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PSYCHOSES BY ATTACKS FROM SUBVERTED MAST CELLS: A ROLE FOR ARTERIAL INTRAMURAL FLOW BADLY STEERED BY THE NASAL GANGLIA?

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SUMMARY

Mechanisms of cortical psychoses are approached by complementing big data-driven genetics and imaging with a putatively subverted neurovascular "reverse plumbing" by arteries. The "cortical spread" of grey matter loss in schizophrenia and the mid-pericallosal "congestion" in fMRI of periodic catatonia - treatable electromagnetically along arteries - are interpreted in terms of the fastest interstitial outflow through the Cerebral IntraMural Reverse Arterial Flow-engine (CIMURAF, Treviranus 2018-19) draining "waste" via arterio-adventitial lymphatics to the neck. Such repetitively sliding segments of CIMURAF are wrung downstream by muscles likely steered by the neurovascular pterygopalatine ganglion. At the pericallosal artery, along its ideal long straight segment, this likely happens diverging from the mid-callosum towards the front and the back. In the case of a convergent inversion a mid-callosal clash will result, which is observable in psychoses as a mid-callosal high-flow-spot simultaneously with hyper-perfusions of branches and "backwatering" of pial vessels with reactive waste - till date interpreted psycho-mathematically. CIMURAF might also accelerate the perivascular intrusion of MCs by flushing autocrine signals (of which electro-magnetism moves the dipoles) through a putative periadventitial counter-current. Psychoses plausible occur through tryptase-mediated attacks operated by mast cells against oligodendrocytes` cytoskeleton (Medic 2009) and probably via complement-4 (Schizophrenia WG, 2014) against neurons. Usually MCs are essential long-lived "orchestrators" of homeostases and immune or barrier defences interacting with nerves, immunocytes, organs, and routes. MCs after somatic programming as to "destination & destiny" (Treviranus 2017a, 6.2., 2018) rapidly intrude also into the brain`s parenchyma, first within the lymphatics and then putatively by crossing-over to extraluminal arterial routes. MCs transverse the BBBs, while macrophages only trespass in "disease" (Faraco et al. 2017). Both can be "subverted" by a list of microbes (and putatively blown up by COVID-19 within walls). Enuresis and MCs' reactions to clozapine add to the interactive support from (epi-)genetics and imaging.

Key words: *psychoses - Intramural Peri-Arterial Drainage - microbial subversion of mast cells - Covid-19 - clozapine and enuresis*

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INTRODUCTION

> *"This is the great error of our day (...): the physicians separate the soul from the body."*
> *Plato*

Research on psychoses struggles to reconcile big data with macro-physiological mechanisms (Ruzzo & Geschwind 2016) and thus witnesses a "near complete absence of clearly associated biological changes." (Dhindsa & Goldstein 2016). Here a convergent "tangible", yet little tested, theory, involving the most rapid (neurovascular) interstitial fluid outflow within in the cerebral arterial walls (CIMURAF) and its external reverse acceleration of adventitial mast cells (Treviranus 2019a,p) is proposed as a main cause of cortical immuno-vascular dysfunction in the context of "psychoses". Mast cells (MCs) are prototype neuro-immune partners (Forsythe 2019), and emerge as ubiquitous players (Singh et al. 2016, Daniel 2019), also inside the brain (Neumann 1890, Olsson 1964, Dines & Powell 1997, Skaper et al. 2012, 2018, Gilfillan et al. 2011, Karagkouni et al. 2013, Silver & Curley 2013). MCs guard the lymphatic and blood vessels (Kunder et al. 2012), and the BB-barrier (Theoharides 1996), which they can pass, what macrophages in health cannot (Faraco et al. 2017).

Yet MCs also act as assailants of oligodendrocytes (ODCs; Medic 2009) and probably of neurons. In SCZ ODCs indeed are diminished in layer 3 (BA9) and VI of (BA9) of the PFC by 20-25% and in WM (Vostrikov et al. 2018).

Here some "real-biological" hypotheses are applied to the symmetrical mounting of cortical damage in SCZ (Sun et al. 2009) and the perfusion-related findings in periodic catatonia (perCat; Foucher et al. 2019).

