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Brain Medicine in Action: An Interdisciplinary Training Ground for Complex Brain Disorders

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Disclosures

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- Azrieli Foundation
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Objectives

1. Introduce the concept of brain medicine
2. Outline the development of a new fellowship and clinical program for complex brain disorders
3. Practice brain medicine in action through clinical case discussions

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The Concept

- The brain is the body's most complex organ
- Modern medicine's focus on increasing physician specialization has led to fragmented care for patients

"...in order to further developments in the neurosciences, we have to eliminate barriers between disciplines…the ground we are now breaking in the science of the brain and mind is common ground."

- Joseph B. Martin

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Neuro-surgery

Neurology	Psychiatry	Geriatrics	Neurosurgery	Physiatry
Neurodegenerative disorders Traumatic brain injury Stroke **Epilepsy** Functional **disorders** **Autoimmune/ demyelinating disorders**	Affective disorders Dementia Delirium Catatonia Psychosis Functional **disorders** **Autism spectrum**	Dementia Stroke **Delirium** Pain	Stroke Traumatic brain injury Brain Cancers	Stroke Traumatic brain injury Chronic Pain

Physiatry

Psychiatry (Geriatric Psychiatry)

Brain Medicine focuses on the holistic assessment and treatment of complex brain disorders with pathology in

A	• Affect
B	• Behaviour
C	• Cognition

Having symptoms from **>1 ABC domains** associated with **worse functional outcomes** (Borda M.G. et al 2020; Deleo, F. et al., 2020; Petkus, A. et al; 2020).

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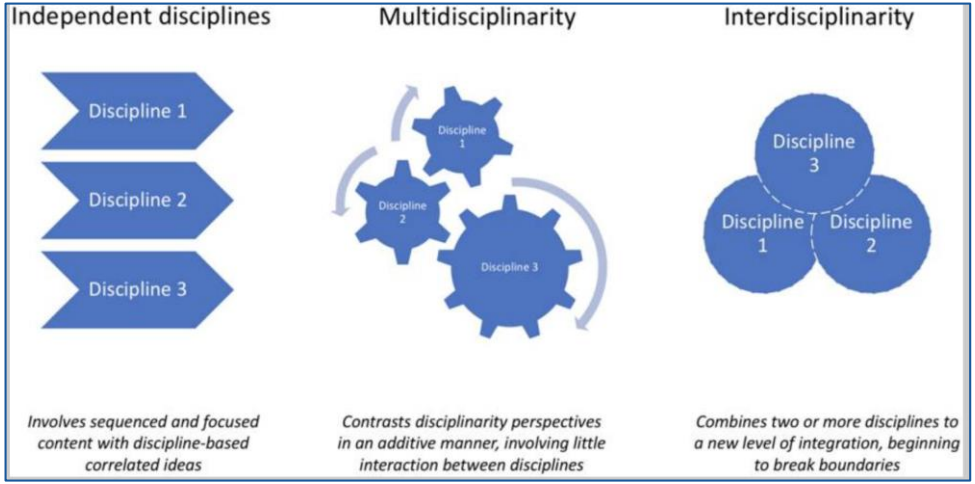
The Vision

Build an **innovative model of fellowship** to improve physician competencies and patient care delivery

Interdisciplinary approach

- "interdisciplinarity" refers to the *integration* [emphasis added] of knowledge across disciplines"

  (Frodeman, 2014)



Gohar et al. Driving Medical Innovation Through Interdisciplinarity: Front Med 2019.

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Azrieli Brain Medicine Fellowship

- **Joint initiative University of Toronto**
  - Faculty members across psychiatry, neurology, neurosurgery and medicine
  - **Cross-city** Toronto Academic Health Sciences Network (TAHSN+)
- **Different routes of entry** from residency training
  - Neurology, Psychiatry, Geriatrics, PM&R, Neurosurgery
- **Competency-based** medical education; tailored fellowship experience

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Path of an Azrieli Brain Medicine Fellow

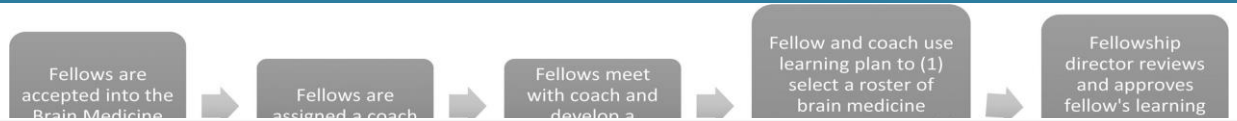

Chart 1

Sample Weekly Fellowship Schedules for Trainees From Different Specialties of Origin, July to December 2020

