-focused ultrasound thalamotomy**

(A) Freehand spiral drawing by patient 2 immediately before (left) and immediately after (right) thalamotomy, showing the change from having difficulty in putting pen to paper to improved drawing ability. Video footage of this patient undertaking this task can be seen in the appendix. (B) As part of the clinical rating scale for tremor (CRST), patients are asked to complete several line drawings. Drawing at baseline (left) and at 3 months (right) after treatment.

MR-guided focused ultrasound thalamotomy for essential tremor: a proof-of-concept study

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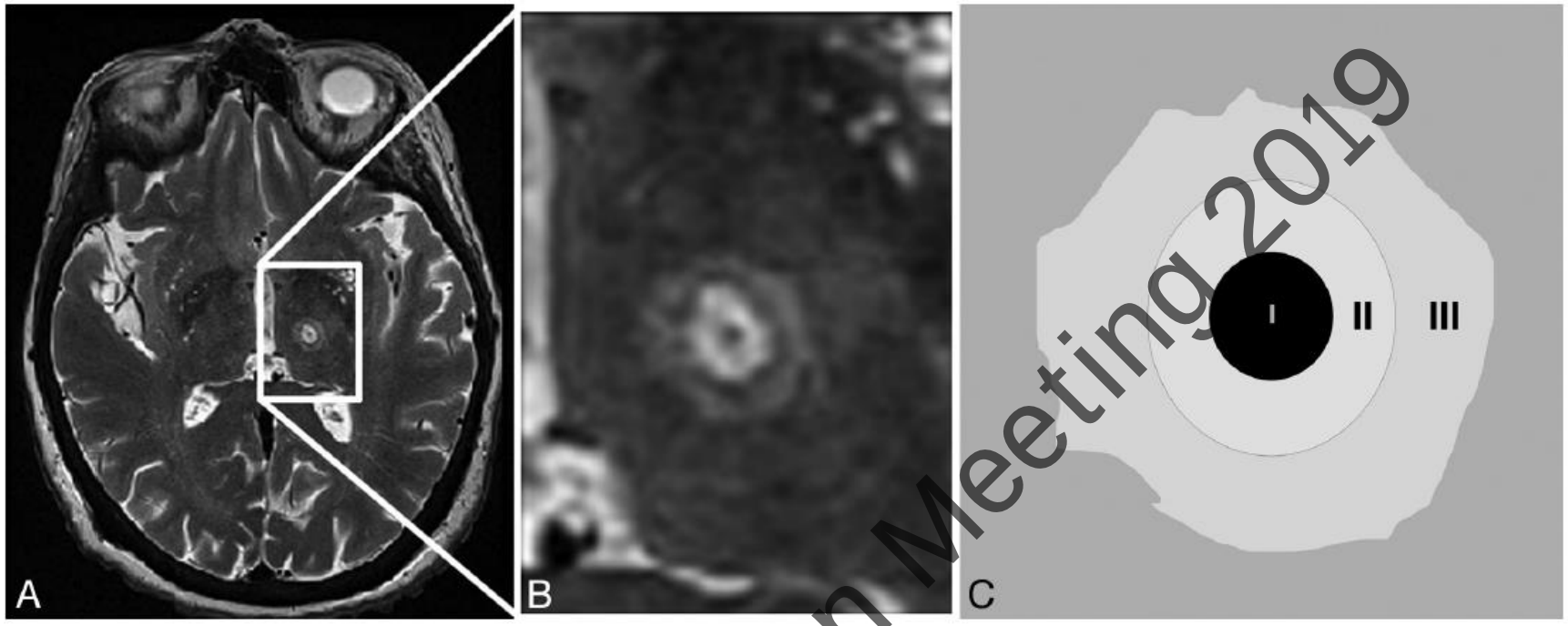

FIG 1. Schematic representation of zones I, II, and III visualized on T2-weighted imaging and the corresponding T2-weighted image of the lesion. On T2-weighted imaging, the patient developed 3 concentric zones at the site of lesioning: a hypointense zone I at the center; a strongly hyperintense zone II demarcated by a hypointense rim; and finally, a fuzzy, slightly hyperintense zone III at the periphery.

CONCLUSIONS: MR imaging–guided focused sonography can accurately ablate a precisely delineated target, with typical imaging findings seen in the days, weeks, and months following the treatment. Tremor control was optimal early when the lesion size and perilesional edema were maximal and was less later when the perilesional edema had resolved.

