



### **Research Article**

# Mindset kinetics and some depression status: A new quantitative model under biochemical - toxicology approach?

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**Keywords:** Depression; Mindset kinetics; Toxicology; Theory of constraints; Mindfulness; Neuroscience; Biochemistry



### **Abstract**

**Depression:** According Pubmed Health: Depression is a state of low mood and aversion to activity that can affect a person's thoughts, behavior, feelings and sense of well-being (moderate or severe).

Can we consider some depression status due to high amount of some stressant stimulus? Or continuous stress in a limited (or long) period? How can react mindset and brain in management an high amount of negative stressing thinking? Observing some relevant literature also mindset kinetics must be considered to better classify this kind of disorder under a specific endogenous –exogenous biochemical-toxicological aspect.

Concept like Kinetics, reaction velocity limits, saturation of the systems, residual buffer properties are currently used in biochemistry and related discipline.

This concepts can be applied also in some depression condition to better explain some phenomena?

## Introduction

Depression is one of the most prevalent and debilitating of the neuro- psychiatric disorders. According many Studies cognitive therapy is as efficacious as antidepressant medications at treating depression, and it seems to reduce the risk of relapse even after its discontinuation. Cognitive-behavioral therapy and antidepressant drugs probably engage some similar neural mechanisms, as well as mechanisms that are distinctive to each. A better specification and knowledge and of these mechanisms might to be used to guide therapy selection and to improve clinical outcomes. Today great enphasys concern the neuro transmitter's status and its implication as main pharmacological strategy.

But are we sure that is the only point of view to consider in this kind of disorder?

Starting from the effective efficacy level of actual pharmacological therapy and the number of relapses in some patients is relevant to observe this disorder under a new light (the same also efficacy of some non-pharmacological therapy).

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This work is produced starting from a medicinal chemistry and biochemistry approach (kinetics) related to some endogenous or exogenous noxa that can produce unbalances of brain-mind. Every biological system present a determinate limit and also brain-mind systems: an over stimulation of stressant stimulous for long time or in acute can produce great effect in more receptive subject. Single individual resilience ability and residual biochemical buffer systems can help in balance the system. Theory of depression consider in example etiopathogenetic (genetic, biochemistry), psycoanalitic factors and other that contribute to the global status of a subject.

Depression conditions can be compared to a psychological manifestation of the spirit which although has been influenced by hormonal level and many other biological factors however has really only relationship with hormones or neurotransmitters? Are this the only factors involved?

In example drinking coffee you would become stressed and angry but anger is a product of someone's provoking you, it has nothing to do with coffee for caffeine. Even if this substatia can enhance global reactivity.

Yes losing hope is slowing down someone's daily activity but this is only related to the serotonin level?

In other example: pain is related to the endorphin level but pain in example product of the deposit of crystals in the joints, could be a pressure on trigeminal or sciatic nerve: therefore pain is not a product of endorphin level itself but a secondary effect of Pathologic moves. Therefore manipulating serotonin and messing up with so many nervous circuits must cause new disorder which we call them side effects (In ex serotoninergic syndrome).

Neurotransmitter manipulation like in anxiety and antipsychotic and antidepressant drugs have been introduced after 70s, and the psychomedical community and giant Pharma and guaranteeing their income is trying to pathologize day after day some in our opinion natural behavioral process of the spirit. So Tomorrow happiness could be considered as disorder? And as well as yesterday too much energy of children was considered not physiologic? Today some prestigious healthcare institution is talking about also a pregnancy mood disorder? It is ridiculous. Why the medical community is trying to pathologize everything in next time?

Is universally known that many psycologic or behavior discipline can help unman being in correctly manage stressant stimulus (mindfulness, yoga and many other discipline). In all this discipline we observe in example great inside concentration activity excluding external stressant stimulus. So depression can be considered more related to quality of thinking or to the amount of negative thinking (and related time involved)?

Why the time can help some people to be more resilient after negative stressant stimulus?