Specialty	Monday	Tuesday	Wednesday	Thursday	Friday
Psychiatry					
Morning	Neurostimulation	Neuropathology	Brain medicine clinic	Neuropsychiatry consult–liaison service	Academic project (neuroethics research project)
Afternoon	Movement disorders clinic	Neuroradiology			
Neurology					
Morning	Neurostimulation	Rehabilitation psychiatry clinic	Brain medicine clinic	Virtual behavioral neurology	Academic project (master teacher program)
Afternoon	Rapid access addiction medicine clinic		Procedural headache clinic	Functional neurological disorder clinic	

ACADEMIC MEDICINE

ACADEMIC MEDICINE

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Brain Medicine Clinic Model

- Brain medicine ‘in action’
  - Longitudinal training environment for fellows
- Interdisciplinary clinical care model
  - Integrated patient assessments by multiple brain medicine specialists “one stop shop”
  - **Neurology, psychiatry (core) +** geriatrics, neurosurgery, physiatry, neuroradiology
  - Comprehensive seamless care for patients
  - Enhance navigation of patients to community resources

Brain Medicine Clinic

Inclusion Criteria for Patients:

- >18 years old
- Presence of complex brain disorder, defined as a chief complaint(s) that involves **2/3** of the **A**ffect, **B**ehaviour and **C**ognition domains (ABC)
- They are screened as likely to require access to at least two Brain Medicine related specialities (geriatric medicine, neurology, neurosurgery, physical medicine & rehabilitation, or psychiatry)
- Started Pre-Pilot January 2021, 0.5 days a week, ~100 new patients

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Brain Medicine Clinic: Population

Low Symptom Severity (LSS): Disturbances in A+B/A+C/B+C

High Symptom Severity (HSS): Disturbances in A+B+C

Table 1. Demographic and clinical characteristics of patients seen in the BMC from inception to August 2022 grouped according to symptom severity.

Characteristics	LSS (n = 51)	HSS (n = 41)	Total (n = 92)	p-value
Age, *years* (mean, SD)	54.96 (16.32)	56.00 (14.35)	55.42 (15.40)	0.74
Sex (n, % female)	27 (52.94%)	23 (56.10%)	50 (54.35%)	0.76
Relationship status (n, %)				0.14
Single	12 (24.00%)	4 (9.76%)	16 (17.58%)	
With a partner	28 (56.00%)	32 (78.05%)	60 (65.93%)	
Divorced/separated	6 (12.00%)	4 (9.76%)	10 (10.99%)	
Others	4 (8.00%)	1 (2.44%)	5 (5.49%)	
Educational attainment (n, %)				<0.05
Primary school	6 (12.24%)	2 (5.26%)	8 (9.20%)	
High school	12 (24.49%)	13 (34.21%)	25 (28.74%)	
College	18 (36.73%)	21 (55.26%)	39 (44.83%)	
Post-graduate	13 (26.53%)	2 (5.26%)	15 (17.24%)	
Employment status (n, %)				0.77
Employed	13 (26.53%)	9 (23.68%)	22 (25.29%)	
Self-employed	2 (4.08%)	2 (5.26%)	4 (4.60%)	
Not working	22 (44.90%)	21 (55.26%)	43 (49.43%)	
Retired	12 (24.49%)	6 (15.79%)	18 (20.69%)	
Living condition (n, %)				0.12
Alone	11 (22.00%)	4 (9.76%)	15 (16.48%)	
With others	39 (78.00%)	37 (90.24%)	76 (83.52%)	
Age of symptom onset, *years* (mean, SD)	49.78 (18.81)	50.95 (15.33)	50.30 (17.28)	0.75
Family history (n, %)				0.94
Dementia	19 (26.76%)	17 (29.82%)	36 (28.13%)	
Other neurologic disease/s	10 (14.08%)	8 (14.04%)	18 (14.06%)	
Other psychiatric disease/s	24 (33.80%)	17 (29.82%)	41 (32.03%)	
Other medical condition/s	7 (9.86%)	4 (7.02%)	11 (8.59%)	
None	11 (15.49%)	11 (19.30%)	22 (17.19%)	
Substance use history (n, %)				0.56
Alcohol	10 (16.67%)	11 (25.00%)	21 (20.19%)	
Cannabis	5 (8.33%)	4 (9.09%)	9 (8.65%)	
Smoking	12 (20.00%)	4 (9.09%)	16 (15.38%)	
Others	2 (3.33%)	1 (2.27%)	3 (2.88%)	
None	31 (51.67%)	24 (54.55%)	55 (52.88%)	
Neurologic exam (n, %)				0.18
Without findings	25 (58.14%)	19 (51.35%)	44 (55.00%)	
With pertinent findings	15 (34.88%)	14 (37.84%)	29 (36.25%)	
With non-pertinent findings	3 (6.98%)	4 (10.81%)	7 (8.75%)	
Disability status (n, %)				0.19
Receiving support on retirement?	8 (11.27%)	11 (26.83%)	19 (20.65%)	
Not receiving support?	43 (60.56%)	30 (73.17%)	73 (79.35%)	
Referral source (n, %)				0.38
Primary care	22 (46.81%)	10 (27.78%)	32 (38.55%)	
Neurology	15 (31.91%)	17 (47.22%)	32 (38.55%)	
Psychiatry	8 (17.02%)	6 (16.67%)	14 (16.87%)	
Geriatrics	1 (2.13%)	2 (5.56%)	3 (3.61%)	
Other sources	1 (2.13%)	1 (2.78%)	2 (2.41%)	

