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Beyond Impulsivity: Behavioral Disinhibition in ADHD

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Abstract

There is a general behavioral disinhibition beyond impulsivity in ADHD that leads to risk taking behaviors such as careless driving, substance use, and many other negative consequences or complications. Behavioral disinihibtion (BD) as a frontal and specifically prefrontal cortex pathology, has been seen long in injuries and pathologies to this area of the brain, leading to uncontrolled behavior, is a centerpiece of symptoms cluster in ADHD-HI (Hyper-Impulsive) subtype. The first aim of this paper is to confirm the existence of a behavioral disinhibition beyond the already general recognized one in cognitive domain. The second goal of the study is to identify if there is a link between this phenotype and risk taking, misconduct behaviors and substance use. Lastly we have sought to determine whether there is a correlation between major symptom clusters of ADHD, -i.e. hyperactivity and impulsivity to behavioral disinhibition.

The result of this original study confirms the common presence of behavioral disinhibition as a major symptom cluster in ADHD-HI. We were also able to show a positive correlation exists between the symptoms of hyperactivity and impulsivity with behavioral disinhibition. Furthermore, there is an even stronger link between behavioral disinhibition and risk taking, misconduct behaviors, and substance use, than with hyperactivity and impulsivity. In conclusion, behavioral disinhibition in untreated ADHD demands recognition, treatment, and prevention.

Introduction

Impulsivity, considered a cardinal symptom of Attention Deficit Hyperactivity Disorder (ADHD) of the hyperactiveimpulsive subtype (ADHD-HI) in DSM5, has been ill-defined. Behavioral illustrations that apply more to verbal's such as "blurting out answers before questions have been finished" and "interrupting or intruding on others, e.g., butting into conversations or games" [1] are limited in scope. Here we redefine impulsivity as "acting on impulses without considering the consequences of the actions" that we believe to be more proper definition and applicable in the assessment and more understandable clinically by the patients. Beyond the impulsivity, we draw attention to a general "behavioral disinhibition" or lack of control over one's actions and behaviors in ADHD-HI.

Impulsivity and behavioral disinhibition (BD) have been discussed in the literature interchangeably at times and at others, impulsivity has been over-generalized [2-4]. BD has been discussed mostly in dementia, intoxication by alcohol and other illicit and licit substances, and brain injuries [5-8], while impulsivity has been observed and reported across several psychiatric disorders such as ADHD, substance use disorders, depression, mania, antisocial and borderline personality disorders among others [9-11]. Therefore impulsivity has been recognized as a heterogenic behavioral trait with diverse underpinning neuro-pathophysiologic mechanisms and pathways, mostly limbic-cortico-striatal with the involvement of Dopamine and Serotonin [9]. Impulsivity has been mostly defined as "poor self-control", "quick and wrong decision making without forethought or regard for potential consequences". Impulsivity seems mostly require a

"cue" predictive of reward that is measured in labs by SSRT (Stop Signal Reaction Time). That is how impulsivity has also been associated with binge eating and drinking where the food and alcohol are cues and immediate gratification instead of delaying rewards are sought [9, 11].

Since both impulsivity and BD co-exist in ADHD-HI, we distinguish between the two, as our subjects related different behaviors to each phenotypes, though they seem to be very closely associated. Behavioral disinhibition in ADHD has been reported as early as 1972 by Douglas [12], then Quay [13] and Barkley [14], and has been considered an inherent component of ADHD. BD by these authors and others later on has been perceived as a phenomenon of "poor impulse control", "poor self-regulation", and "response inhibition", and considered to be a deficiency of "executive function" rather than a general behavioral disinhibition. It has also been included in the inattentive ADHD subtype (ADHD-I), while it may apply only to the ADHD-HI subtype. Our hypothesis is that behavioral disinhibition underpins post-morbidities (a new term that we coin to denote cause-and-effect or a secondary complication of a primary condition, opposed to comorbidities that occur in parallel) such as risk taking, misconduct behaviors and substance use disorders that are secondary consequences of untreated ADHD.

Method

Our sample consists of 134 adults (19 years old and over, 82 males, 52 females) (For age and sex distribution, see **Table 4**), who conducted on online test from our website www.adhdrevisited.com from December 2015 to May 2018 and their diagnoses were confirmed by clinical interviews, based on DSM5 ADHD criteria. We subdivided the ADHD symptoms into three clusters of inattention (**Table 1**), hyperactivity (**Table 2**), impulsivity and behavioral disinhibition (**Table 3**).

1	Are you often inattentive, easily distracted, not able to			
-	sustain attention?			
2	Are you often not able to give close attention to details or			
	makes careless mistakes in schoolwork, work, or other			
	activities?			
3	Do you often seem not to listen when spoken to directly?			
4	Do you often not follow through instructions and fail to			
	finish schoolwork, chores, or duties (not due to			
	oppositional behavior or failure to understand			
	instructions)?			
5	Do you often have trouble organizing tasks and activities?			
6	Do often avoid, dislike, or don't want to do things that			
	take a lot of mental effort for a long period of time (such			
	as schoolwork or homework)?			
7	Do you often lose things needed for tasks and activities			
	(e.g. toys, school assignments, pencils, books, or tools)?			
8	Are you often forgetful in daily activities?			

 Table 1: Inattentive symptoms cluster.

1	Are you or when younger have been hyperactive, restless,			
	could not sit still, fidget a lot, running around and			
	climbing things?			
2	Are you having or when younger had often trouble			
	playing or doing leisure activities quietly?			
3	Are you or when younger were often "on the go" or often			
	acts as if "driven by a motor"?			
4	Do you or when younger used to often talk excessively?			
5	Do you often having trouble waiting one's turn?			
6	Are you impatient, easily getting bored, cannot wait for			
	things?			