Observing other scientific discipline in example the light properties in physics discipline: it can be considered under double condition: As ondulatory properties or as particle (and every properties verified esperimentally).

(In example see the quantum theory in chemical physics): 2 different point of view of the same phenomena (Figures 1,2).

So can we think some mindset-brain process under multiple aspect phenomena?

Thinking but also amount of thinking and the global quality of thinking (positive or not) is a relevant factor to better understand mindset status. And is very interesting



observe if the brain show limits to manage this stressant conditions? The kinetics of this phenomena can help us to better clear some psycologic- psychiatric, neurlogic condition? A global saturation of the system, in example due by high stimulous as today we see in modern world, can contribute to the efficiency of the systems? And what can be the effect in a saturated system to sostitute negative stress with positive?

In order to correctly evaluate the global system the negative-positive stress balances must be compared in example to a receptorial model with agonist antagonist in competition (pharmacological molecules) and observe the effect when positive stimulus increase related the amount of negative (Figure 3).

And to correctly set the problem is useful to weigh stressant negative stimulus to correctly evaluate a physio-pathologic condition?

Why 2 centuries ago in medical textbooks there wasn't described ansia as pathology? Some psycologic- psychiatric condition changed in last centuries in medical and social approach?

Contribute to this phenomena high amount of new stressant agents? (Media, internet, civilization, business conditions et other recent conditions).

After high stressant periods a download of metabolic - neurotransmitters and other molecule is a natural pathway? Is a conservative strategies? It can be compared to an ibernant metabolic process in some animals?

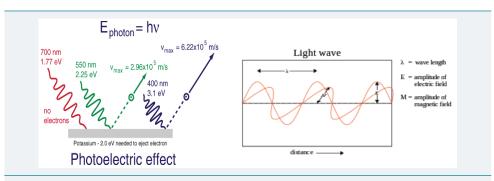


Figure 1: Corpuscular and ondulatory theory of light.

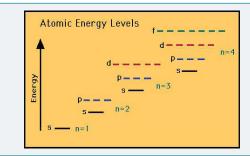


Figure 2: Quantum theory, orbital energy, quantized energy level (not linear but quantized).

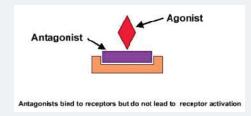


Figure 3: An antagonist molecule can bind to the receptor avoiding the agonist link.

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### **Material and Methods**

With an observational approach and analyzing scientific literature from biomedical databases (PubMed and other like university library database) we try to verify if mindset kinetics profile can influence the depressive tract. Then we try to produce an experimental tests hypotesys to verify the buffer properties of brain-mind and kinetics involved in some brain- mind phenomena.

Mindset kinetics is also deeply involved in many kind of thinking and abilities or behavior like: Catastrophic thinking, extreme thinking, Mental traps, too rapid conclusion approach, conflict management, Emotion management, positive vision, personal Goal setting, isolation, to search help ability and resilience, self-esteem and self-motivation, critical thinking approach, Love our self-ability.

And also other like: ability to Change the frame of the situation in complex situations, Rethinking the problems, Mental training, change negative thinking with pleasure activity, Stress management (coping strategy), Living and thinking at the present moment(not in past or in future), Emotional indifference and intelligence, Forgives ability, Contemplation exercise (mindfulness) to reduce stressing situations, No guilt sense (to make more free your mind and thinking), Dream up (to brake the negative thinking), Make more umor in the difficulties, Take distance from your negative thinking (mindfulness), Verify our sense attribution to the stressant situation, Open to new experiences, social intelligence, Neophyte behavior, Learn new experience (positive), Use better the opportunities, No fear for new situation).