LSS: Low symptom severity. *HSS*: High symptom severity. *p-value*: <0.05 indicates significant difference between LSS and HSS. *SD*: Standard deviation.

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Case 1:

54 y.o female, married therapist with one child with Autism Spectrum Disorder

PMHx: Hypertension, hypothyroidism, hysterectomy, migraine without aura (monthly), post-partum depression & anxiety

Medications: Multiple supplements (Vitamin B12, Vitamin D, ashwagandha, Omega 3, calm magnesium)

Social History: Born in Canada, Master's degree in social work, non-smoker, alcohol recreationally and no recreational drug use.

Family History: Alzheimer's Type Dementia in mother (age of onset 79)

Case 1:

RFR: Rule out dementia

HPI: Presents with a six-year history of worsening cognitive concerns, walking into a room and forgetting why, leaving on appliances, forgetting to lock doors, forgetting appointments, difficulty with remembering words and writing. She reports that she is unable to follow patients over time and so has paused working. Reports "brain fog" and "not being the same person".

Physical Exam: Mental Status Examination notable for tearfulness when discussing her cognitive symptoms

Cognitive Testing: MoCA 22/30 (-2 serial 7's, -1 repetition, -4 recall (able to recall all with category cue), -1 orientation); BNA-SF 108/114 (-2 serial 7's, -4 semantic fluency)

No abnormalities on complete neurological exam (no primitive reflexes, apraxia, parkinsonism, abnormal movements)

Other information to know?

Came alone and provided detailed description of cognitive complaints with use of notes or collateral history

Extreme distress around cognitive symptoms, out of keeping with degree of functional impairment

Expanded Social history: Supportive relationship with husband, though required marital counselling in the past as couple coped with child's ASD diagnosis and behavioural challenges. 3 children and 2 older children have recently left the home.

Childhood history: High achiever at school, identifies as introvert with some friends (not a wide circle of friends). At home she experienced parents as having high expectations of achievement and felt like attention and affection was attached to these expectations. Older brother who died of substance use in his mid-20's. A few close friends for support but difficult to see as "everyone has their own life".

Felt a lot of responsibility when mom diagnosed with AD later in life and ultimately mom moved into a LTC.

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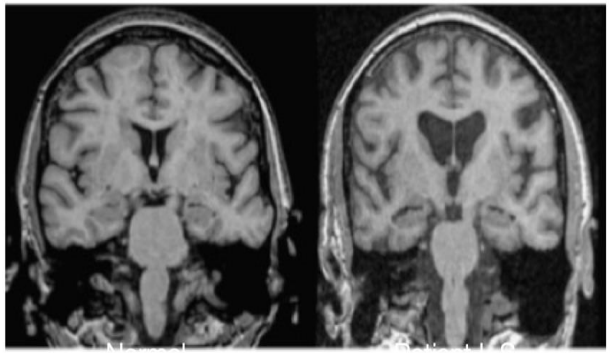
Case 1: Investigations

CASE

Screening blood work unremarkable:
TSH, B12, CBC, lytes/extended lytes, LFTs, Cr

Neuroimaging



Thoughts on diagnosis?
Next steps?

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Interactive biopsychosocial formulation

	Neuro	Bio	Psycho	Social
Predisposing				
Precipitating				
Perpetuating				
Protective				

Interactive biopsychosocial formulation

	Neuro	Bio	Psycho	Social
Predisposing	Family history of dementia and mental illness (mom, brother) Increased neurodegenerative risk factors (vascular risk factors, depression)	Hypothyroidism	Obsessive-compulsive personality traits Need for control Self-esteem sustained by accomplishment	Caregiving responsibilities Prominent advocate in disability community
Precipitating	Increasing social isolation	Advancing age Psychosocial stress Menopause	Role transition	Children leaving home COVID-19 pandemic interfering with social engagement
Perpetuating	Decreased cognitive stimulation, not working Migraines and vascular disease Poor sleep Ongoing low mood	Hypothyroidism, vascular risk factors	Concern for loss of independence Hyperattentive to any deficits/failures	Experience of being a caregiver for someone with neurodegenerative disease Taking on less responsibility vocationally due to cognitive concerns (reinforcing cycle)
Protective	High educational attainment (Master's level) Lifestyle choices (non-smoker, no alcohol etc)	Brain and general health focused lifestyle	Engagement with diagnosis Help-seeking with acceptance of psychological supports Hopefulness	Strong family support Maintaining friendships High SES

Case 1: Diagnosis

Functional cognitive disorder

Table 2. Proposed operational definition of FCD (based on [9]).