 Table 2: Hyperactivity symptoms cluster.

1	Do you often blurt out answers before questions have
	been finished?
2	Do you often interrupt or intrude on others (e.g., butts
	into conversations or games)?
3	Are you impulsive (acting on impulses and not
	considering the consequences of actions)?
4	Have you been behaviourally disinhibited, such as being
	out of control, destroying things and annoying others?
5	Have you been risk taking such as cycling or driving
	carelessly?
6	Do you or have used any illicit substances?

 Table 3: Impulsivity & Behavioral Disinhibition symptoms cluster.

Age Gro up	Num ber of Subj ects	# of Male s	# of Fema les	Age Ran ge	Age Mean	Age Med ian	Ag e Mo de
Adu lts (>18)	134	82 (61.1 9%)	52 (38.8 1%)	58- 19 (39)	29.09 774	26	22

Table 4: Subjects age and sex statistics.

We merged the two DSM5 questions for the inattentive subgroup of "often has difficulty sustaining attention in task or play activities" and "is often easily distracted" into one question "Are you often inattentive, easily distracted, not able to sustain attention?", but gave it a 2 point value while other questions had a 1 point value. In the hyperactivity symptoms cluster, we merged the DSM questions of "often fidgets", "often leaves seat in situations when remaining seated is expected", and "often runs about or climbs in situations where it is inappropriate" into one question "Are you or when younger have been hyperactive, restless, could not sit still, fidget a lot, running around and climbing things?" and gave it a 3 point value. The DSM criteria of "often has difficulty

waiting for his or her turn" that implies "impatience" and "boredom" and based on our clinical observation are cardinal symptoms of ADHD; we re-phrased to the question "Are you impatient, easily getting bored, cannot wait for things?" and gave it a 2 point value. Although it is not clear in DSM5 whether impatience and boredom are part of the hyperactivity or impulsivity symptom cluster, we included them in the hyperactivity section.

We added our definition of impulsivity, "acting on impulses without considering the consequences of the actions" to the two questions in DSM5 "blurting out, or butting into conversations or games" and "often interrupting or intruding on others". We also added a question relating to behavioral disinhibition (BD), "Have you been behaviorally disinhibited, such as being out of control, destroying things and annoying others?" and a question about risk taking to this category "have you been risk taking such as cycling or driving carelessly" and a question on substance use, "do you or have you used any illicit substance" (**Table 5**).

1	Don't think before speak and got into trouble for saying inappropriate things before thinking
2	Very impulsive and react very quickly and emotionally rather than rationally
3	Still get into troubles for bad decision makings without thinking and considering the consequences at work and in personal life
4	Have thrown people off for acting on impulses
5	Now regret aftermath of my impulsive behaviors but not when younger
6	Being ridiculed by peers and punished by parents for being impulsive

 Table 5: Examples of Impulsivity (acting on impulses without thinking).

Examples of impulsivity (such as acting on impulses), BD, and risk taking behaviors recorded by some individuals in the comment box in their tests are shown in (**Table 6, 7 & 8**). We also included two questions to measure "Novelty Seeking" and "Reward Seeking" in ADHD, "Are you novelty seeker (getting bored easily with old things and looking for new things or changing things?" and "Are you reward seeker (seeking reward when doing things/tasks, or driven by rewards?" We matched the 66% positive response diagnostic criterion of DSM5 for inattentive and hyperactivity symptom clusters. When >66% or 2/3 of the questions in each symptom cluster was positive, we summarized them into one under "inattention" and "hyperactivity" in our data (Appendix 1). Since impulsivity is a cardinal diagnostic symptom scluster

(**Table 6**), we put them all under one column whenever 2 out of three received a positive response (Appendix 1).

1	Used to scream and say bad words for no good reasons to
	others or just to the air
2	Annoying others and destroying
23	Has been told to be out of control
4	Breaking and damaging things
5	Drawing all over the walls
6	Being punished often for being out of control
7	Still out of control and do things out of logic
8	Would dance on the desks in school
9	Often was in trouble as a child
1	Was aggressive and combative
0	
1	Throwing knives into the couch and around
1	
1	Take apart things like electronics without putting them
2	back together
1	Broke all the doors and walls in the house
3	

Table 6: Examples of Behavioral Disinhibition.

Results

First we tested the validity rate of each definition of impulsivity by DSM5, "blurting out, or butting into conversations or games" and "often interrupting or intruding on others" with our re-definition of "acting on impulses without considering the consequences of the actions" through correlation analysis (using Correlation Coefficient calculation) of these with the cardinal symptom clusters of ADHD, inattention, hyperactivity, and also BD, risk taking behaviors and substance use (Table 8). Each definition of DSM5 correlated with the inattention 0.0725 (7.25%) and 0.0697 (6.97%), while our re-definition correlated 0.0731 (7.31%), but with hyperactivity, the DSM definitions correlated 0.2080 (20.80%) and 0.0756 (7.56%), while our impulsivity re-definition was correlated higher (0.2248 or 22.48%) (**Table 7**).

in /m			
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as			
of			
control and get more angry than peers			
ng			
-			

Table 7: Examples of Risk taking behaviors.