THE INTRAMURAL FLOW OF ARTERIES DRAINING BRAINS'S INTERSTITIUM TO ADVENTITIAL LYMPHATICS

Arteries resurface in neuropsychiatry (Meynert 1867/-68, Reynolds & Trimble 2009, iCross-Disorder Group 2019) and have joined psycho-neuro-immunology (Hanson & Gottesman 2005, Maes et al. 2000) while feeding the cerebral 17-fold performing capillaries (Wilhelm et al. 2016) falling ill in SCZ (Uranova et al. 2010, Delgado-Marín et al. 2019). Brain cells are – without buffering – dependent on vessels for heat and waste removal and the supply of energy, oxygen, water, and nutrition. The interstitial one among the extracellular spaces separates brain cells by 1/5 of total brain volume and hereby distances adhesive and charged cells

by around 40 nm so that waste products may escape by diffusion (Kaur et al. 2020).

Arteries` role here is reactivated through a model (Cerebral IntraMURal Reverse Flow; details: Treviranus 2018p, 2019a,p) postulating their pervasive "aortic blueprint" (whereby neuron-driven muscles only switch coaxial tubes; see Figure 1) to realize brain´s quickest "Intramural PeriArterial Drainage (IPAD)" (Albargothy, 2018) of interstitial fluid - between sliding peri-muscular basement membranes. Besides histo-topological correspondences (Figure 1, 2) CIMURAF added the energetic drive from vascular smooth muscles (VSMCs) – now a part of IPAD; Aldea et al. 2019). Atrophy by being correlated in psychoses with the rarely far, but usual "one-hop" *dys*-functional connectivity support atrophy (somehow) to be driven by the latter (Shafiei 2019) – or by another cause: While the "epicenter" here points to the cingulate, where both salience and DM-networks border, it hereby also points to the long, straight pericallosal artery (pCallA), where CIMURAF should deploy accelerations. Conversely at the subgenual u-turn of the pCallA depressant MCs could "fly off the adventitial track», e.g. in depressant mastocytosis (Boddaert et al. 2017). Here the neuronal massacre of depression occurs (Drevets et al. 2008), nullifying ECT (Liu et al. 2015, Qiu et al. 2018).

The VSMCs only (repetitively) twist membraneous tubes co-axially in a segment which thereby is moved *up* stream (!) under neural command, hereby simultaneously creating and undoing pairs of slight hyperboloid "candy-cracker" stenoses (interiorly constraining the arterial wall enough to move fluid upstream within a sliding closed segmented "ring" loaded with "waste"-clearing fluid to move between the membranes wrapping the VSMCs, Figure 2, a segment which nevertheless has radially open shutters towards the perivascular space creating a parallel flow overcoming less resistance). Since such accelerations of the segment (as in the guts` peristalsis) are thought to be directed by neurovascular commands (e. g. from PPG), intramural (intralaminar) pressure should build up and be relieved by the moving stenoses to an average. Segments moved by contrary commands instead should pressurize a section between them more, and eventually transmit peaks to branches, which thus would be injected by "waste", which could well transport various principles leading e. g. to degranulations from MC-guardians at the BBB. Conversely divergent moves of two segmented "rings" would cause a negatively pressured segment eventually suctioning from the wall of branches.

Vascular, arterial factors at first sight seem to be non-contributing to psychoses (Keshavan & Kaneko 2013) since they occur at similar rates in vascular and Alzheimer's dementia, the latter worsening under blocked drainage (Wang et al. 2019). Yet CADASIL a small vessel and subcortical stroke disorder with enlarged perivascular Virchow-Robin spaces (VRS) with intact BBB (Rajani et al. 2019) tells otherwise, as it seems to be interpretable in terms of CIMURAF: The proposed sliding surfaces between the membranous wrapping of VSMCs of its "aortic blueprint" could act as a molecular grinding mill between these VSMCs (Liu et al. 2017), and such could cause the molecular fragmentation of Notch-3 noted in CADASIL (Young et al. 2019). Notch-molecules replace MCs` canonical c-kit at every step of adhesion (Murata et al. 2019) and vascular remodeling (van Engeland et al. 2019). CIMURAF was the first model to propose a muscular suction driving force for the observed diffusive ECS solute transport - besides not qualified (Asgari et al. 2016) pulsation - and actually inverse trans-astrocyte flow (Treviranus 2019). CIMURAF also questions macro-electromagnetic therapies (Argyelan et al. 2019, McWirther et al. 2015), fluctuations influencing fMRI (Wittaker et al. 2019) or outlasting ECT (Cabral-Calderin et al. 2016, Bächinger et al. 2017), as well as EEG-microstates (da Cruz et al. 2020).