### **Results**

### From literature

According article mindset kinetics under a toxicological aspect "in order to evaluate stressing situation are fundamental: kind of stress (in example HIGHor not); amount of global stressing condition, simultaneous;

Duration of stimulus (cronic conditions?) individual status (resilience? stress management ability, depression) psycologic but also genetic; kinetics." [1] and in article Attitudes and skills in business working setting: a HR management tool 2017: "ability to Treat great problem in a simply way. Learning by the errors, lifelong learning, Root causes analysis procedure (you can make errors but what is crucial is your ability to rise on), Delegate more, Time management (to do list and other management instruments), give priority, Rethinking the great problems, searching help in every situation, zero thinking ability, take your time ability to give response.

Change the frame of the situation. Mental training, no extreme thinking, lose comfort zone. Orientation attitudes (to be oriented in all situation), what your goal, what your task, what resource you need to do better a works (resource, help, instruments, strategies) to say no ability negotiation, conflict management, Positive thinking, Not catastrophic thinking, No negativity in working settings, Not to think to be at the center of the world, Pay attention to Mental traps, no rapid conclusion, No preconception, Think to your positive things happened in the day, Hard works to have more results help in work difficulties, Stop negative thinking with pleasure activity, Thinking Oriented to solution not only to problems, Positive results drive towards more self-motivation, Use Entertainments as motivational force, No mental traps, No mental limits, Trust in your instinct" [2].

"Stress Management and Coping Strategy Mindfulness: Living and thinking at the present moment (not past or future) (Constantly thinking to troubles make the mind weaker). Stop thinking (for 6 seconds), take a pause form trouble, Stop to the judgment, Emotional indifference, Forgives ability (mindfulness), No intrusive thinking, Changing sense of situation, Context, Make one think on the same time, learn go slowly, no multitasking Meditation technique is one hobby. Give value to the others, listen the



other thinking in the right way. Contemplation (mindfulness) is to reduce stress. No guilt sense (to make freer your mind). Massages, stretching, Sports, music, arts are hobbies. Holidays are to reduce stress. Dream up (to break negative thinking). Laugh, sense of humor, minimize, and leave drift the problems. Make humor in the difficulties. Stop the working connections when you are not at work or in office (if possible). Remember that life is also out of office (family, friends, social). Build positive relationship (friends, family and other). Learn to forgive mobbing management, to search emotional support ability, Attention to the distortion in, communication (up, down and between), Hear but not Listen (think before to the real sense of what other says to you), Pay attention to informal notice about you and to the your images other see. Take distance from your thinking (mindfulness), Verify our sense attribution to the situation, No too much rapid response, Say you're thinking with calm, No anger explosion, Open to new experiences, Neophyte behavior, Learn some new experience (positive), Use well the opportunities, No fear for the new situation, Make Glide the situation, To complain frequently results in negative cycle, Search social support, family, friends, Searching fellow, alliances, Rapidly stop the cause of trouble, before they increase(kill the monster before it increase), Take time to give response (time to correctly think to the solution), Deep knowledge in mobbing preventing activity (normative, law, office, strategies), Request of write order about strange request, Register every strange situation, Send write letter to chief officer and to chief UR Manager office, Pay attention to your body, emotional energy level, rest, Coaching supportive use" [2].

According Erin P Gillung et al., "Major depressive disorder (MDD) is the leading cause of disability in the developed world, yet broadly effective treatments remain elusive. Up to 40% of patients with depression are unresponsive to at least two trials of antidepressant medication and thus have "treatment-resistant depression" (TRD). There is an urgent need for cost-effective, non-pharmacologic, evidence-based treatments for TRD. Mindfulness-Based Cognitive Therapy (MBCT) is an effective treatment for relapse prevention and residual depression in major depression, but has not been previously studied in patients with TRD in a large randomized trial" [3]. According article A NEW PHYSIO-ANATOMIC BRAIN MAP 2017 "Why many area and brain systems are interested by pharmaceutical industry activity and other no?

