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Discussion forum

Neuroscience, neuroimaging and the law

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1. Introduction

Violence is a phenomenon we are daily confronted with in the media and everyday life. Yearly more than one and a half million of humans are reported to lose their lives due to violence. Violence has links to aggression, an almost universal phenomenon in animal kingdom that may in some instances serve the purpose of survival of species (e.g., the maternal aggression for defending offspring). Violence is classified according to target and mode. Our focus here is on the individual violent behavior toward others and contributions from neuroimaging to understanding its putative neurobiological underpinnings and reframing the "nature-nurture" debate.

Historical tracing of the nature-nurture discussion concerned with the etiology of individual violent and criminal behavior reveals back and forth shifts from biological to environmental determinism. At one pole of the dialectics, we find incisive arguments for an incorrigible biological determinism, at the other, an embracement of a naïve environmental causality (Heide and Solomon, 2006; Caspi et al., 2010). Despite persistence of terminologies such as "genes of violence" or "born to be criminal" in both scientific literature and media, a careful review of recent advances in neuroscience, genetics, epigenetics and neuroimaging nowadays paints a more nuanced and complex picture of the current neuroscientific understanding of the underpinnings of the individual violent behavior. Individual violent behavior can be viewed as a complex behavior that arises from a dynamic and likely time-sensitive interplay between genes and environment (including personal and cultural environment). Advances in the epigenetic field have taught us that genes (nature) and environment (nurture) cannot anymore be seen as separate, additive entities. Instead environmental factors can influence gene expression and brain development and synaptic plasticity in a time-dependent fashion. This suggests a role for time-sensitive environmental manipulations and opens a pathway of hope for designing violence prevention strategies.

2. Possible brain bases of violence and anti-social behavior

As Paus (2005) underlined, the initial search for neural correlates of aggressive behavior targeted pathological, anti-social forms of aggression in individuals who suffered brain trauma or individuals without known history of brain damage who committed severe violent acts. More recently the scope of this search has broadened, aiming to additionally unearth the neural underpinnings of so-called normative, developmental physical aggression and its resolution mechanisms. [Developmental aggression – in the form of hitting, biting – is a common occurrence in childhood, starting around age 1 year, arguably peaking around 3.5 years of age and decreasing afterwards (Tremblay, 2008)].

The first descriptions of Phineas Gage more than 160 years ago (Harlow, 1848) already suggested that brain damage – particularly of the ventromedial or orbital frontal cortex – may lead to changes in personality (impulsivity), social behavior and cognition. Working in railway construction, Phineas Gage had had an accident whereby a crowbar longer than 1 m entered and exited his forehead after a dynamite explosion. Gage survived, but – though this is nowadays controversially discussed – lost his foresight and planning abilities. Several decades after Harlow, other researchers emphasized the importance of prefrontal cortex for behavioral and emotional regulation and character formation (Welt, 1888).

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The studying of brain–behavior relationships took a new dimension with the advent of a wide range of structural and functional brain imaging techniques, which allow refined analyses of structure–function relations (Paus, 2005; Glenn and Raine, 2008). Studies of patients with lesions of ventromedial prefrontal cortex underscored the importance of the integrity of this area for experiencing guilt and capacity for affective theory of mind (that is linked to empathy) (Krajbich et al., 2009). The employment of neuroimaging in the case of a family father, who suddenly engaged in pedophilic behavior with his own children, enabled positive outcomes (Burns and Swedlow, 2003). During his imprisonment he was diagnosed with a right orbitofrontal cortex tumor. Its surgical removal resulted in complete remission of his pedophilic behavior and urges and subsequent family reintegration.

Identifying early biomarkers and protective and predisposing environmental factors is nowadays seen as imperative for designing violence prevention strategies. Developmental studies point to conditions associated with various anti-social behaviors that may be precursors of later violent behavior, such as conduct disorder. This may explain the increase in neuroimaging studies targeting young population (Crowe and Blair, 2008).

Carrying out imaging studies in youth poses several challenges, however (Paus, 2010). Children and adolescents with conduct disorder are far from being a homogenous population, a fact that was unfortunately neglected by certain studies (Hodgins et al., 2009). Some children with conduct disorder present with callous-unemotional traits and low anxiety levels, while others, on the contrary, experience co-occurring anxiety disorders. This differentiation is important not only for interpreting imaging studies data, but also for designing effective treatment strategies. For example, in comparison with other children with conduct disorder, those endorsing callous-unemotional traits do not respond to normative forms of punishment, such as time-out (Hawes and Dadds, 2005). Attention-hyperactivity deficit disorder is a possible comorbidity of children and adolescents with conduct disorder, but magnetic resonance imaging (MRI) selection limitations may affect data acquisition and interpretation in children or adolescents who are highly prone to move during scanning. Several brain imaging studies evaluated children with conduct disorder with a wide age distribution (Hodgins et al., 2009). Recently large-scale magnetic resonance normative developmental studies point however to non-linear and sex-differentiated development of the human brain, calling for developmental and sex-sensitive imaging investigating approaches (Paus, 2010).