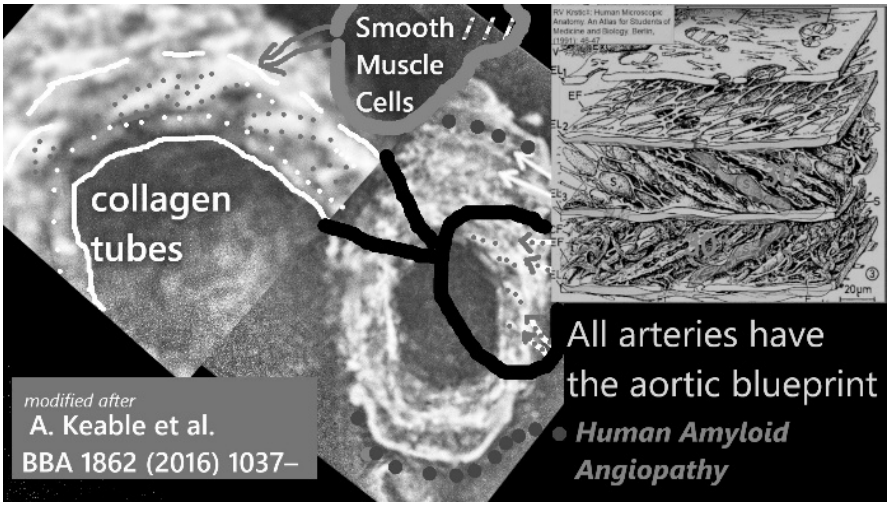

Figure 1. The „pervasive aortic blueprint" of the CIMURAF-model allows to identify probable obliquely running vascular smooth muscle cells from transverse histological cuts of cerebral arteries attained by Human Cerebral Amyloid Angiopathy aggregating Aβ flowing between the basement membrane wrappings of the VSMCs (Keable et al. 2016). RUQ: Krstić 1984

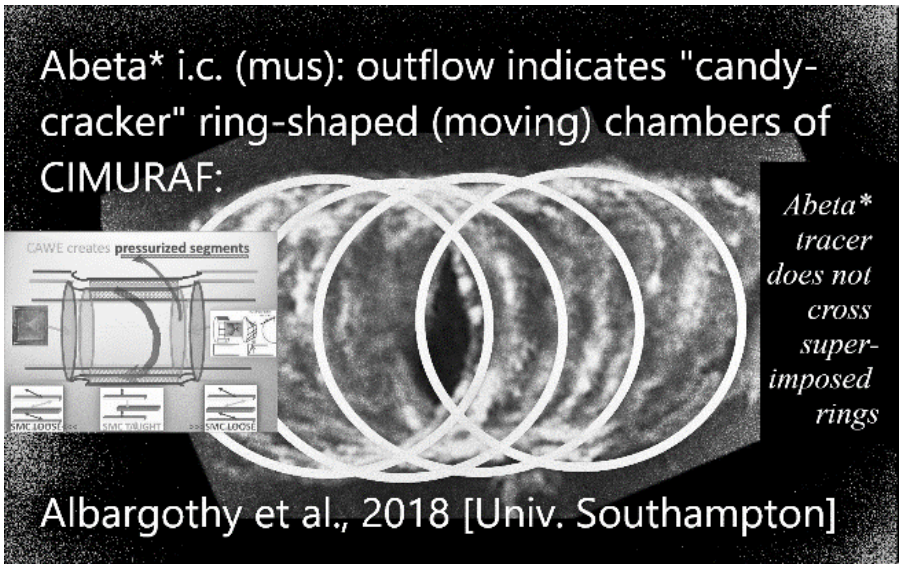

Figure 2. The image from the leading intramural IPAD-model (Albargothy et al. 2018; Fig 1e; CCBY) "shows Aβ tracer (…) within the wall of the artery in a spiral or ladder-type distribution" - which by superimposing white rings seems more compatible with *separate rings of tracer* as CIMURAF would predict them to be created by sliding twisted segments (see insert)