ORIGINAL RESEARCH
BRAIN

Imaging Findings in MR Imaging–Guided Focused Ultrasound Treatment for Patients with Essential Tremor

M. Wintermark, J. Druzgal, D.S. Huss, M.A. Khaled, S. Monteith, P. Raghavan, T. Huerta, L.C. Schweickert, B. Burkholder, J.J. Loomba, E. Zadicario, Y. Qiao, B. Shah, J. Snell, M. Eames, R. Frysinger, N. Kassell, and W.J. Elias

AJNR Am J Neuroradiol 35:891–96 May 2014 www.ajnr.org

REVIEW

Movement Disorders, Vol. 30, No. 11, 2015

Therapeutic Advances in Tremor

Alfonso Fasano, MD, PhD[1] and Günther Deuschl, MD[2]*

TABLE 2. Selection of active trials enrolling tremor patients, as submitted to the US NIH database (https://clinicaltrials.gov)

NCT Number	Study Title	Condition(s)
Medication		
02277106	Evaluate SAGE-547 in Patients With Essential Tremor	ET
02197104	Citocoline for Treatment of FXTAS	FXTAS
01961297	Voice Tremor in Spasmodic Dysphonia: Central Mechanisms and Treatment Response	Dystonia
01958177	Clinical Study to Evaluate the Safety and Efficacy BMMNC in Cerebellar Ataxia	Cerebellar Ataxia
01864525	Effects of Octanoic Acid for Treatment of Essential Voice Tremor	ET
Botulinum neurotoxin		
02427646	Use of Kinematic Assessment of Hand Tremor Pre- and Post- Treatment With Botulinum Toxin Type A in Essential Tremor and Parkinson Disease	ET and PD
02334683	Compare Two Guidance Techniques for Botulinum Toxin Injections for the Treatment of Limb Spasticity and Focal Dystonia	Spasticity and dystonia
02207946	Botulinum Toxin A to Treat Arm Tremor	ET
02419313	Investigation of the Efficacy and Safety of IncobotulinumtoxinA (Xeomin) in Parkinson's Tremor: A Customized Approach	PD
Transcranial magnetic stimulation		
02441985	rTMS Therapy for Primary Orthostatic Tremor	Primary Orthostatic Tremor
02443181	Demand-driven Management of Essential Tremor	ET
02387346	The Cerebellum as a Potential Treatment Site for PD Motor Symptoms	PD
02370108	The Study of Rest Tremor Suppression by Using Electrical Muscle Stimulation	PD
01792336	Transcranial Magnetic Stimulation for Focal Hand Dystonia	Dystonia
Deep brain stimulation		
02418858	Functional Outcomes of Awake vs Asleep Deep Brain Stimulation (DBS) for Essential Tremor	ET
02384421	Adaptive Closed Loop Neuromodulation and Neural Signatures of Parkinson's Disease	PD
02288468	One Pass thalamic aNd subthalamic stimulatiON	PD
02264925	Thalamic LFPs and VIM DBS in Essential Tremor: Correlation, Evolution, and Therapeutic Perspectives	ET
02119611	Deep Brain Stimulation Therapy in Movement Disorders	ET and PD
02087046	Deep Brain Stimulation (DBS) for the Suppression of Tremor	ET
02071446	Local Fields Potentials Recorded From Deep Brain Stimulating Electrodes	ET, PD and dystonia
01945567	Randomised Crossover Trial of Deep Brain Stimulation of Differential Posterior Subthalamic Area Regions in Parkinson's Disease and Tremor	PD
01934881	Voltage Adjustment Only Versus Combined Parameters Adjustment in PD Patients Treated With Bilateral STN DBS	PD
01909531	Deep Brain Stimulation (DBS) Data Base Study	ET and PD
01809613	Functional Magnetic Resonance Imaging (fMRI) During Deep Brain Stimulation (DBS) to Treat Parkinson's Disease	ET, PD and dystonia
01681641	Managing Changes in Life After Deep Brain Stimulation for Parkinson's Disease	PD
01581580	Deep Brain Stimulation Surgery for Movement Disorders	ET, PD and dystonia
Gamma knife radiosurgery		
02406105	An Effectiveness and Toxicity of CyberKnife Based Radiosurgery for Parkinson Disease	PD
02255929	Gamma Knife Radiosurgery for Treatment of Essential Tremor	ET
02095600	Radiosurgery for Drug Resistant Invalidating Tremor	Tremor
01734122	Stereotactic Radiosurgery for Essential Tremor and Parkinsonian Tremor	ET and PD
MRI-Guided Focused Ultrasound		
02289560	Continued Access Protocol: ExAblate Transcranial MR Guided Focused Ultrasound for the Treatment of Essential Tremors	ET
02252380	ExAblate Transcranial MRgFUS for the Management of Treatment-Refractory Movement Disorders	ET, Holmes Tremor, PD, dystonia
02037217	ExAblate Transcranial MR Guided Focused Ultrasound in the Treatment of Essential Tremor	ET
01827904	ExAblate Transcranial MR Guided Focused Ultrasound for the Treatment of Essential Tremors	ET
01772693	ExAblate Transcranial MR Guided Focused Ultrasound for the Treatment of Parkinson's Disease	PD
Others		
02370134	Development of Parkinson's Glove for Detection and Suppression of Hand Tremor	PD
02067702	Limb Cooling in Essential Tremor	ET
01989013	Effect on Parkinson's Disease After Therapeutic Induction of CranioSacral Integrated Therapy	PD
01940406	The Essential Tremor (ET) and Parkinson Disease (PD) Tremor Acute Stimulation Study	ET and PD
01860794	Evaluation of Safety and Tolerability of Fetal Mesencephalic Dopamine Neuronal Precursor Cells for Parkinson's Disease	PD

Questions

Album Cover
Devon Band - Muse : " The 2nd Law"

Coloured image from MRI Tractography