The same we can think a new method to measure brain status observing some individual characteristics as:

All this indicators can be added to create a single data to verify a normal status giving more objectivity. Is not a new procedure but we think is innovative is to create a complexive map using this information. This approach can be useful in some field as forensic science, jurisdictional settings, HR management, and many other (Emotional Systems). Depression level, anxious status, schizophrenia, emotional status, or other pathological condition as Parkinson, coma, epileptic status, exiting status, dementia, migraine, sleep profile, hormonal status. And all other brain condition. Using for example statistical analysis methods in order to not have a relative condition that modify according the society evolution level but a more objectivable parameter to use in stabile way (nor relative). (What cells involved and related intensity of signal and objectivable effect). Information that come from directly from the cell or systems involved. We can have a physiology and anatomic information complete related whit the efficacy of some drugs or substances. This approach start from observing some brain disease (or systemic) and the effect due by some iatrogenic or toxic substanties and the drugs (used in therapy).

All this condition are often under pharmacological therapies and the related receptor profile. (The same we can consider the profile of addict's substanties and related receptor). We can see that in many situation we have an abuse or misuse of some psychotropic drugs also in young people and this phenomena is growing every year. Have we a single indicator to verify a normal or abnormal brain status? or we are



obliged to live in a psychological status managed by pharmacological molecules? "[4]. Dean J et al. written: "Major Depressive Disorder (MDD) is one of the most common and debilitating mental disorders; however, its etiology remains unclear. This paper aims to summarize the major neurobiological underpinnings of depression, synthesizing the findings into a comprehensive integrated view. A literature review was conducted using Pubmed. Search terms included "depression" or "MDD" AND "biology", "neurobiology", "inflammation", "neurogenesis", "monoamine", and "stress". Articles from 1995 to 2016 were reviewed with a focus on the connection between different biological and psychological models. Some possible pathophysiological mechanisms of depression include altered neurotransmission, HPA axis abnormalities involved in chronic stress, inflammation, reduced neuroplasticity, and network dysfunction. All of these proposed mechanisms are integrally related and interact bidirectionally. In addition, psychological factors have been shown to have a direct effect on neurodevelopment, causing a biological predisposition to depression, while biological factors can lead to psychological pathology as well. The authors suggest that while it is possible that there are several different endophenotypes of depression with distinct pathophysiological mechanisms, it may be helpful to think of depression as one united syndrome, in which these mechanisms interact as nodes in a matrix. Depressive disorders are considered in the context of the RDoC paradigm, identifying the pathological mechanisms at every translational level, with a focus on how these mechanisms interact. Finally, future directions of research are identified" [5].

Shin YC: "Various types of stress affect mental health in the form of mood disorders, anxiety disorders, and suicidal ideation. Recently, the increasing suicide rate in the working-age population has become a major mental health concern in Korea. Thus, we investigated what kind of stress influence depression, anxiety, and suicidal ideation in Korean employees. The study participants were 189,965 employees who attended health screenings and responded to the Center for Epidemiologic Study-Depression Scale, the Beck Anxiety Inventory, and a questionnaire on the major causes of stress and suicidal ideation. We investigated the major causes of stress by gender and age categories and used binary logistic regression to determine the impact of the causes of stress on depression, anxiety and suicidal ideation. Of several stress causes, workrelated stress was the most prevalent, regardless of age category and gender, followed by interpersonal relationships. However, interpersonal relationships and financial problems were the predominant causes of stress related to depression or suicidal ideation. This research suggests that despite the fact that work is the most common cause of stress for Korean employees, stress related to life problems other than work has a greater influence on the mental health of Korean employees" [6].

According Harvey et al., "The purpose of the present study was to address 1) whether exercise provides protection against new-onset depression and anxiety and 2) if so, the intensity and amount of exercise required to gain protection and, lastly, 3) the mechanisms that underlie any association. A "healthy" cohort of 33,908 adults, selected on the basis of having no symptoms of common mental disorder or limiting physical health conditions, was prospectively followed for 11 years. Validated measures of exercise, depression, anxiety, and a range of potential confounding and mediating factors were collected. Undertaking regular leisure-time exercise was associated with reduced incidence of future depression but not anxiety. The majority of this protective effect occurred at low levels of exercise and was observed regardless of intensity. After adjustment for confounders, the population attributable fraction suggests that, assuming the relationship is causal, 12% of future cases of depression could have been prevented if all participants had engaged in at least 1 hour of physical activity each week. The social and physical health benefits of exercise explained a small proportion of the protective effect. Previously proposed biological mechanisms, such as alterations in parasympathetic vagal tone, did not appear to have a role in explaining the protection against depression. Regular leisure-time exercise of any

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intensity provides protection against future depression but not anxiety. Relatively modest changes in population levels of exercise may have important public mental health benefits and prevent a substantial number of new cases of depression" [7].