THE PERICALLOSAL ARTERY & INTRAMURAL ARTERIAL OUTFLOW

The pCallA-complex next to (peri-)callosal regions supplies the anterior 2/3 of the medial and superomedial hemispherical surfaces. The corpus callosum (CCALL) in front is supplied by the pCallA, alias segments A2 to A5 of the anterior cerebral artery (ACA). While in 1/3 the pCallA ends on the precuneus, in nearly 2/3 the frontal supply is continuous with branches from the posterior cerebral artery (PCA) via the outer perisplenial circle (and an inner plexus cooling the fibres) fed in 88% by the occipital medial artery (Blaauw & Meiners 2020).

The callosal drainage occurs via the internal cerebral veins (Kahilogullari et al. 2008, Wolfram-Gabel & Maillot 1992). The centerfold pCallA's networks branch out laterally (Kakou et al. 2000) providing a topological alternative to psycho-mathematics.

Subregions like the subgenual one of the anterior cingulate cortex (sgACC) (Touroutoglou & Dickerson, 2019) constitute driving hubs of functional macroconnectivity (FC). The posterior CC (pCC) provides internally-directed cognition within the DMN, while its dorsal part tunes the brain´s metastability and focus (Leech & Sharp 2014).

The pCallA supplies the inter-hemispheric linker CCALL (Roland et al. 2017) and the gyrus cinguli related to effort and need (Heilbronner & Hayden 2016) averaging rewards (Aberg et al. 2020). In SCZ the WM of the CCALL shows early and lasting (cognition-hampering; Ohoshi et al. 2019) micro- and only late, posterior macro-losses (Madigand et al. 2019) - as if by an early (maybe arterial) hit followed by progression (Thompson et al. 2009).

The spectrum towards schizophrenia

A cortical "spread of psychosis" emerges from longitudinal imaging of schizophrenia (SCZ; Velakoulis et al. 2006, Bellanis et al. 2010, Pantelis et al. 2003, 2005, Dietsche et al. 2017) through at times revealing sagittally shifted windows of neuro-progression (Lewandowski et al. 2020).

Besides cortical processes, such of the striatum are key to prodromata and SCZ (Hubl et al. 2017, McCutcheon et al. 2019), while still adding the L-sided hyperperfusion of sensorimotor cortex to that of the putamen (Foucher et al. 2018).

Not parkinsonism or dyskinesia, but other neuromotor anomalies like (maybe only arterially explainable) "soft signs" (NSS) are prevalent in SCZ and in homogenous proportion among patient's relatives (sparing complex fine movements; Schäppi et al. 2018) – whilst predicting grey matter-losses (GM) in FEP. These unexplained symptoms fluctuate independently (Bachmann & Schröder 2018). NSS do not correlate with cortico-subcortical disbalance (Schröder et al. 1998), but with schizotypal traits (Galindo et al. 2016), whereby these manifest clearer cingulate than subcortical changes (Derome et al. 2020a,b).

Periodic catatonia

In up to 12% of SCZ the WKL-classification (Foucher et al. 2020) distinguishes the in 27% familial periodic catatonia (perCAT) as a notably qualitatively disordered motricity with initially insufficient compromise of other systems. PerCAT shows a (in 5/6 also affective) bipolar dimensional, recurrent-progressive course (Cercle d`excellence 2020). Among segregated cortico-subcortico-thalamo-cortical circuits (CSTCs) perCat seems to

spread from those to the lateral (LMA) and supplementary (SMA; Walther et al. 2017) motor areas (Haber & Calzavara 2008), to the one to ACC (destabilizing effort), and earlier to that to OFC (destabilizing mood), yet potential deficits of the caudal cingulate motor area of cingulate cortex (CgCx) match its core kinetic deviations including mutism.