The DSM5's "blurting out, or butting into conversations or games" correlated with BD, risk taking and substance use, 0.2537 (25.37%), 0.2799 (27.99%), and 0.0873 (8.73%), respectively, and "often interrupting or intruding on others" correlated 0.0938 (9.38%), 0.0841 (8.41%) and 0.1369 (13.69%) respectively. Our re-definition of impulsivity correlated with BD, risk taking and substance use much higher (0.4765 or 47.65%; 0.5004 or 50.042%; and 0.2878 or 28.78%) (**Table 8**).

	Inatte ntion	Hypera ctivity	B D	Ris k tak ing	Subst ance use	Nov elty seek ing	Rew ard seek ing
Blurti	.0725	.2080	.25	.27	.0873	.201	.081
ng out			37	99		3	3
Interr	.0697	.0756	.09	.08	.1369	.060	.005
upting			38	41		8	6
Actin	.0731	.2248	.47	.50	.2878	.352	.131
g on			65	04		6	9
impul							
ses							

Table 8: Correlation between three impulsivity symptomclusters and Inattention, Hyperactivity, BehavioralDisinhibition (BD), risk taking and substance use in totalsubjects-N 134.

Among all the subjects of the three subtypes, the rates of each symptom clusters were as following: Inattention 98.50%; Hyperactivity 76.86%; Impulsivity 74.63%; Behavioral Disinhibition 67.16%; Risk taking behaviors 65.67%, Substance use 52.98%, Novelty seeking 80.60%, and Reward seeking 70.15% (Appendix 1). There were only 13 subjects with ADHD-I (Inattentive subtype, with no hyperactivity or impulsivity) comprising 9.7% of the total subjects (Appendix 2), and 81 subjects with ADHD-HI (Hyperactive & Impulsive) comprising 60.45% of the total subjects (Appendix 3), and 121 subjects with ADHD mixed subtype (Hyperactive or Impulsive) comprising 90.30% of the total subjects (Appendix 4). A statistic summary and comparison between the subtypes and symptom clusters is seen in (**Table 9**).

ADHD-I	9.7%
ADHD-HI	60.45%
ADHD-Mixed	90.30%
Inattention	98.50%
Hyperactivity	76.86%
Impulsivity	74.63%
Behavioral Disinhibition	67.16%
Risk Taking Behavior	65.67%
Substance Use	52.98%
Novelty seeking	80.60%
Reward Seeking	70.15%

Table 9: Subtypes and symptom Cluster Statistics.

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Finally a correlation analysis between each cardinal symptom clusters of Inattention, Hyperactivity, Impulsivity and Behavioral Disinhibition (BD) were made with each other and risk taking behaviors, substance use, novelty and reward seeking among all the total 134 subjects (Table 10). Inattention showed a higher positive correlation with hyperactivity (0.0754 or 7.54%), then with impulsivity (0.0731 or 7.31%) and the lowest with BD (0.0428 or 4.28%). Hyperactivity correlated higher with BD (0.5282 or 52.83%) than with impulsivity (0.2248 or 22.48%). BD correlated the highest respectively with hyperactivity (0.5283 or 52.83%), with impulsivity (0.4765 or 47.65%), with risk taking behavior (0.9502 or 95.02%), with substance use (0.32.15 or 32.15%), with novelty seeking (.04103 or 41.03%), and with reward seeking (0.1922 or 19.22%) than any other symptom clusters including impulsivity (Table 10).

	Inattenti	Hyperactivi	Impulsivit	BD
	on	ty	У	
Inattention	.1000	.0754	.0731	.04
				28
Hyperactivi	.0754	.1000	.2248	.52
ty				83
Impulsivity	.0731	.2248	.1000	.47
				65
BD	.0428	.5283	.4765	.10
				00
Risk	.0032	.5717	.5008	.95
Taking				02
Substance	.0415	.2261	.2878	.32
use				15
Novelty	.0952	.4333	.3526	.41
Seeking				03
Reward	.0803	.0936	.1319	.19
Seeking				22

Table 10: Correlation between Risk taking and substance use with Inattention, Hyperactivity, Impulsivity and Behavioral Disinhibition (BD) in total subjects-N 134.

Discussion

According to Grafman et al. [15] in their handbook of neuropsychology, "disinhibition" is a lack of restraint manifested in several ways, affecting motor, emotional and cognitive domains with signs and symptoms e.g. impulsivity, disregard for others and social norms, aggressive outbursts, misconduct, oppositional and risk taking behaviors. Disinhibition is a common symptom following brain injury, or lesions, and dementia particularly of the frontal lobe and orbitofrontal cortex [16-18]. Behavioral disinhibition (BD) as a result of damage to the frontal lobe could also be seen as a result of consumption of alcohol and central nervous system depressants drugs, e.g. benzodiazepines that disinhibit the frontal cortex from self-regulation and control, particularly in the young and aged brains [6-8]. Therefore BD seems to be a general umbrella that covers a wide range of behaviors,

including but not limited to impulsivity or in the cognitive domain.

It is widely believed that the prefrontal cortex (PFC) with its frontal-subcortical circuits serves as a source of inhibitory control over other brain areas. The three principal behaviorally relevant circuits originate in the 1) dorsolateral prefrontal cortex, 2) orbitofrontal cortex, and 3) anterior cingulate cortex. Circuit-specific marker behaviors associated with each circuit are executive dysfunction (dorsolateral prefrontal-subcortical motoric disinhibition (orbitofrontal-subcortical circuit). circuit), and apathy or emotional inhibition (medial frontalsubcortical circuit) [19-20]. The basal ganglia forms one of the most complicated systems in the brain, with extensive connectivity to other subcortical regions, e.g. limbic system and the higher cortical regions, specially frontal cortex, composed almost entirely of inhibitory GABAergic neurons and affected by dopamine. This extensive neural network controls the initiation and continuation of motoric, emotional, behavioral and cognitive functions at a relatively selective, fine-grained level [21-24].

