

## **THE GOBLETS (MAJOR DEPRESSIVE DISORDER)**

Our thoughts appear to burn with a dry heat, a seemingly slow but progressive eradication of previous states of existence and frames of mind, as the seat of each individual personality is decidedly aflame, the part commonly referred to as the frontal lobes, to elaborate what is presenting itself is chronic inflammation giving way to an all-consuming darkening of mood associated with cognitive difficulties and murky recall of events, at least those positive in nature, all when it is of the uttermost importance to remember who we are and how we got here, to this point, to a life marked by chronic eradication, and how to get out with guns blazing. And yes—we are totally serious, the push back needs to be a bitch, and the aforementioned inflammation simmers in what is referred to as the occipital lobe, right angular gyrus, parahippocampal gyrus, and lateral prefrontal cortex, and as such there is a rise in the concentrations of proinflammatory cytokines and glucocorticoids and a hyperactivity of the hypothalamic-pituitary-adrenal axis in response to various threats to homeostasis, so there is no stability here, there, anywhere, how can there be when these losses keep mounting, and the neuroendocrine and immune system are rendered lax, there are thyroid abnormalities present with elevated T4 levels, low T3, elevated rT3, a blunted TSH response to TRH, positive antithyroid antibodies, and an elevated CFS TRH concentration resulting in what feels like another loss in the midst of multiple devastations, the loss of one's energy, as energy metabolism is the most recognized target of thyroid hormone action, and furthermore, there are microbial signatures of dysbiosis present in the intestinal microbiome with an elevated risk presented by bacteria *Morganella* and *Klebsiella*, the ones causing infections in hospital patients, and there it is, although this does not explain it, as none of these bodily processes are really it, the *it* we are looking for, the *why* we are losing ourselves, in distress and gloom, all just symptoms here, and naming them doesn't lead us much further neither in terms of actual causality nor responsibility, responsibility as inducers of inflammation are surrounding us in our daily lives, novelties brought on by industrial production since the Second World War, and we are in- and enflamed going up in flames, engulfed in what our lives have become whilst tormented by what they otherwise could have been, and we are desperately and vehemently searching. So we go back, to find the someone or something responsible, at least another part of the picture, and there's the epigenetic changes of our ancestors, the changes in their miRNA expression, covalent histone modifications, and methylation of DNA, stemming from the bioaccumulation of mercury, lead, and arsenic present in fish and shellfish, mussels and other bivalves, the most widely accepted bioindicators of chemical pollution in coastal and estuarine waters since around 1960, and these compounds bring forth losses at a rapid pace, another being the loss of traditions of coastal populations and the identity and recognition of oneself that comes with it. Ingesting industrial waste and deep pockets, the soft tissues of shellfish integrate with our own.

We count to 1. Then we count some more.

## **THE GOBLETS (GENERALISED ANXIETY DISORDER)**

Fear is a basic biological process, and we are scared of the fire, we are. We are scared of ourselves, us, of who and what we are in the face of adversity, as we are in the midst of adversity, and the amygdala, heavily connected with cortical regions including the limbic cortex, is working to formulate and retrieve emotional and fear-related images with input from the hippocampus, thalamus, and hypothalamus, tumultuous projections of the present, past, and future, all run by fear, and it is all coming and it already happen and it is here. And alas, we are here, us, in the face of stressor exposure, with a downpour of bodily processes not to be consciously controlled, and the issue was already negative experiences that were unpredictable and out of our control, and what else is new, certainly not negative feedback loops, and it's called emotional hyperreactivity with amygdala hyperresponsivity and reduced tonic parasympathetic activity (i.e., reduced heart rate variability) along with greater tonic sympathetic activity levels, with implications for higher resting levels of emotional arousal and greater sensitivity to affective shifts from a neutral or relaxed state to one that is negative, and there we are, in adversity. To elaborate, it is chronic inflammation leading to, in a range of processes, cognitive difficulties including information processing, all in the brain, on adversity, and our blood harbours serotonin, brain-derived serum neurotrophic factor, cortisol and microRNA, to continue the saliva in our mouths holds the markers of cortisol, lysozyme, and alpha-amylase, and how about the microbial signatures of dysbiosis in the intestinal microbiome with an overgrowth of bacteria such as *Escherichia-Shigella*, *Fusobacterium* and *Ruminococcus gnavus* in our intestines, and even asleep, the stress-responsive neural systems of the nervous system are on high alert, not allowing restorative sleep, signalling that it is not safe to relax, which it cannot be, because something is burning, or rather, it is *all* burning, so we step back, and there's the epigenetic changes of the forefathers/mothers, changes in miRNA expression, covalent histone modifications, and methylation of DNA, and then we are one step closer, perhaps, as fear, it turns out, can leave permanent epigenetic marks on DNA, marks to be passed down to offspring, as the experiences of a parent, before even conceiving offspring, markedly influence both structure and function in the nervous system of subsequent generations, and there are so many events to choose from, lifetimes of systemic violence and aggression and hierarchical thinking and what not. Acts of war, poverty, disease, and fire, and why we call it a disorder, this recurring anxious state, and not just the order of things, as they are and were, is sometimes hard to know, but again, who knows with this inflamed brain, and DSM-5<sup>1</sup> and its European equivalent probably know better.