After averaging fMRT-signals during 6 tasks the remnants mirrored the, possibly vascular, "trait" (Foucher et al. 2018) as a high-flow-spot on the mid-medial CgCx with hyperperfusions on the L side in the same coronal segment: of the precentral gyrus, posterior Broca, and supplementary motor area (SMA) (Foucher et al. 2020). The Bernese perCat-similar patients replicated this with a slightly more anterior high-flow-spot plus again an orthogonal catatonia-correlated hyperperfusion of both SMA and L ventral premotor focus, "compensating" (Walther et al. 2017) for a disconnected 1st CSTC through ACC or rather 5th through SMA (Numbering backwards on Figure 3, Alexander et al. 1986). These high-flow-spots could result from "clashing" inversions of normally divergent CIMURAFs: both to the mid-callosum (instead towards the front and rear ends).

Patients with perCAT are relieved by a robotorized rTMS (Zorn et al. 2012) tracing an individual path (probably) along the MCA-branches (communicating over the top with those of the pCallA; Ugur 2005). On fMRT/PET-overlap images during Alzheimer's hallucinations less perfusion and tissue of the R anterior insula (as from a distal MCA-superior division disorder) again correlate with the L mid-cingulate gyrus (Blanc et al. 2014).

The intriguing link between enuresis and severe mental disorder

Cerebral micturition control (Griffiths 2015) refers to storage and voiding (Harvie et al. 2019), and the thalamus, active in both, relays bladder sensations from the brainstem's PAG towards the prefrontal decider to void (Arya & Weissbart 2017): in childhood enuresis this path is disconnected on the L. Equally the L medial orbital superior frontal gyrus, in front of the knee of the CCALL – a hub amidst all other players like the CgCx above the "knee" - was less active (Zhu et al. 2019).

The rate of (strongly hereditary) childhood enuresis in SCZ (as noted since Kraepelin) is twice that in siblings and thrice the basic prevalence (21% vs. 11% vs. 7%), while implicating an (early spreaded) prolongation of prodromata by 2 years, and worse cognition. While cognition suffered only in the fluency tests, late micturition control correlated *per se* with less GM. In SCZ this was most significant at a spot on the R superior frontal gyrus. In controls likely GM scars persist and a strong urge comes with a broad activation of the PFC manifesting a zone of GM loss again from the medial PFC down to the sgACC (Hyde et al. 2008). Late onset of enuresis in SCZ (36%) has been twice that in BPAD and predicted negative symptoms (Hollis 2003).

All these areas (besides some lesser temporal and occipital ones) could be reached by a toxic intrusion along the pCallA and to the left MCA (since it supplies the routes of bladder interoception signals through ACC and insula). This unique developmental and also more actual and variegate "intoxication" could stem from adventitially intruding MCs, if they would ascend within the carotid sheath from the crossing of the lymphatic thoracic duct with the aortic arch – assuming that ascending lymphatics at that level would open up to expel the fluid column in order to hasten transport of epitopes to lymph nodes from some bladder or nail infection. Acute episodes of SCZ in non-adults do present with 20% UTIs versus 13% in MDD (e. g. Carson et al. 2017), and bladder infections can be latent (Gilbert et al. 2019).

AN IMMUNO-LYMPHO-ARTERIAL FRAMEWORK OF CONCATENATED HYPOTHESES

The overall framework used evolves as follows: **A.** The perfusion patterns deranged in psychoses, as referred to the sagittal supply of the brain branching off laterally over the cortex from the pericallosal artery (pCallA), **B.** are put into relation with the intramural reverse CIMURAF maximally generated within the straight pCallA. **C.** The pseudo-peristaltic neurovascular steering by the pterygo-palatine ganglion (PPG) instructs, **D.** the CIMURAF to wring out - by "candy-cracker twists" - interstitial fluid towards arterio-adventitial lymph vessels (Droszs 2008, Xu 2007, Bocharov 1968), while the meningo-lymphatics reach the same carotid sheath (jugular) deep cervical lymph nodes along veins (Aspelund et al. 2015, Louveau et al. 2018, Pal et al. 2020, Absinta 2017). **E.** A putative adventitial perivascular flow parallel to CIMURAF (by open radial shutters of such sliding wrung segments) would trigger known counter-flow movements of immunocytes like MCs (by flushing all but rear autocrine signals; Treviranus 2019b,p). **F.** Long-lived MCs - after chemico-physical programming (Csaba 2014) at bodily barriers as to "destination & destiny" (6.2, Treviranus 2017b) – reach the brain via lympho-adventitio-arterial routes. **G.** The MCs` "orchestration" of also cerebral agendas for metabolic, morphological, "Freudian" sexual, reproductive, stress-, and defense responses is often hidden - as in acupuncture (Jung et al. 2017). **H.** MCs modulate the complex double-layer-dural immune responses (Coles et al. 2017) and move along arteries, lymphatics, and calvarial channels (Cai et al. 2019). **I.** MCs invade the thalamus balancing sleep and the «cognitive complexity divide» (Treviranus 2017, 2018, Morrow & Fitzpatrick 2017). **J.** MCs irritate the cortical surfaces escalating "epileptoïd" symptoms towards psychosis (Blumer et al. 2004, Bob et al. 2006) and, **K.** after descending via the arachnoid trabeculae (Engelhardt & Marchetti 2020). **L.** by their proteases (Douahier et al. 2014) attack