There is evidence from animals and human brains imaging studies that not only frontal lobe, but also a sophisticated neural network from subcortical to higher cortex are actively in dynamic concert to control our thoughts, emotions and behaviors or otherwise we lose the control and being impulsive and disinhibited **[25-27]**. There is also ample evidence that the modulation of dopamine (DA) levels as well as dopaminergic areas in the brain affect impulsive choice behavior, seeking immediate vs. delayed reward and perhaps general disinhibition. **[27,28]** Moreover dopamine has a significant role in the development of prefrontal cortex during early development and its impact on behavioral inhibition and cognition **[29]**.

ADHD since when it was labeled "Minimal Brain Dysfunction" and "Hyperkinetic Disorders" to the recent years has been known as a generalized disinhibition in domain of cognition, manifested as executive dysfunction or inattention; also in the motoric domain as hyperactivity, restlessness; and behaviorally as impulsivity, risk taking behavior, conduct disorder, and drug seeking; as well emotionally as aggression, anger, temper tantrum and irritability, due to PFC pathology causing disinhibition across these different domains [**30-39**]. Some authorities have even suggested heterogeneity in ADHD, and separated the ADHD-HI and ADHD-I s two separate pathological entities due to BD being a centerpiece in the pathophysiology of ADHD-HI as a disinhibitory disorder [**40-41**].

Behavioral disinhibition has been also associated with the externalizing disorders or behaviors, such as conduct disorder, substance use, and novelty seeking [42]. BD has also been shown to be a hereditary phenotype of ADHD linked with its underlying pathology of PFC [43-44]. In a large study on 16,099 children and adolescents, ages 6 to 18 years, the individuals with greater ADHD trait scores had worse

response inhibition, slower response latency, and the ADHD traits and inhibition were shown to be co-heritable [45]. Disordered dopamine neurotransmission is implicated in mediating impulsiveness and disinhibition across a range of behaviors and disorders including addiction, compulsive gambling, ADHD, and dopamine dysregulation syndrome. It has been shown that pharmacologically enhancing dopamine activity increases impulsivity by enhancing the diminutive influence of increasing delay on reward value (temporal discounting) and its corresponding neural representation in the striatum [46]. The lesions in the ventromedial part of the prefrontal cortex (VMPFC), which is part of the orbitofrontal cortex (OFC), has been shown to cause the individuals to discount, or neglect, the future consequences of their decisions, leading to behavioral disinhibition and risk taking [47].

In this study, we have shown that first of all the impulsivity in DSM5 is ill-defined and insufficient, but our redefinition of impulsivity as "acting on impulses without considering the consequences of the actions" correlates more with the other cardinal symptoms of ADHD. Our impulsivity definition of "Acting on impulses" correlated higher with the inattention (7.31%), and more so with hyperactivity (22.48%), BD (47.65%), risk taking (50.04%) substance use (28.78%), novelty seeking (35.26%) and reward seeking (13.19%) than with DSM5 symptom definition of impulsivity as "Blurting out" 7.25%, 20.80%, 27.99%, 8.73%, 20.13% & 8.13%. Interrupting and intruding into others fared the least, correlating with inattention 6.97%, with hyperactivity 7.56%, with BD 9.38%, with risk taking 8.41%, with substance use 28.78%, with novelty seeking 6.08% & with reward seeking 5.6% (Table 8). In summary while "blurting out" scored better than "interrupting and intruding on others" for impulsivity, our re-definition of impulsivity as "acting on impulses" fared much higher with inattention, hyperactivity, BD, risk taking, substance use, novelty & reward seeking.

Lastly we showed that BD correlated much higher with hyperactivity than impulsivity (52.83% Vs. 22.48%), with impulsivity than hyperactivity (47.65% Vs. 22.48%), and higher with risk taking than hyperactivity and impulsivity even to our re-definition (95.02% Vs. 52.83% & 50.08% respectively). BD correlated higher with substance use than with hyperactivity and impulsivity (32.15% Vs. 22.61% & 28.28%). While only hyperactivity correlated marginally higher with novelty seeking than BD (43.33% Vs. 41.03%), BD correlated higher with novelty seeking than impulsivity (41.03%Vs.35.26%), and much higher than hyperactivity and impulsivity with reward seeking (19.22% Vs. 9.36% & 13.19%) (**Table 10**).

As it was discussed in the introduction, impulsivity and BD have been used interchangeably and not differentiated sufficiently at a phenomenonologic or symptomatic descriptive level, though it is more so at an underlying neruopathophysiologic level **[47,48]**. A look at some examples that our sample reported about their impulsive vs. disinhibitory

behaviors demonstrate this differentiation at a symptomatic level better. "not thinking before speaking and getting into trouble for saying inappropriate things before thinking"; "react very quickly and emotionally rather than rationally"; "get into troubles for bad decision makings without thinking and considering the consequences at work and in personal life" seem to be different with the following examples of BD by the subjects. "Screaming and saying bad words for no good reasons to others or just to the air"; "Annoying others and destroying"; "Being told to be out of control"; "Breaking and damaging things"; "Dancing on the desks in school"; "Being aggressive and combative"; "Taking apart things such as electronics without putting them back together"; "Breaking all the doors and walls in the house" seem to be general disinhibitory problems and not impulsive behaviors in response to a cue or for immediate gratification and reward seeking.

