

**Chapter x**

Implicit Cognition: An Intermediate Phenotype for Addiction?

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### ***3.4 Implicit cognition as an endophenotype?***

While current evidence is scarce and indirect, we suggest that the pathways described above may connect various genetic variations influences to implicit cognition in addiction. Initial findings have connected some of the above genes to some forms of addiction-related implicit cognitive processes. Genetic influences involving attentional bias for alcohol have been found in a study with young adolescents and young adults (177). A dot probe task with alcoholic drinks and soft drinks was used to assess attentional bias to alcohol pictures. The risk variant in the *OPRM1* gene (the G-allele) was associated with a relatively strong attentional bias for alcohol in young adolescents, while the *DRD4 DRD4 7+* repeat VNTR was found to be associated with an attentional bias for alcohol in young adults. While we know of no other study relating attentional bias for alcohol to genetic factors, it should be noted that in research on anxiety, one of the above sources of genetic variation – serotonin-related polymorphisms related to stress - has been associated with attentional bias for emotional stimuli (178-181), see for a meta-analysis (182). A stronger attentional bias could be explained from increased emotional salience of stimuli and thereby a stronger influence on learning processes. It is well possible that in a subgroup of individuals with an attentional bias for threatening stimuli, this bias is coupled with a bias to approach alcohol (as a way to cope with the stress). Similar processes could influence the development of automatic associations, in two ways matching the basic dichotomy of internalizing and externalizing pathways to addiction. Interactions involving genes and implicit cognition have also been found for implicit memory associations (183). Only for subgroups with high-risk variants in *ALDH2* or *COMT*, were alcohol-coping associations (assessed with an IAT, see above) predictive of drinking behavior. Finally, as mentioned above, the risk variant of a polymorphism in

the *OPRM1* gene has been found to be related to relatively strong automatic approach tendencies for alcohol and other appetitive stimuli in male heavy drinkers (103).

Hence, individuals for whom drug use compensates for a genetic lack of sensitivity to normal reinforcement would form a group at risk for developing addiction-related approach tendencies. Individuals with a genetic tendency to experience strong negative emotions could experience greater reinforcement for drug use because it helps them avoid those emotions. In both cases, individuals with strong executive function would be better able to overcome the effects of these tendencies (see Figure 1).