oligodendrocytes (ODCs) and probably also neurons coated with complement-4 (C4), as reflected by genetics (Schizophrenia WG, 2014). **M.** MCs as first defendants against unknown germs at barriers and nail folds (Ito et al. 2015) are targeted by their "subversions".

Mast cells: the reason for the might of clozapine?

While Clozapine (CLZ) is uniquely effective at least in early SCZ and perCAT (Lin et al. 2016), e. g. by dampening thalamo-cortical glutamatergic transmission (Fukuyama et al. 2019), therapeutic consumers are threatened by unwanted side-effects mostly from its metabolites (which can be modulated e.g. by fluvoxamine; Polcwiartek & Nielsen 2016, Lu et al. 2018): weight gain, enuresis and obstipation are common (Every-Palmer et al. 2017, Luche & Francois 2020), and myocarditis or hematological can be rapidly lethal (Leung et al. 2019, De Berardis et al. 2018). Unfortunately many attempts to work around these costs through variant molecules have been unfruitful, while its receptor-profile and short stay on the D2-receptor are shared by various competitors (Nucifora et al. 2017). CLZ via the clathrin-mediated endocytosis prevents MC-activation via IL-37 and MrgX2 (Murakami et al. 2018) - and cell entry by COVID-19 - and inhibits the focal adhesion protein paxillin mediating MCs`cytoskeleton responses

Table 1. Subversive (self-serving) manipulations of mast cells by pathogens

Pathogen	Mechanism	Source (et al.)
Dengue virus	IgG-enhanced uptake	Rathore & St John 2020
COVID-19 ?	IL-1-excess, HA, proteases	Kritas 2020
COVID-19 ?	? Cytokine storm	Kunder 2011
COVID-19 ?	Pulmonary endothelitis	Theoharides 2020
COVID-19 ?	MC sustain B-cell function	Palm 2016
COVID-19 – NO RISK?	MCAS, mastocytosis	Valent 2020
MIS-C/Takotsubo	MC-Etosis (Treviranus 2019)	Riollano-Crus 2020
HIV-1	CXCR4, CCR5, function, death	Taub 2004
HIV-1	Colonize MCs and switch to Tc	Jiang 2015
HHV-8 Kaposi sarcoma	Angiogenic, MC-IgE-reaction	Ayers 2018, Byakwaga 2020
Cytomegalovirus (CMV)	TRAIL-triggers apoptosis	Smith 2013
Listeria monocytogenes	Broad changes	Jobbings 2013
Bartonella spp., Brucella spp.	Genome manipulation, LPS anti TRL4	Ben-Tekaya 2013
Bartonella quintana	LPS: Protects VSMCs from MC via Toll-like receptors	den Dekker 2012 Matera 2008
Salmonella typhimurium	SptP suppresses MCs	Choi 2013
Staphylococcus aureus	Own uptake into MC	Abel 2011
Staphylococcus aureus	Invasion via VEGF , release SP, IL-33	Johnzon 2016
Group B Staphylococcus	Provoked degranulation	Gendrin 2015
Chlamydia pneumoniae	In Mφs metabolic switch	Itoh 2014
Chlamydia pneumoniae	MCs attack beta-cells	Rodriguez 2015
Chlamydia pneumoniae	Metabolic switches	Rodriguez 2015
Mycobacterium tuberc.	Tbc stops extracellular traps	Campillo-Navarro 2018
Mycobacterium tuberc.	Tbc enters MC	Muñoz 2009
Mycobacterium tuberc.	T7S protein, survival in Mφs	Jin 2019
Mycobacterium marinum	Colonizes MCs	Siad 2016
Toxoplasma gondii	Block IgE-response via PLCγ	Smith 2013
Toxoplasma gondii	Adenosine production	Mahamed 2012
Candida albicans	Temporal MC response	Lopes 2015
Candida albicans	Protective uptake into MC	Trevisan 2014
Toxocara canis	Increase of MC number	Carlos 2011
Parasitic worms	ES-62 targets PKC	Bell 2015