Prathikanti S et al., "Conventional pharmacotherapies and psychotherapies for major depression are associated with limited adherence to care and relatively low remission rates. Yoga may offer an alternative treatment option, but rigorous studies are few. This randomized controlled trial with blinded outcome assessors examined an 8-week hatha yoga intervention as mono-therapy for mild-to-moderate major depression. Investigators recruited 38 adults in San Francisco meeting criteria for major depression of mild-to-moderate severity, per structured psychiatric interview and scores of 14-28 on Beck Depression Inventory-II (BDI). At screening, individuals engaged in psychotherapy, antidepressant pharmacotherapy, herbal or nutraceutical mood therapies, or mind-body practices were excluded. Participants were 68% female, with mean age 43.4 years (SD = 14.8, range = 22-72), and mean BDI score 22.4 (SD = 4.5). Twenty participants were randomized to 90-minute hatha yoga practice groups twice weekly for 8 weeks. Eighteen participants were randomized to 90-minute attention control education groups twice weekly for 8 weeks. Certified yoga instructors delivered both interventions at a university clinic. Primary outcome was depression severity, measured by BDI scores every 2 weeks from baseline to 8 weeks. Secondary outcomes were self-efficacy and self-esteem, measured by scores on the General Self-Efficacy Scale (GSES) and Rosenberg Self-Esteem Scale (RSES) at baseline and at 8 weeks.

In intent-to-treat analysis, yoga participants exhibited significantly greater 8-week decline in BDI scores than controls (p-value = 0.034). In sub-analyses of participants completing final 8-week measures, yoga participants were more likely to achieve remission, defined per final BDI score  $\leq$  9 (p-value = 0.018). Effect size of yoga in reducing BDI scores was large, per Cohen's d = -0.96 [95%CI, -1.81 to -0.12]. Intervention groups did not differ significantly in 8-week change scores for either the GSES or RSES. In adults with mild-to-moderate major depression, an 8-week hatha yoga intervention resulted in statistically and clinically significant reductions in depression severity [8].

Piotr Gałecki et al., "Separating emotions from cognition seems an impossible task in a human being's everyday experiences, similarly to the functional separation of frontal lobes and hippocampal formations. The majority of emotional experiences are linked with cognitive processes, and emotions are an indispensable element of cognition (the so-called principle of cognition compatibility with mood). This principle affects not only memory processes but also includes perception, attention, or linguistic abilities. It seems that the so-called "reptilian brain" is in charge of steering our choices, while "rational" frontal lobes are always one step behind. The pace of evolutionary changes does not keep up with the intensity of civilization changes. Therefore, symptoms of depression may be one of the forms of adaptation to excessively high requirements of the environment. When summing up our deliberations regarding the etiology of depression, can we simply claim that Nature has not finished its work? We will leave this question without an answer" [9].

Ferrari fet al., "Depressive disorders are heterogeneous diseases, and the complexity of symptoms has led to the formulation of several aethiopathological hypotheses. This heterogeneity may account for the following open issues about antidepressant therapy: (i) antidepressants show a time lag between pharmacological effects, within hours from acute drug administration, and therapeutic effects, within two-four weeks of subchronic treatment; (ii) this latency interval is critical for the patient because of the possible further mood worsening that may result in suicide attempts for the seemingly ineffective therapy and for the apparent adverse effects; (iii) and only 60-70 % of treated patients successfully respond to therapy. In this review, the complexity of the biological theories that try to explain the molecular mechanisms of these diseases is considered, encompassing (i) the classic "monoaminergic hypothesis"