Moreover the underlying reward seeking of impulsivity that is seen in other psychiatric disorders such as substance use, binge eating and drinking **[49]** correlated higher with substance use (25.50%) and with impulsivity (13.19%) than novelty seeking that seems to be more associated with ADHD-HI (23.53%). Novelty seeking fared higher in our data with BD and risk taking (41.03% & (40.04%) than reward seeking (19.22% & 18.10%) (**Table 11**).

	Novelty Seeking	Reward Seeking
Impulsivity	.03526	.1319
BD	.4103	.1922
Risk Taking	.4004	.1810
Substance use	.2353	.2550

Table 11: Correlation between Impulsivity, BD, Risk Taking,Substance use and Novelty and Reward Seeking in totalsubjects-N 134.

Novelty and reward seeking also like impulsivity and BD have been used interchangeably in the literature and linked to dopamine and striatal-prefrontal circuit function. Novelty or sensation seeking has also been thought to be linked psychopathologically to reward seeking [32, 50]. But despite this misconception, novelty-seeking has been shown to be positively correlated with Substantial Nigra/Ventral Tegmental Area (SN/VTA) activation of striatum elicited by novel cues that did not predict reward, whereas rewarddependence was related to activations elicited by novel cues that predicted reward. The positive correlation between SN/VTA responses to novelty and novelty-seeking scores has been associated with a negative correlation with rewardrelated SN/VTA activation and memory enhancement. In a better word, novelty-seekers tend to show generally up regulated, novelty-induced exploratory behavior, even when novelty does not predict reward [51].

Our results here confirm previous reports that ADHD is associated with higher novelty-seeking scores and a decreased

reward anticipation response. Along this line adults with ADHD have also shown decreased activation in the ventral striatum during the anticipation of gain, but increased activation of the orbitofrontal cortex in response to gain outcomes. Ventral striatal activation in adults with ADHD during gain anticipation has been negatively correlated with self-rated symptoms of hyperactivity and impulsivity [52,53]. This aligns with our result that reward seeking is more in line with impulsivity and substance use than novelty or sensation seeking that is more in line with BD, risk taking (Table 11)

It has been extensively and for long shown in the literature that the negative consequences of untreated ADHD being mostly due to its impulsivity component that now behavioral disinhibition needs to be added to. The Cambridge Study in Delinquent Development [54], a prospective longitudinal survey of males from ages 8 to 32 years old have reported the prediction of adolescent aggression, teenage and later on adult violence and convictions for violence in untreated ADHD. Another longitudinal analytic study of a cohort of 435 boys has found strong connection between juvenile delinquency and ADHD, starting even as early as preschool age, escalated at school entry, and persisted into adolescence [55]. Genetic studies have also reported association between ADHD and risk of aggressive behaviors [56].

A review of the outcomes of 351 ADHD studies has also demonstrated complications of untreated ADHD in academic, antisocial behavior, careless driving and accidents, substance use/addictive behavior, self-esteem, and social function domains, that improved with treatment [57] ADHD has also been shown to be associated with earlier onset of polysubstance use disorders independently of psychiatric comorbidity. The substance use among ADHD is so high that at least one out of 4-5 substance users may have undiagnosed and untreated ADHD as early as age 10 that in turn could increase the risk of conduct and oppositional defiant disorders in childhood and adolescents that in turn could increase the risk of anti-social and other delinquent behaviors and even personality disorders in adulthood [58, 59]. Impulsivity and more so behavioral disinhibition as we showed in our studies are the leading phenotypes to these ADHD post-morbidities.

Adults with ADHD are also at increased risk of accidents, trauma and workplace injuries, particularly traffic accidents, increased rates of substance abuse and criminality, that all could improve with treatment [60]. A large national sample of the United States population [61] adults aged 18 years and older during the 2004-2005 has shown that impulsivity is quite high in general population (about 17%), particularly among males and younger individuals, and associated with a broad range of psychiatric disorders, particularly drug dependence, personality disorders, bipolar disorder and ADHD. This report asserts that impulsivity is associated with behavioral disinhibition, attention deficits, and lack of planning, risk taking and dangerous behaviors to the individuals and others, including driving recklessly, starting fights, shoplifting,

perpetrating domestic violence and trying to hurt or kill with higher risk of lifetime trauma and substantial physical and psychosocial impairments [61].

While there are extensive reports in the literature of the post-morbidities or complications of untreated ADHD, there is lack of pathophysiologic explanations or association of which elements or phenotypes of ADHD being causal. In this paper for the first time to our knowledge, we expanded the earlier reports of behavioral disinhibition (BD) that have been more studied in the cognitive domain and termed more as "response inhibition" to a general behavioral domain. We showed that the general BD in ADHD-HI is associated more than other phenotypes or symptom clusters of inattention, hyperactivity and impulsivity to risk taking behaviors, substance use, and novelty or sensation seeking. Therefore we hypothesize that BD could be the underpinning endophenotype leading to any misconduct, careless and reckless behaviors without considering the negative consequences onto the individual, others, and the society at large.

As discussed impulsivity is a multi-faceted behavior associated with many psychiatric conditions, including mood disorders, particularly suicidality, personality disorders, substance use, and in connection with the serotonergic in addition to the dopaminergic functions of the brain and is not limited to ADHD [62-65]. But ADHD-HI could be a unique disorder to have both impulsivity and behavioral disinhibition in connection with the pre-frontal lobe pathology and dopaminergic deficiency, leading to risk taking, careless, reckless and misconduct behaviors, not only on a impulse and cue-based, but in general and not much reward-conditioned like other impulsive disorders. Further replication studies to reconfirm our results and also to directly bridge between BD and all risk and careless behaviors of untreated ADHD are required to prevent these costly post-morbidities of this condition.