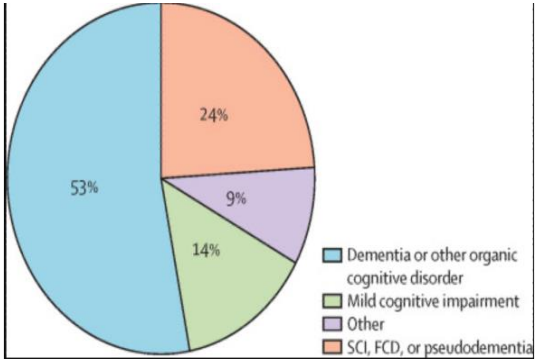
1. One or more symptoms of impaired cognitive function.
2. Clinical evidence of internal inconsistency.[a]
3. Symptoms or deficits that are not better explained by another medical or mental disorder.[b]
4. Symptoms or deficit that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning or warrants medical evaluation.[c]

a: Internal inconsistency indicates a worse self-reported performance compared to objective evidence, or inconsistency between situations, or at different time points (i.e., variability over time, not stability nor a pattern of decline).

b: Patients may have comorbid medical or psychiatric disorder as well as FCD.

c: A minimum of 6 months duration should be considered.

Specifier: Specify if: with/without a linked co-morbidity.



McWhirter et al. Lancet Psychiatry 2020

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Case 1: Functional Cognitive Disorder

Table 3. "Archetypal" FCD features (based on [11]) as a possible heuristic for diagnosis.

- Young age (50 s)
- "Attended alone" sign (= no immediate access to collateral history)
- Brings written list of symptoms (*La maladie du petit papier*)
- Positive family history of dementia (usually in an elderly relative, i.e., not a monogenic form of dementia)
- Disturbed sleep
- Disturbed mood
- Positive for subjective memory complaint on brief screener (e.g., Subjective Memory Complaint Likert scale)

Table 4. Features unlikely to differentiate FCD from other causes of memory complaint (based on [11]).

- Patient gender
- Patient handedness
- Referral source (primary or secondary care)
- Scores on simple cognitive screening instruments

Other positive features:

- Resistance to reassurance
- Repeated medical consultations
- Failure on performance validity tests

Pennington C, Ball H, Swirski M. Functional Cognitive Disorder: Diagnostic Challenges and Future Directions. Diagnostics (Basel). 2019 Sep 28;9(4):131.

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Case 1: Approach

- Evidence-based psychotherapy to treat psychiatric comorbidities
- Resource Navigation (patient navigator)
- Psychoeducational resources
    - Neurosymptoms.org
    - FND Hope
    - Overcoming functional neurological disorders
- Developing program to provide specific psychotherapies for FCD
- Functional cognitive rehabilitative approach (guided by PM&R)

Competencies From This Case

Fellows would gain the following competencies:

Domain	Competency
Affect	Recommend +/- deliver evidence-based psychotherapy for disordered affect
Cognition	Perform a neurobiopsychosocially-relevant clinical history and assessment relevant to symptom complaints across all cognitive domains including attention/concentration, language, memory, visuospatial function and executive function Recognize and evaluate for all potentially relevant biopsychosocial contributions to impaired cognition

Case 2:

55 y.o male, married with two children

RFR: Cognitive impairment

PMHx: No diagnoses prior to stoke July 2022 but limited healthcare contact; R MCA stroke July 2022 with hemorrhagic transformation, new diagnosis of atrial flutter, CHF, DM type 2, Hypertension, Hypercholesterolemia, BPH

Medications: None pre-stroke. Post-stroke: Amiodarone 200mg po OD, Apixaban 5mg po BID, Candesartan 8mg po OD, Digoxin 0.125mg po OD, Metoclopramide 5mg po TID, Metoprolol 200mg po BID, Ondansetron 4-8mg po BID, Pantoprazole 40mg po OD, rosuvastatin 10mg po OD, Tamsulosin 0.8mg po O5

Social History: Born in Canada, Master's degree in Education, remote history of smoking (quit 2007)

Family History: Father: multiple sclerosis, Mother: Hypertension and atrial fibrillation, Maternal grandfather dementia

Case 2:

HPI: July 2022 - bronchitis diagnosis and then acute stroke symptoms with left sided weakness → code stroke with M2 clot, given TPA with hemorrhagic conversion and then EVT. Admitted to ICU post procedure with complicated hospital course (aspiration pneumonia, atrial fibrillation, delirium with hallucinations). Eventually went to Rehab discharged Dec 2022

Neuro deficits: left sided neglect/inattention, anosognosia, mild left sided residual weakness/numbness, mild dysphagia

Emergence of depression towards end of hospital visit. Possible apathy syndrome.