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alongside the updated hypothesis according to which long-term therapeutical action of antidepressants is mediated by intracellular signal transduction pathways and (ii) the hypothalamic-pituitary-adrenal axis involvement. Although these models have guided research efforts in the field for decades, they have not generated a compelling and conclusive model either for depression pathophysiology or for antidepressant drugs' action. So, other emerging theories are discussed: (iii) the alterations of neuroplasticity and neurotrophins in selective vulnerable cerebral areas; (iv) the involvement of inflammatory processes; (v) and the alterations in mitochondrial function and neuronal bioenergetics. The focus is put on the molecular and theoretical links between all these hypotheses, which are not mutually exclusive but otherwise tightly correlated, giving an integrated and comprehensive overview of the neurobiology of depressive disorders" [10].

According Forsyth et al "The purpose of this article is to describe changes in positive and negative thinking in adult inpatients with depression who attended an Advanced Practice Nurse-led Cognitive Behavioral Therapy group on 1 inpatient unit in a large medical center.

A descriptive design with a retrospective cohort chart review was conducted (n = 427). Positive and negative thinking were measured by the Automatic Thoughts Questionnaire at admission and at discharge.

A paired t-test revealed a significant change (p = 0.001) in both positive and negative thinking in the desired direction between admission and discharge. It is important to measure clinical improvements" [11].

Trick L et al., "Depression is common in people with long term conditions, and is associated with worse medical outcomes. Previous research shows perseverative negative thinking (e.g. worry, rumination) predicts subsequent depression and worse medical outcomes, suggesting interventions targeting perseverative negative thinking could improve depression and medical outcomes. Previous studies recruited healthy individuals, however. This review aimed to determine the temporal relationship and strength of prospective association of perseverative negative thinking with depression, anxiety and emotional distress in people with long term conditions.

Four electronic databases were searched for studies including standardised measures of perseverative negative thinking and depression, anxiety or emotional distress, and which presented prospective associations. Findings were narratively synthesized.

Thirty studies were identified in a range of long term conditions. Perseverative negative thinking and subsequent depression, anxiety or emotional distress were significantly correlated in the majority of studies (bivariate r=0.23 to r=0.73). 25 studies controlled for confounders, and in 15 perseverative negative thinking predicted subsequent depression, anxiety or emotional distress. Results varied according to condition and study quality. Six of 7 studies found bivariate associations between depression, anxiety or emotional distress and subsequent perseverative negative thinking, though 2 studies controlling for key covariates found no association. Few studies assessed the impact of perseverative negative thinking on medical outcomes.

Strongest evidence supported perseverative negative thinking predicting subsequent depression, anxiety and emotional distress in people with long term conditions. Further prospective research is warranted to clarify the association of perseverative negative thinking with subsequent poor medical outcomes" [12].

And Saori Nishikawa et al written: "Previous studies have demonstrated an association between negative life events (NLEs) in childhood and resilience/posttraumatic growth (PTG) with regard to the pathogenesis of major depressive disorder. We hypothesized that the type and timing of NLEs interact to influence



mental health in the general youth population. Therefore, the present study aimed to examine the effects of NLE timing and intensity on current depressive symptoms, and to determine the direct and indirect effects of NLEs/resilience on PTG and depression among non-clinical adolescents. Data were collected from 1,038 high-school students across seven high schools in Fukui, Japan, during their freshman and sophomore years (648 boys and 390 girls, mean age = 15.71, SD = 0.524). Respondents completed a set of questionnaires designed to evaluate the type and timing of NLEs, depressive and traumatic symptoms, and PTG. Cluster analysis was used to divide participants into three groups based on outcomes: "cluster 1" (n = 631), for whom depressive scores were significantly lower than other two subgroups (p < 0.05, for both); "cluster 2" (n = 52), for whom levels of current and past perceived stress associated with NLEs were significantly higher than those of the other two subgroups (p < 0.05, for both); "cluster 3" (n = 374), for whom perceived stress at the time of NLE was significantly higher than that of participants in the cluster 1 (p < 0.05) group, but not the cluster 2 group. Our findings indicated that exposure to NLEs at a younger age resulted in stronger negative outcomes and that NLE timing and intensity were associated with PTG and current symptoms of depression. Furthermore, path analysis demonstrated that associations between perceived stress at the time of NLEs were direct and indirect predictors of current depression via PTG and that posttraumatic stress symptom and PTG mediate the association between NLEs/trait-resiliency and current depression. In conclusion, our findings suggest that event intensity, NLE timing, and gender may play a role in emotional vulnerability during adolescence" [13].