MCs are the rapid initial opponents of most microbes – e. g. via extracellular traps (Möllerherm et al. 2016); whereafter – by e.g. potentiating IL-33 (Zhou et al. 2020) – they orchestrate adaptive immune responses (Toniato et al. 2017) not only against worms (Shimokawa et al. 2017) like the top SCZ-associated Toxocara canis (Arias et al. 2012, Carlos et al. 2011), as antigen presenters and activators of distant lymph-nodes via cytokine-pellets (Kunder 2009).
Thus MCs qualify as prime targets of "subversion" by microbes, which includes ligands of MC receptors, intrusive molecules, colonization and metabolic upset of MCs, and changes to their niches

to IgE-signaling (Han et al. 2015). CLZ is indeed unique among antipsychotics for inhibiting MC-degranulation (Seol et al. 2004), but also dopaminergic modulation of innate immunity (Mackie et al. 2018). The response of SCZ to CLZ follows one of the few polymorphisms: that of protein G-protein subunit-beta 3 (GNB3; Samanaite et al. 2020), which again is involved in various MC-related pathologies and in thermogenesis (Özdemir et al. 2017, Zhang et al. 2019).

In lymphocytes of persons with SCZ epigenetic DNA-methylations (CpG) seem to be both anomalous in certain segments (Teroganova et al. 2016) and specifically changed by CLZ: a) particularly at genes involved in „cell substrate -" and "cell matrix-adhesion" allowing for integrin-centered migration along routes, while such related b) to CREB-binding protein (CREBBP) uniquely (among 29.134 CpG!) seemed to halve symptoms linearly after CLZ (Kinoshita et al. 2017). Only a weak, yet rare support resulted for CREBB from a parallel investigation and for GNB3 (and some transmitter-related genes) from a meta-analysis (Gillespie 2019).

Among countless processes (Pardo et al. 2017) CREBBP constrains B-cell response and MHC-class-II-activation (Jiang et al. 2017). Importantly, since it acetylates the oncogen K-ras (Dixon et al. 2016), it likely inhibits the key MC-activating c-kit-receptor pathways (Khalaf et al. 2007). While kit supports the adhesion and survival of MCs, Notch only supports adhesion (Murata et al. 2014, 2019), the latter being low in SCZ and BPAD (Hoseth et al. 2018).

Both weak effects on CREBB and GBN3 – awaiting replications – also match requirements of the "Destination & Destiny"-hypothesis (Treviranus 2013, 2019), which implies that MCs are programmed to advance along arteries (like kanban-tranfer charts along rail-switches) through serial decisions at bifurcations according to a set of adherence molecules "imprinted" at the start to match differential matrix partner molecules leading to cerebral destinations.

Since MCs are likely to modulate CSTCs not only in the 1st medial loop to ACC (Treviranus 2017, 2018), an analogous action of MCs on the 2nd medial loop to the dorsolateral PFC (dlPFC; a functional area subserving 4D-modeling, i.e. Thought) as a possible strong contributor to SCZ could explain the effects of CLZ via MC-stabilization, since it selectively reactivates dlPFC (Samanaite et al. 2020).

Mast cells: How great agents become subverted by microbes?

MCs like macrophages (Féger et al. 2002, Conti et al. 2019) become subversively targeted by pathogens (Table 1) and then - also via the lymphatics (Tsunoda 2017) - do derange the brain (Girolamo et al. 2017, Severance & Yolken 2020, Radua et al. 2018). In Covid-19 persons with already subverted MCs could be most at risk, and a MC-stabilizer is a candidate drug (Theoharides 2020).

CONCLUSIONS AND OUTLOOK

The above imaginable mechanistic steps draw some interactive support and thus are hoped to deploy some traction towards more real-biological psychosis research.

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