Limitations

We limited our data to adult age group, as we are working on the collected data on children and adolescents to be published soon as well. The collected sample were selfreferred and tested, with the option of being anonymous, unless those who referred to our clinic as well for clinical assessment and treatment. The questions on our re-definition of impulsivity and BD have not previously been validated by others, and our finding of positive correlation with other symptom clusters of ADHD, i.e. hyperactivity and impulsivity is the first validation of these parts of questionnaire.

Conclusion

Behavioral disinhibition (BD) has been recognized in ADHD at least since 1973 by Pontius [**30**] when the condition was labeled as MBD (Minimal Brain Dysfunction) and known to be associated with Frontal lobe pathology. In later years

since the understanding of ADHD from a "hyperkinetic" or hyperactive condition moved to a more cognitive deficiency condition with emphasis on difficulties in sustain attention, working memory and executive function, BD was recognized as a cognitive deficit and labeled mostly as "response inhibition". But since ADHD-HI is a pathophysiological condition of the brain striatum in connection with the frontal, particularly the prefrontal cortex, so BD like hyperactivity and impulsivity is not only a cognitive deficit endophenotype, but a general symptoms cluster, affecting motoric, emotional and behavioral domains as well.

Therefore in the present research through our collected data in a group of adult ADHD, we showed the presence and significant correlation of BD in ADHD-HI along with hyperactivity and impulsivity. We demonstrated that BD is not only a cognitive deficit and issue, but a general behavioral problem leading to many post-morbidities or complications of untreated ADHD, involving risk taking, substance use and other misconduct behaviors. BD in fact was more associated with risk taking behavior, substance use than impulsivity that needs re-defining in DSM. We also showed that our new definition of impulsivity has more validity and stronger correlation with other cardinal symptom clusters of ADHD. Furthermore there was a differentiation between impulsivity and BD, in behavioral disinhibition being more associated with novelty than reward seeking that impulsivity is linked with.

In closing remarks, behavioral disinhibition needs to be recognized as a general behavioral symptoms cluster, a centerpiece and cardinal diagnostic symptom of ADHD-HI, due to its significance in leading to many costly consequences or post-morbidities such as risk taking, misconduct behaviors and substance use. In fact the screening of ADHD should not be only on academic under-achievements, but also on individuals with risk taking, such as driving carelessly and uncontrolled behaviors leading to many irreversible consequences.

References

- 1. Diagnostic and statistical manual of mental disorders: DSM-5. Arlington, VA: American Psychiatric Association 2013.
- 2. Moraleda-Barreno E, Díaz-Batanero C, Pérez-Moreno PJ, Gómez-Bujedo J, Lozano OM (2018) Relations between facets and personality domains with impulsivity: New evidence using the DSM-5 Section III framework in patients with substance use disorders. Personal Disord 9: 490-495.
- **3.** Curry I, Luk JW, Trim RS, Hopfer CJ, Hewitt JK, et al. (2018) Impulsivity Dimensions and Risky Sex Behaviors in an At-Risk Young Adult Sample. Arch Sex Behav 47: 529-536.
- 4. Um M, Hershberger AR, Whitt ZT, Cyders MA (2018) Recommendations for applying a multi-dimensional

model of impulsive personality to diagnosis and treatment. Borderline Personal Disord Emot Dysregul 5: 6.

- Starkstein SE, Robinson RG (1997) Mechanism of disinhibition after brain lesions. J Nerv Ment Dis 185: 108-114.
- **6.** Silveri MM, Rogowska J, McCaffrey A, Yurgelun-Todd DA (2011) Adolescents at risk for alcohol abuse demonstrate altered frontal lobe activation during Stroop performance. Alcohol Clin Exp Res 35: 218-228.
- 7. Cservenka A, Herting MM, Nagel BJ (2012) Atypical frontal lobe activity during verbal working memory in youth with a family history of alcoholism. Drug Alcohol Depend 123: 98-104.
- **8.** Spear LP (2018) Effects of adolescent alcohol consumption on the brain and behaviour. Nat Rev Neurosci 19: 197-214.
- **9.** Dalley JW, Roiser JP (2012) Dopamine, serotonin and impulsivity. Neuroscience 215: 42-58.
- **10.** Herman AM, Critchley HD, Duka T (2018) Risk-Taking and Impulsivity: The Role of Mood States and Interoception. Front Psychol 9: 1625.
- **11.** Stojek MM, Fischer S, Murphy CM, MacKillop J (2014) The role of impulsivity traits and delayed reward discounting in dysregulated eating and drinking among heavy drinkers. Appetite 80: 81-88.
- **12.** Douglas VI (1972) Stop, look, and listen: The problem of sustained attention and impulse control in hyperactive and normal children. Canadian Journal of Behavioural Science 4: 259-282.
- **13.** Quay HC (1988) Attention deficit disorder and inhibition systems: The relevance of the neuropsychological theory of Jeffrey Gray. In L. M. Bloomingdaly & J. Seargent Eds), Attention deficit disorder: Criteria, cognition, intervention. New York: Pergamon 117-126.
- **14.** Barkley RA (1997) Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. Psychol Bull 121: 65-94.
- **15.** Grafman Jordan, François Boller, Rita Sloan Berndt, Ian H Robertson, Giacomo Rizzolatti (2002) Handbook of Neuropsychology. Elsevier Health Sciences 103.
- **16.** Jarive HF (1954) Frontal lobe wounds causing disinhibition; a study of six cases. J Neurol Neurosurg Psychiatry 17: 14-32.
- **17.** Lane KS, St Pierre ME, Lauterbach MD, Koliatsos VE (2017) Patient Profiles of Criminal Behavior in the Context of Traumatic Brain Injury. J Forensic Sci 62: 545-548.
- **18.** Hughes LE, Rittman T, Robbins TW, Rowe JB (2018) Reorganization of cortical oscillatory dynamics underlying disinhibition in frontotemporal dementia. Brain 141: 2486-2499.
- **19.** Cummings JL (1995) Anatomic and behavioral aspects of frontal-subcortical circuits. Ann N Y Acad Sci 769: 1-13.
- **20.** Munakata Y, Herd SA, Chatham CH, Depue BE, Banich MT, et al. (2011) A unified framework for inhibitory control. Trends Cogn Sci 15: 453-459.
- 21. Tabibnia G, et al. (2011) Different forms of self-control