We count to 2. Then we count some more.

### ***THE GOBLETS (POST-TRAUMATIC STRESS DISORDER)***

Something happened in the past, that plays in the present, and we were also happening in the past, we were there, and something happen to us and now it is present. It recurs, the event, it flares up and bristles, and as such there is something wrong with time, it has come

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<sup>1</sup> The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* is the taxonomic and diagnostic tool published by the American Psychiatric Association (APA). In the United States, the DSM serves as the principal authority for psychiatric diagnoses.

undone in a myriad of spatial and material expressions, it turns out time may never have been chronological after all, but was threaded all the way through with ghostly echoes, and by now what happened to us seems a burnt temporality, even, as it flares and bristles with airborne cinders, and our neurons keep firing, firing, firing, in time, but again, what time, they are confounded and confused by the past not being a pure past staying in the past, and we are too. In the midst of this our bones and muscles start to simmer with a dry fervent heat, our bones and muscles, they seem to burn with an inner fire in a slow but progressive process, it turns out it is not just time that is unhinged, it is the material too, to elaborate it is chronic inflammation and cognitive difficulties including memory processing presenting in our brains, there is an endocrine dysfunction in the blood and the immune system, and microbial signatures of dysbiosis in the intestinal microbiome within the intestines of our guts, and furthermore, even asleep, the stress-responsive neural systems in the nervous system are on high alert, not allowing restorative sleep, signalling that it is not safe to relax, which it cannot be, because something is burning, or rather, it is *all* burning, so we step back, and even though we would like to say that time itself is the trauma, as it has us drooping to the ground, quite literally, we know our bodies will, and death has always awaited us, and it is known and known, but there is something else, more specific, as bits and pieces are taken from us throughout, pieces of our health and clarity, of time with our families, and the systems we live under, political and socioeconomic, are made for someone else's gain, and most of these come entangled with decisions made affecting our bodies, life-threatening events, war, assault, abuse and natural disasters, and in 1986 Chernobyl was the site of an uncontrolled nuclear explosion as the No. 4 reactor in the Chernobyl Nuclear Power Plant blew, to this day the health effects of this explosion on the general population are considered 'uncertain', as the entangled effects defy measurement, at least our sort, and there it is, the traumatic event, still recurring, flaring and bristling.

We count to 3. Then we count some more.

### ***THE GOBLETS (MYALGIC ENCEPHALOMYELITIS/CHRONIC FATIGUE SYNDROME)***

Bones and muscles appear to burn with a dry fervent heat, they seem to burn with an inner fire in a slow but progressive process, aka the heat is on, etc., and so forth. And in the middle of this, amongst a range of other fatigue(d) symptoms, a difficulty or slowness in the eye whilst focusing on objects is detected, especially those close up and kept close for a reason. Sometimes objects matter as they too, populate and help build our lives, and, as such, the current tiredness in reaching for them, for anything, is insurmountable. Focus and