Aside from frontal lobes, an impressive amount of work has focused on amygdala. Amygdalar malfunctioning was proposed to be involved in anti-social behavior and other social behavior deviances. Impulsive-affective forms of violent-aggressive behavior were linked to a functional hyperactivity of the limbic system (amygdala) in patients with various psychiatric or neuropsychiatric conditions (Siever, 2008). Psychopathy that can be accompanied by both instrumental and impulsive forms of violence seems however to be associated with a lower functional activity of the amygdala across various tasks (e.g., Marsh et al., 2008). Face-emotion processing is important for social behavior and the amygdala was identified to be part of the face processing neural network (Tahmasebi et al., 2011). Several conditions may be associated with various patterns of engagement of amygdala during face-emotion processing (Staniloiu and Markowitsch, 2010). In youth with psychopathic (callous-unemotional) traits reduced amygdala activation to fearful expression was found (Marsh et al., 2008).

A recent study that reported that poor fear conditioning at age three predicted criminal activity in adulthood ignited an even more pronounced interest in the amygdala and speculations about its role in the emergence of violent criminal behavior (Gao et al., 2010). Our and other researchers' experience with patients with relatively selective bilateral amygdala damage, due to a rare genetic condition – Urbach–Wiethe disease – shows that indeed they have abnormalities of fear reactions and experience, as well as some social behavior deficits (Markowitsch et al., 1994; Markowitsch and Staniloiu, 2011). However there have been no reports of increased risk for violence in these patients, according to our knowledge. This points to several important aspects of structure–function relations interpretations. As animal studies suggest, depending on its onset, amygdala damage may have a differential impact on the development of its connected structures, leading to various phenotypes. The employment of different MRI scanners may explain incongruent findings of amygdalar volume, such as in adults with psychopathy. Amygdalar malfunctioning as evidenced by imaging studies, might not reflect amygdala's deficiency per se, but a connectivity issue. Amygdala is a hub that integrates emotion with cognition and has multiple connections with subcortical and cortical areas. In fact, one study reported in adult men with psychopathy microstructural changes of the uncinate fascicle that links fronto-temporal areas (Craig et al., 2009). Furthermore, particular neural circuits are engaged to support specific tasks in a given context. Context (including culture) is an important ingredient that has to be taken into consideration when performing imaging studies and there are indeed suggestions that the amygdala may be sensitive to context, including cultural influences (Markowitsch and Staniloiu, 2011).

3. Imaging genetics, violence and anti-social behavior

The heritability of physical aggression was estimated to be around 50% (Brendgen et al., 2005) (40–80%, depending on methods and subjects), underscoring that complex behaviors result from gene-environment interplays (Meyer-Lindenberg et al., 2006). Several gene variants may increase susceptibility to violent behavior. Except for a minority (Brunner et al., 1993), these variants are common in general population and are not solely implicated in the chain leading to violence, but together with other genes and/or interacting environmental factors.

The promoter polymorphism associated with low expression of the monoamine-oxydase-A enzyme (MAOA) gene in vitro (low active allele-MAOA-L) is common in population, but was found by a seminal study to predict higher risk for impulsive violence in New Zealander white men of European heritage only in association with a history of severe

maltreatment in childhood (Caspi et al., 2002; Kim-Cohen et al., 2006). As opposed to what some people may have wrongly interpreted as genetic determinism, the results of this study in fact emphasize the complex influence of environmental factors on gene expression, which may be time-dependent (taking place during certain windows of vulnerability). Indeed both recent animal and human data draw attention to the role of early life experiences in modifying gene expression via epigenetic mechanisms (McGowan et al., 2009). Furthermore the study of Caspi et al. (2002) suggests that the effects of MAOA gene and its interacting genes and/or environmental factors may differ between ethnic groups (perhaps partly due to specific gene–gene interactions effects), indirectly pointing to the risk of possible misuse of genetic information (Caspi et al., 2010).

Despite terms such as "genes of violence" still being part of the media and literature repertoire, it is widely known that genes in fact do not code for violence, but for proteins. Certain genetic variations may lead to subtle molecular abnormalities, which, in conjunction with other genetic and/or environmental factors, could alter synaptic plasticity, neural circuits and information processing, which may in turn influence one individual' s predisposition for violent behavior.

How genetic polymorphisms resulting in subtle molecular abnormalities shape brain structures and functions and account for interindividual variability constitutes the focus of imaging genetics. Employing structural and functional MRI and using a candidate gene approach, Meyer-Lindenberg et al. (2006) showed that MAOA-L was associated with sex-differentiated morphological and structural changes of the cortico-limbic system in healthy carriers, such as reduced volumes of amygdala, cingulate cortex, hippocampus, larger volumes in lateral orbitofrontal cortex (only in males), hyperactivity of the amygdala during emotional tasks and reduced regulation of the amygdala by the orbitofrontal and anterior cingular cortex.

4. Conclusions

Individual violent behavior is a complex behavior that arises from a dynamic and likely time-sensitive interplay between genes and environment. Advances in the field of epigenetic suggest the possibility of modifying at least some of the genes' effects through environmental manipulations, such as changes in lifestyle habits or specific psychotherapeutic interventions. A crucial task for the future is to describe valid environmentally mediated factors that interact with genes to increase the risk for individual violent behavior. This will benefit from taking multiple research approaches (both cross-sectional and longitudinal) and involving several disciplines. Longitudinal prospective developmental studies, coupled with genome wide association studies, a rigorous characterization of the phenotypes (both behavioral and neuropsychological) and a broadening of the conceptual understanding of the environment to encompass elements of the personal (lifestyle habits), family and socio-cultural environment are needed to further our understanding of the gene and environmental factors' contribution to the risk for violence and design timely and optimally tailored preventive and treatment strategies.

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