Now presenting with:

- Stepwise decline in short term memory, attention and concentration, executive function apraxia
- Disturbed affect with lability & apathy resulting in poor self-care, inability to work, disengagement from family life
- High degree of caregiver burnout from partner
- ADL dependence (toileting - fecal incontinence, bathing and dressing)

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Case 2:

Physical Exam:
MSE notable for dishevelled appearance, lability, paucity of speech, concrete thought form, passive suicidal ideation

Cognitive Testing: MoCA 23/30 (-2 serial 7's, -1 clock drawing,-2 repetition, -1 abstraction, -2 delayed recall, additional word with category cue, -1 orientation, BNA-SF 95/114 (-1 serial 7's, -1 memory, semantic fluency 16, -1 clock, -12 executive function (phonemic fluency 10, -2 similarities)

Neurological examination:
Cranial nerves: Saccadic extraocular movements, mild left nasolabial fold flattening +ve palmomental reflex bilaterally, bilateral ideomotor apraxia, mild left neglect
Motor: Mild spasticity in left arm, 4+/5 pyramidal pattern weakness in left arm and leg, reflexes 2+ symmetrical
Sensation: reduce to temperature over left hemibody
Gait: Instability, hemiplegic pattern wide based gait with scissoring. Required walker for stability.

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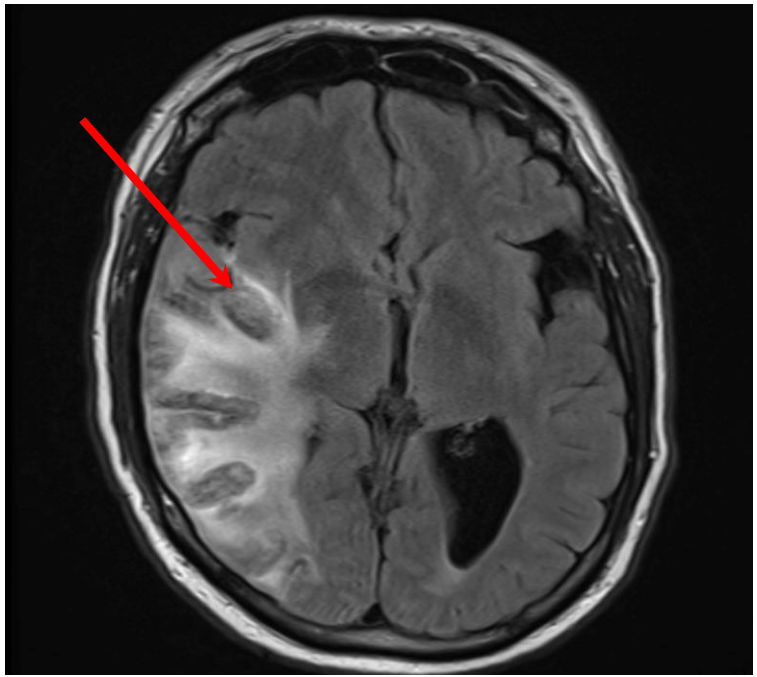
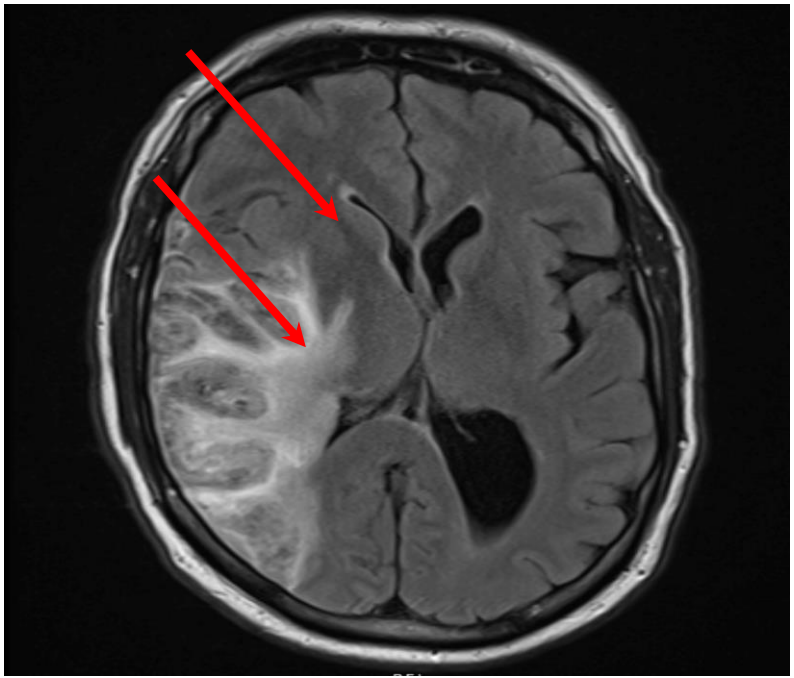
Case 2:





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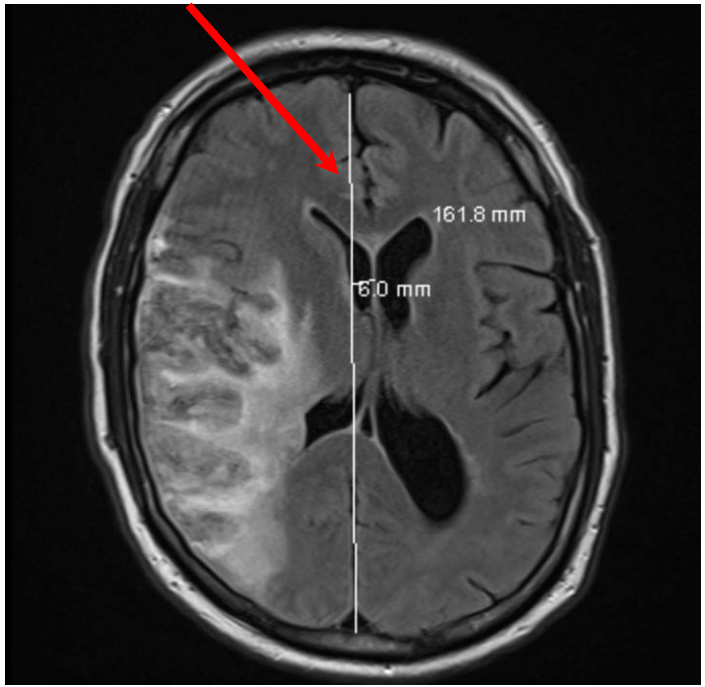
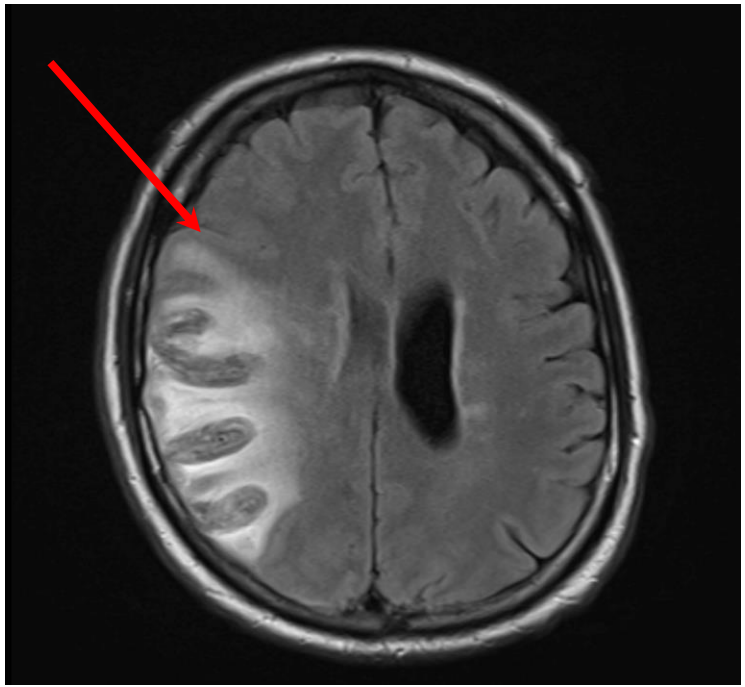
Case 2:





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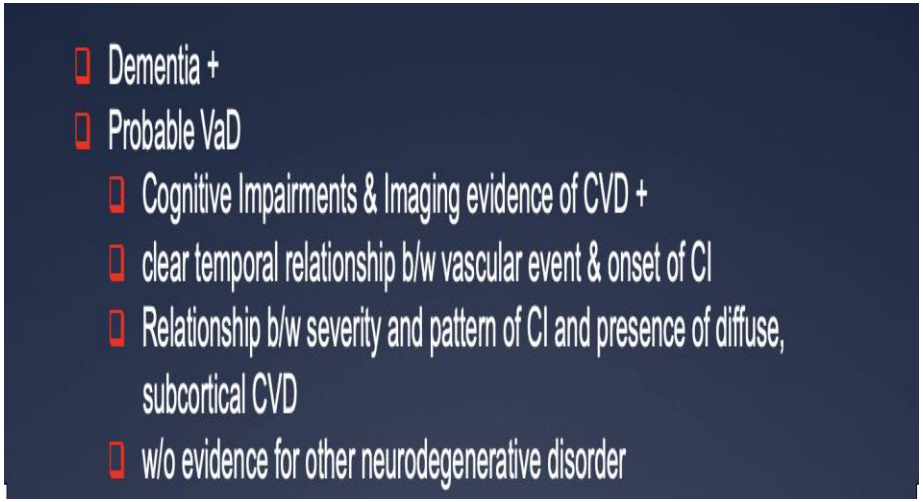
Interactive biopsychosocial formulation