share a neurocognitive substrate. J. Neurosci 31: 4805-4810.

- 22. van Gaalen MM, Brueggeman RJ, Bronius PF, Schoffelmeer AN, Vanderschuren LJ (2006) Behavioral disinhibition requires dopamine receptor activation. Psychopharmacology (Berl) 187: 73-85.
- **23.** Wei W, Wang XJ (2016) Inhibitory Control in the Cortico-Basal Ganglia-Thalamocortical Loop: Complex Regulation and Interplay with Memory and Decision Processes. Neuron 92: 1093-1105.
- **24.** Wiecki TV, Frank MJ (2013) A computational model of inhibitory control in frontal cortex and basal ganglia. Psychol Rev 120: 329-355.
- **25.** Kalenscher T, Ohmann T, Güntürkün O (2006) The neuroscience of impulsive and self-controlled decisions. Int J Psychophysiol 62: 203-211.
- **26.** Bechara A, Tranel D, Damasio H (2000) Characterization of the decision making deficit of patients with ventromedial prefrontal cortex lesions. Brain 123: 2189-2202.
- **27.** McClure SM, Laibson DI, Loewenstein G, Cohen JD (2004) Separate neural systems value immediate and delayed monetary rewards. Science 306: 503-507.
- **28.** Wade TR, de Wit H, Richards JB (2000) Effects of dopaminergic drugs on delayed reward as a measure of impulsive behavior in rats. Psychopharmacology (Berl.) 150: 90-101.
- **29.** Diamond A (2002) A model system for studying the role of dopamine in prefrontal cortex during early development in humans. In: Johnson MH, Munakata Y, Gilmore RO, editors. Brain Development and Cognition: a Reader. Blackwell Press 2002: 441-493.
- **30.** Pontius AA (1973) Dysfunction patterns analogous to frontal lobe system and caudate nucleus syndromes in some groups of minimal brain dysfunction. Journal of the American Medical Women's Association 28: 285-292.
- **31.** Mattes JA (1980) Role of frontal lobe dysfunction in childhood hyperkinesis. Compre-hensive Psychiatry 21: 358-369.
- **32.** Chelune GJ, Ferguson W, Koon R, Dickey TO (1986) Frontal lobe disinhibition in attention deficit disorder. Child Psychiatry Hum Dev 16: 221-234.
- **33.** Shue KL, Douglas VI (1992) Attention deficit hyperactivity disorder and the frontal lobe syndrome Brain and Cognition 20: 104-124.
- **34.** Niedermeyer E, Naidu SB (1997) Attention-deficit hyperactivity disorder (ADHD) and frontal-motor cortex disconnection. Clin Electroencephalogr 28: 130-136.
- **35.** Nigg JT (2001) Is ADHD a disinhibitory disorder? Psychol Bull 127: 571-598.
- **36.** Depue BE, Burgess GC, Willcutt EG, Ruzic L, Banich MT (2010) Inhibitory control of memory retrieval and motor processing associated with the right lateral Prefrontal cortex: evidence from deficits in individuals with ADHD.Neuropsychologia 48: 3909-3917.
- **37.** Ellis AJ, Kinzel C, Salgari GC, Loo SK (2017) Frontal alpha asymmetry predicts inhibitory processing in youth with attention deficit/hyperactivity disorder.

Neuropsychologia 102: 45-51.