reach, suddenly precarious things of the past, or at least waning, as we try hard to hold on to things, objects, relationships, what matters most, and more. So much slips when falling to the ground and currently the ground is not the literal ground, but somewhere horizontal to spend large amounts of time as nights and days turn biochemical dysfunction at the skeletal muscular level with more to go. To elaborate, it is chronic inflammation and cognitive difficulties including memory processing in the brain, several biomarkers of inflammation and sustained immune responses in the blood, microbial signatures of dysbiosis in the intestinal microbiome, and even asleep, the stress-responsive neural systems are on high alert, not allowing restorative sleep, continuously signalling that it is not safe to relax, which we of course know it cannot be, because something is burning, or rather, it is *all* burning, so we step back, we try for something like a semblance of causality and responsibility, and there it is, the epigenetic changes of our forefathers/mothers, changes in miRNA expression, covalent histone modifications, and methylation of DNA, and we are a step closer, towards one piece of the puzzle or whatnot, and how about organochlorine pesticides, their exposure typically through inhalation or ingestion, the mouth, the lungs, the stomach, but also through water, foodstuffs, air, dermal exposure, and/or vertical transmission from mothers to offspring during pregnancy and lactation, and it is enough to bring it on, the bleak realisation of other's agendas and what they can do, and, to continue on, many pesticide company controversies seem to have been wiped from google search, although a number of studies still linger on PubMed, it's not all scrubbed, still something there, and how about chlorinated hydrocarbons used extensively from the 1940s and throughout the 1960s in agriculture and mosquito control, and they were alive then, one's relatives, even parents, and they had bare hands/lungs/open mouths.

We count to 4. Then we count some more.

### ***THE GOBLETS (OBSESSIVE-COMPULSIVE DISORDER)***

We inhale and an interference occurs: a minuscule piece is drawn in with the air, the something or someone starts its passage within the body's cavities and there seems to be no option here for refusal or rebuke, its molecules vibrate in their given receptors and start a downpour of bodily processes, none of which we consciously control. We feel dirty. And with a jolt, we realise there are all sorts of these "others" riding the streams of our circulatory system, conjugating in our intestines, continuously producing and secreting hormones in the endocrine system, and what not, and action is needed. And these thoughts of contamination are intrusive and recurring and we suddenly realise they might not even be ours, really, somehow we are *being* thought, and there are fires everywhere, such a dry heat, and it

seems our inflamed circuits are doing the thinking, they are the current hotspots, to elaborate it is chronic inflammation within the corticostriatal circuitry of OCD in the orbitofrontal cortex (OFC), ventromedial prefrontal cortex (vmPFC), dorsal anterior cingulate cortex (dACC) and striatum, abnormal activity in the brain structure and function related to cognitive deficits in tasks of non-verbal memory, response inhibition, interference control, cognitive flexibility, and visuospatial working memory all within the brain, and a dysregulation of our immune function based on alterations in innate and adaptive immune-related parameters such as proinflammatory cytokine levels, antineural antibodies, or hypothalamus-pituitary adrenal axis dysregulation in the immune system, to continue our blood also exhibits peripheral serotonergic abnormalities and 5-HT<sub>2A</sub> receptor-binding characteristics, all shipped around by veins and arteries, and how about microbiome lower species richness/evenness (α-diversity, Inverse Simpson) and lower relative abundance of the three butyrate producing genera *Oscillospira*, *Odoribacter*, and *Anaerostipes* within the intestines, and furthermore, even asleep, the stress-responsive neural systems are on high alert within the nervous system, not allowing restorative sleep, signalling that it is not safe to relax, which it cannot be, because something is burning, or rather, it is *all* burning, so we step back, as we do, looking for the responsible part or parties, or any kind of multifactorial causality, because we don't accept genetic determinism and full responsibility of the individual in mental disorders, they don't get off that easy, those that capitalize on us, how can they, to continue we know the obsessions and compulsions associated with OCD are related to sexuality, aggression, and contamination, and it's the latter that is our struggle, and we understand thoughts of bodily contamination have recurred well beyond Louis Pasteur's germ theory, but we still feel his theory especially contributed to an ontology that retains us as victims, prey in a hostile world living as a separate species in isolation from "others", so let's just start there, with this cultural component, as the continued aetiology takes us, amongst other places, to living in polluted places, especially early on in life, breathing in air containing, amongst other substances, polycyclic organic hydrocarbons, organophosphate flame-retardants, phthalates, benzothiazoles, musk compounds, plasticisers, lead, nickel, cadmium, arsenic, and magnetite, and there is an overlap here with a risk of neurodevelopmental disorders with an obsessive-compulsive disorder comorbidity.

We count to 5. Then we count some more.