	Neuro	Bio	Psycho	Social
Predisposing				
Precipitating				
Perpetuating				
Protective				

Interactive biopsychosocial formulation

	Neuro	Bio	Psycho	Social
Predisposing	Multiple undiagnosed and unmanaged vascular risk factors	Sedentary lifestyle	Avoidance of addressing issues that elicit fear/anxiety	Lack of engagement with healthcare providers
Precipitating	Large right MCA territory stroke	Bronchitis and prolonged complicated hospital admission, delirium Deconditioning	Threat to self-esteem due to loss of independence related to major health concern	Need for caregiving within the family system Displacement from family due to health care needs
Perpetuating	Poor mobility, social interaction, and cognitive stimulation post-stroke Extensive dead brain tissue	Multiple unmasked medical comorbidities requiring optimization	Ambivalence regarding role in family secondary to new functional status	Deteriorating relationship with partner & children Financial stress
Protective	High educational attainment Smoking cessation Risk factors managed Young age (neuroplasticity)	Young age Adherence to medical treatment of comorbidities and rehabilitation	Ultimately desire to stay part of family and regain function	Ongoing family support despite strained relationships High level of health literacy within the family

Vascular Dementia



Single strategic infarct

- **Caudate nucleus:** Unilateral or bilateral lesions
  - **Dorsolateral caudate**: Psychomotor depression, apathy
  - **Ventromedial caudate:** Psychomotor hyperactivity, disinhibition, impulsiveness
- **Hippocampus:** Usually bilateral
- **Thalamus: Dorsomedial or anterior nucleus**
- **Right MCA infarct (right parietal)**:
  - acute delirium, inattention/neglect syndrome

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Apathy

Apathy → quantitative reduction of goal-directed activity compared to previous function

- Apathy dimensions: cognition, behaviour, emotion, social interaction
- Associated with functional decline, caregiver burnout, institutionalization, increased mortality
- Differs from anhedonia due to degree of emotional blunting/indifference

Diaschisis implicated in development of apathy post-stroke

"Emotional neutrality" differentiates apathy & MDE

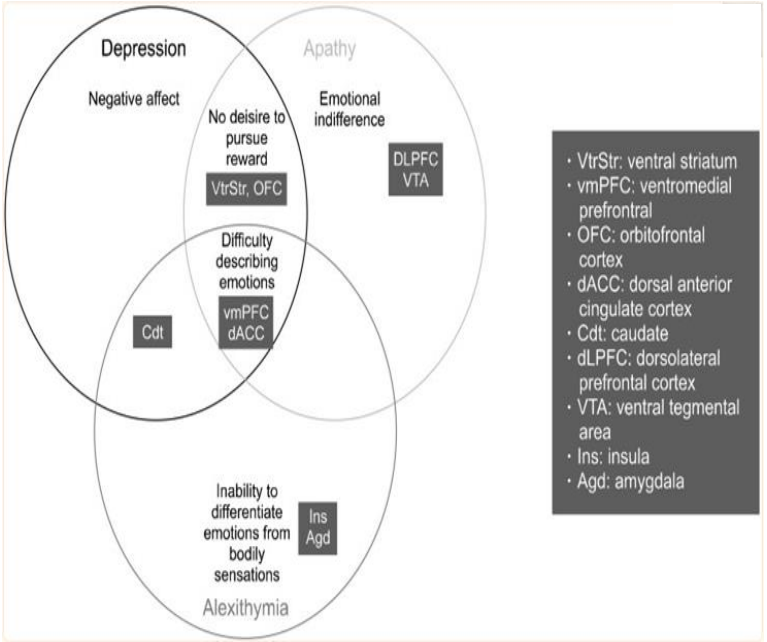

FIG. 1
Broad clinical and neuro-scientific distinctions between depres-sion, apathy and alexithymia (5.13).

Fahed & Steffens, Apathy; Neurobiology, Assessment, & Treatment.
Clinical Psychopharmacology Neuroscience. 2021 May 31, 19(2), 181-189.