- **38.** Ishii S, Kaga Y, Tando T, Aoyagi K, Sano F, et al. (2017) Disinhibition in children with attentiondeficit/hyperactivity disorder: Changes in [oxy-Hb] on near-infrared spectroscopy during "rock, paper, scissors" task. Brain Dev 39: 395-402.
- **39.** Ueda S, Ota T, Iida J, Yamamuro K, Yoshino H, et al. (2018) Reduced prefrontal hemodynamic response in adult attention-deficit hyperactivity disorder as measured by near-infrared spectroscopy. Psychiatry Clin Neurosci 72: 380-390.
- **40.** Nigg JT, Willcutt EG, Doyle AE, Sonuga-Barke E (2005) Causal heterogeneity in attention-deficit/hyperactivity disorder: Do we need neuropsychological subtypes? Biol Psychiatry 57: 1224-1230.
- **41.** Nigg JT (2003) Response inhibition and disruptive behaviors: toward a multi-process conception of etiological heterogeneity for ADHD combined type and conduct disorder early-onset type. Ann N Y Acad Sci 1008: 170-182.
- **42.** Young SE, Friedman NP, Miyake A, Willcutt EG, Corley RP, et al. (2009) Behavioral disinhibition: liability for externalizing spectrum disorders and its genetic and environmental relation to response inhibition across adolescence. J Abnorm Psychol 118: 117-130.
- **43.** Aron AR, Poldrack RA (2005) The cognitive neuroscience of response inhibition: relevance for genetic research in attention-deficit/hyperactivity disorder. Biol Psychiatry 57: 1285-1292.
- **44.** Pliszka SR, Glahn DC, Semrud-Clikeman M, Franklin C, Perez R 3rd, et al. (2006) Neuroimaging of inhibitory control areas in children with attention deficit hyperactivity disorder who were treatment naive or in long term treatment. Am J Psychiatry 163: 1052-1060.
- **45.** Crosbie J, Arnold P, Paterson A, Swanson J, Dupuis A, et al. (2013) Response inhibition and ADHD traits: correlates and heritability in a community sample. J Abnorm Child Psychol 41: 497-507.
- **46.** Pine A, Shiner T, Seymour B, Dolan RJ (2010) Dopamine, time, and impulsivity in humans. J Neurosci 30: 8888-8896.
- **47.** Probst CC, van Eimeren T (2013) The functional anatomy of impulse control disorders. Curr Neurol Neurosci Rep 13: 386.
- **48.** Kim S, Lee D (2011) Prefrontal cortex and impulsive decision making. Biol Psychiatry 69: 1140-1146.
- **49.** Kaisari P, Dourish CT, Rotshtein P, Higgs S (2018) Associations Between Core Symptoms of Attention Deficit Hyperactivity Disorder and Both Binge and Restrictive Eating. Front Psychiatry 9: 103.
- **50.** Rubia K, Smith AB, Halari R, Matsukura F, Mohammad M, et al. (2009) Disorder-specific dissociation of orbitofrontal dysfunction in boys with pure conduct disorder during reward and ventrolateral prefrontal dysfunction in boys with pure ADHD during sustained attention. Am J Psychiatry 166: 83-94.
- **51.** Krebs RM, Schott BH, Düzel E (2009) Personality traits are differentially associated with patterns of reward and

novelty processing in the human substantia nigra/ventral tegmental area. Biol Psychiatry 65: 103-110.

- **52.** Anckarsäter H, Stahlberg O, Larson T, Hakansson C, Jutblad SB, et al. (2006) The impact of ADHD and autism spectrum disorders on temperament, character, and personality development. Am J Psychiatry 163: 1239-1244.
- **53.** Ströhle A, Stoy M, Wrase J, Schwarzer S, Schlagenhauf F, et al. (2008) Reward anticipation and outcomes in adult males with attention-deficit/hyperactivity disorder. Neuroimage 39: 966-972.
- **54.** Farrington DP (1989) Early predictors of adolescent aggression and adult violence. Violence Vict Summer 4: 79-100.
- **55.** Moffitt TE (1990) Juvenile delinquency and attention deficit disorder: boys' developmental trajectories from age 3 to age 15. Child Dev 61: 893-910.
- **56.** Hamshere ML, Langley K, Martin J, Agha SS, et al. (2013) High loading of polygenic risk for ADHD in children with comorbid aggression. Am J Psychiatry 170: 909-916.
- **57.** Shaw M, Hodgkins P, Caci H, Young S, Kahle J, et al. (2012) A systematic review and analysis of long-term outcomes in attention deficit hyperactivity disorder: effects of treatment and non-treatment.BMC Med 10: 99.
- **58.** Sihvola E, Rose RJ, Dick DM, Korhonen T, Pulkkinen L, et al. (2011) Prospective relationships of ADHD symptoms with developing substance use in a population-derived sample. Psychol Med 2011: 1-9.
- **59.** Biederman J, Petty CR, Dolan C, Hughes S, Mick E, et al. (2008) The long-term longitudinal course of oppositional defiant disorder and conduct disorder in ADHD boys: findings from a controlled 10-year prospective longitudinal follow-up study. Psychol Med 38: 1027-1036.
- **60.** Küpper T, Haavik J, Drexler H, Ramos-Quiroga JA, Wermelskirchen D, et al. (2012) The negative impact of attention-deficit/hyperactivity disorder on occupational health in adults and adolescents. Int Arch Occup Environ Health 85: 837-847.
- **61.** Chamorro J, Bernardi S, Potenza MN, Grant JE, Marsh R, et al. (2012) Impulsivity in the general population: a national study. J Psychiatr Res 46: 994-1001.
- **62.** Booij L, Swenne CA, Brosschot JF, Haffmans PM, Thayer JF, et al. (2006) Tryptophan depletion affects heart rate variability and impulsivity in remitted depressed patients with a history of suicidal ideation. Biol Psychiatry 60: 507-514.
- **63.** Bornovalova MA, Lejuez CW, Daughters SB, Zachary Rosenthal M, Lynch TR (2005) Impulsivity as a common process across borderline personality and substance use disorders. Clin Psychol Rev 25: 790-812.
- **64.** Butler GK, Montgomery AM (2004) Impulsivity, risk taking and recreational 'ecstasy' (MDMA) use Drug Alcohol Depend 76: 55-62.
- **65.** Carli M, Baviera M, Invernizzi RW, Balducci C (2006) Dissociable contribution of 5-HT1A and 5-HT2A receptors in the medial prefrontal cortex to different

aspects of executive control such as impulsivity and compulsive perseveration in rats. Neuropsychopharmacology 31: 757-767.

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