### ***THE GOBLETS (DEMENTIA)***

The us that is we appear to burn with a dry heat, in a slow but steady erasure of who and what we are—were—past tense now coming in as our minds become progressively inflamed, and we were something important to ourselves, our memories and impressions mattered, to elaborate it is chronic inflammation and advancing cognitive difficulties including remembering or recall, all when it is of the uttermost importance to remember how we started losing, and why. The current overwhelm include the occipital lobe, right angular gyrus, parahippocampal gyrus and lateral prefrontal cortex, to continue there are abnormalities in the brain's cholinergic, noradrenergic, serotonergic, and dopaminergic neurotransmitters, the cortical and neuronal systems, the cells of these systems filling up with neurofibrillary tangles, and it is all tangled, the us that is gradually made into something else: cut and paste, rearrange, and it actually is that brutal, and altered gut microbes are suggested as possible contributors to amyloid plaques, as proteins produced by intestinal

bacteria modify the interaction between the immune and nervous system, and we are already losing our language skills in the brain's left hemisphere, so why not here too, in our literal centre, losing our ability to interact, long gone, vascular dysfunctions cause altered brain blood flow and pressure, and that can't be good either, pressure, and how about disturbed circadian rhythms creating sleep disturbances and sleeplessness, although who can sleep in the midst of a fire anyway, because something is burning, or rather, it is *all* burning, both inside and outside the body (if we are still discerning difference this way), and it is a cliché to say but still true though, so we go back, this time to the altered and dysregulated gut microbiome, there's even an altered oral flora and the bloodstream is a pathway, up to no good, and early childhood exposure to broad scale antibiotics is correlated with several gastrointestinal, immunologic, and neurocognitive conditions, and antibiotics as disruptors of gut microbiota can promote the hallmarks of dementia, and there we are gut dysbiosis with a larger population of enterotype III bacteria, and although causality is a slippery slope, it seems our use of broad scale antibiotics is slithery too, the actual drawbacks to their use ranging from the selection for and spread of resistance across multiple bacterial species, to the aforementioned detrimental effect on the host microbiome, the host, i.e. us.

We count to 6. Then we count some more.

### ***THE GOBLETS (INFLAMMATION-ASSOCIATED ANOREXIA)***

Inflamed, our brains are running hot, or rather, a specific neural circuit is, it is running hot in response to a peripheral administration of pro-inflammatory cytokines, such as interleukin-1B or stimulants such as lipopolysaccharide (LPS), and the circuit's neurons light up simultaneously with the whitish fiery glow of a pathway overload, fireworks leading to reduced meal frequency whilst IL-1B induces an aversion to novel foods or sucrose solutions altogether, and then what to do, there goes our (food) culture and our sucrose-based self-medicating, what got us through Monday to Friday, to continue even the consumption of sucrose is rendered less pleasurable (anhedonia), and then what to do and where to go in search of an activation of the brain's reward system, the mesolimbic dopamine, as we are in clear need, and inflammatory heat is not it, comfort nor comfortable, not by a long shot. It initially caught us by surprise that cytokines are capable of acting on our central nervous systems, as we have been taught that the blood-brain barrier prevents blood-borne pro-inflammatory factors and immune cells access to our brains, but it turns out the immunocompetent cells of our nervous systems are capable of detecting pathogen-

associated molecular patterns and of producing pro-inflammatory factors in response to injury and inflammatory challenges, so we shouldn't be surprised that a barrier really is no barrier, even between the blood and the brain, nothing is separate, really, especially when it comes to our bodies, and there is the feeling that we should have known better, and perhaps now we do, it seems things are not what they seemed and that the knowledge system we based everything on has cost us, or maybe it was the sucrose self-medicating costing, or both, but more so what we were never taught, the entanglement and interaction of everything down to its quantum core, so in the midst of this firework of rejection inflamed brains refuse sustenance whilst the world is burning, an inflammatory result all around, although who can eat in the midst of a fire anyway, as it is *all* burning, both inside and outside the body, and it is a cliché to say but still true though, so we go back, we look for environmental factors and an inkling of responsibility or causality, and Dimethylformamide (DMF) is an organic solvent produced in large quantities throughout the world, a colourless liquid used in the chemical industry as a solvent, an intermediate, and an additive, and is readily absorbed following oral, dermal, or inhalation exposure, with air in the vicinity of point sources appears to be the greatest source of exposure of the general population to DMF, the petrochemical sector was responsible for 84% of the reported atmospheric releases, releases from the pharmaceutical industry accounted for 87% of total releases to water as it is used as a solvent in peptide coupling for pharmaceuticals, with more than 40 approved peptide-based drugs in use today, once absorbed in the body it is uniformly distributed and metabolized primarily in the liver with adverse effects, other associated symptoms include nausea, abdominal pain, and anorexia.

We count to 7. Then we count some more.