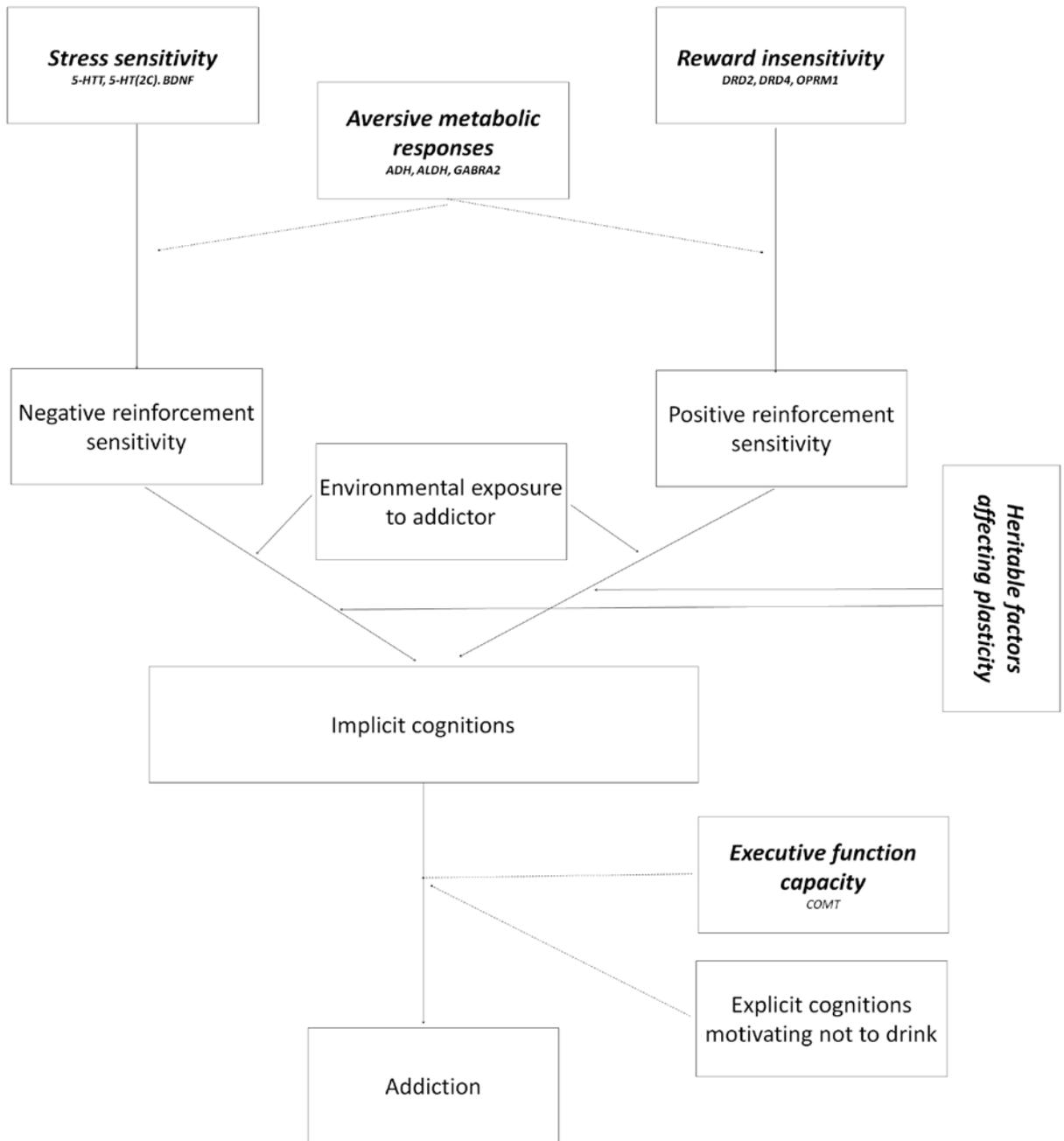


Figure 1. A heuristic model illustrating possible pathways to addiction, involving implicit cognitive processes.

To account for interactions between the various influences that are likely involved in addictive behaviors, an endophenotype for addiction would have to be defined in terms of constellations of pathways, with the common result of a tendency to develop difficult-to-control implicit cognitions directed towards addictive behaviors. There are two such constellations which we argue should be distinguished: the positive and negative reinforcement endophenotype. The positive endophenotype revolves around heritable biological deficits that drug use ameliorates (e.g., decreased ability for dopaminergic stimulation), while the core of the negative endophenotype is a general stress vulnerability that confers added negative reinforcement value on the acute effects of drugs. For example, coping drinking would be considered an expression of the latter pathway, and would be expected to be associated with different genes than individuals with different drinking motivation. On the other hand, other genetic factors would be expected to have common effects in either endophenotype: genetic variation that renders drug metabolism aversive should always be protective, as would factors that increase ECFs.

#### **4. Conclusion**

From an implicit cognition or dual-process perspective, the endophenotype for addiction vulnerability would consist of a set of interrelated genetically influenced factors: (1) non-aversive metabolism of the addictor; (2) enhanced (positive or negative) reinforcement of acute effects; (3) relatively weak ECFs. The “perfect storm” would involve all factors working towards a tendency to addiction. This vulnerability would be expected to be expressed at a behavioral level as a common endophenotype, defined in terms of automaticity development: the ease with which hard-to-control cognitive biases arise from addictor-related reinforcement. The measurement of such an endophenotype would require novel methods for detecting

such vulnerability, possibly involving experimentally controlled tests of automaticity development (for an example of such an approach, see 184). From the perspective sketched above, research focusing on genetic variation and implicit cognition, and in particular the development of implicit cognitive processes, may be highly relevant to understanding the biological basis of the vulnerability to addiction.

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