### **Discussion**

Related the literature observed is relevant to introduce new more objective way to the definition of depression status to be pharmacologically treated to be separated to the subject that take advantages with other non-pharmacological strategies.

In this kind of disorder also mindset kinetics and their specific limits must be considered to evaluate in objective way saturation situation of the system, specific buffer properties and resilience abilities of individuals.

In actual scenario a better objective way to verify the amount of stressing condition, time of exposure and quality must be introduced.

An useful instruments for healthcare professionals and patients.(using also a toxicological approach: what toxic condition, amount and time of exposure and under a biochemical aspect( kinetics, max velocity of a system, saturation) and not only the receptorial status.

Observing biochemistry kinetics law can we think that a Zero Order Kinetics in mindset kinetics can reduce some mind-brain disorder? (Only a determinate quantum of stressing condition in a definite amount of time) (Figures 4-6).

### Conclusion

Scientist like Max Planck, Einstein, Bohr, de Broglie, Schrödinger, Heisenberg et others (involved in theory of quantum chemical physic), E. goldratt (Teory of constraints), Michaelis-Menten (kinetics theory), other biochemical and enzymatic reaction theory must be deeply investigated also in other fields like neuroscience and applied in order to better clear some process (Figure 7).

The factor that can join the organic theories to the psychological approach can be an abnormal- pathological mindset kinetics process or an overuse or saturation in some Psyco- neurologic process.

The single resilience ability or single buffer properties in biochemical receptorial status must be also objectivable.



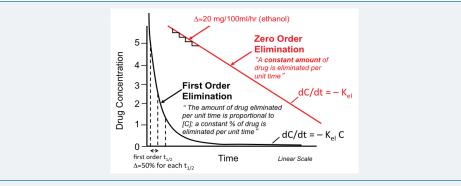


Figure 4: Example of zero order kinetic.

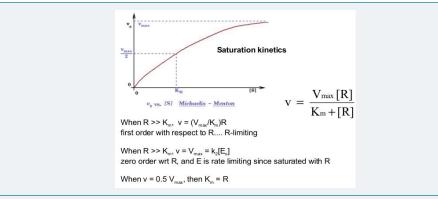


Figure 5: Saturation kinetc.



Figure 6: Mindset buffer model.

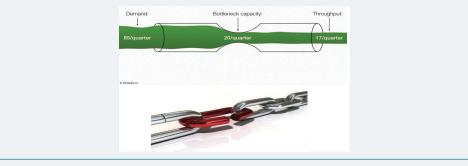


Figure 7: E. Goldratt: theory of constraints. Weakest ring.

So Is crucial to verify in more objective way the global amount of stressan stimulous, time long (acute or prolonged time), quality of stressant condition and the single resilience ablities as well as the buffer biochemical properties and other factors that can be involved (environment, social situation, working condition, health status).

So it is real crucial to introduce new diagnostic objective tests to verify this conditions.

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Considering the stress antstimolus like an endogenous- exogenous toxic condition factor can be interesting to think to new kind of Remedies.

A Toxicology status can be considered also a overuse of a system that can produce great unbalances in physiology in some apparatus.

### **Clarifications**

This paper was not written for any diagnostic or therapeutic intent, only to produce new research hypotesys.

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