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Biological Treatments of Apathy

Treatment should be tailored to etiology:

- *Major Depressive Disorder:* Selective Serotonin Reuptake Inhibitors (SSRI)
- *Vascular Lesions:* Rivastigmine
- *Alzheimer's Disease:* methylphenidate, SSRIs, preliminary evidence for rTMS
  - Here evidence supports that methylphenidate also improves caregiver burden
- *Parkinson Pathologies:* pramipexole, methylphenidate, Acetylcholinesterase Inhibitors
- *Frontotemporal Dementia:* SSRIs, agomelatine? intranasal oxytocin? stimulants?

Fahed & Steffens, Apathy; Neurobiology, Assessment, & Treatment. *Clinical Psychopharmacology Neuroscience*. 2021 May 31, 19(2), 181-189

Treatment Approach

Neurobiological: SSRI optimization, methylphenidate, connection with PM&R, optimization of vascular risk factor management and sleep (e.g. CPAP for OSA), cognitive rehabilitation (PM&R, OT)

Psychological: provided regular family counselling to address anger & burnout

Social: connection to ABI network and other resources for case management

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Competencies From This Case

Fellows would gain the following competencies:

Domain	Competency
Affect	Obtain a patient-centered history around disordered affect
Behaviour	Develop a differential diagnosis for patients presenting with disordered behaviour and propose a rational work-up for the proposed differential
Cognition	Demonstrate appropriate command of the localization of cognitive based disorders within the brain, and provide a neurobiopsychosocial formulation relevant to the patient's presentation

Brain Medicine Vision

> Acad Med. 2023 Jan 30. doi: 10.1097/ACM.0000000000005156. Online ahead of print.

The Brain Medicine Fellowship: A Competency-Based Training Program to Treat Complex Brain Disorders

Sarah Levitt [1], Alex Henri-Bhargava [2], David Hogan [3], Kenneth Shulman [4], Sara Mitchell [5]

Affiliations + expand

PMID: 36719701 DOI: 10.1097/ACM.0000000000005156

Abstract

Problem: Complex brain disorders involve symptoms in the domains of affect, behavior, and cognition. It is increasingly recognized that there is a need for a novel type of physician who can treat individuals with these conditions in an interdisciplinary fashion to best address their complexity. Few training programs have focused on the education of such practitioners.

Approach: The authors outline the development and practices of the Brain Medicine Fellowship, an innovative, competency-based fellowship program at the University of Toronto Temerty Faculty of Medicine that accepts trainees from multiple brain medicine-related specialty training programs to develop expertise in integrative assessment and treatment of complex brain disorders. The authors describe how brain medicine competencies were generated, the current assessment process, and

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Azrieli Brain Medicine Fellows

PAST

"We're looking at brain dysfunction and its many symptoms from every angle, and providing the most holistic care possible."

Dr. Sarah Levitt

PRESENT

"I'm being trained by neurologists, psychiatrists and physiatrists and am learning to detect neuropsychological disturbances in my patients – helping them maximize the benefits they gain from physiotherapy, occupational therapy and speech and language therapy."

Dr. Carl Leochico

FUTURE

The Azrieli Brain Medicine Fellowship promises a broadened clinical perspective that will allow me to better explain to patients the relationship between their brain health and their experience of mind."

Dr. Michael DeDominicis

Conclusions

- Given advances in neuroscience, increasing imperative to re-examine health care provision to patients with complex brain diseases (CBD)
- Azrieli Brain Medicine Fellowship aims to train a new phenotype of physician, the Brain Medicine Specialist, fostering interdisciplinarity amongst brain related disciplines
- The Brain Medicine clinic is designed as both a ‘one-stop shop’ for patient with CBD and a fertile training group for Brain Medicine trainees

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Future Directions

- **Evaluate** Brain Medicine Program from educational, clinical care innovation and outcomes, and patient perspective
- **Expand** model of Brain Medicine to other academic institutions nationally through collaborative efforts
- **Establish** sustainability model

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How to apply:

University of Toronto Fellowships:
Azrieli Brain Medicine Fellowship

https://documents.med.utoronto.ca/Forms/FellowshipsApplication

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Thank you for your attention.

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Thank you:

- Azrieli Foundation
- University of Toronto, Faculty of Medicine, Department of Psychiatry
- Dr. Benoit Mulsant, Dr. Ken Shulman
- Brain Medicine Steering and Competency Committee
- University of Toronto Office of Advancement
- Past, Present and future Brain Medicine Fellows
- Ashley Wilcox, Natalie Rashkoven

DEMENTIA VS DEPRESSION

- Depression
  - Often retained insight
  - Greater concern than family/friends
  - Cognitive testing:
    - Psychomotor slowing
    - Poor effort
    - Memory improves with cueing

- Depression as risk factor and prodrome for dementia, often co-exist
- New late life depression (consider dementia)