Neurosciences and the Human Person: New Perspectives on Human Activities
Pontifical Academy of Sciences, *Scripta Varia* 121, Vatican City 2013
www.casinapioiv.va/content/dam/accademia/pdf/sv121/sv121-posner.pdf

How Genes and Experience Shape the Human Will[1]

Michael I. Posner, Mary K. Rothbart,
Pascale Voelker[2] & Yi-Yuan Tang[3]

In this paper we examine mechanisms underlying *will*. By *will* we refer to the means through which our intentions lead to our thoughts and behaviors. In psychology these mechanisms are variously called self regulation in childhood and self or cognitive and emotional control in adults. In our view all these various names refer to specific brain networks that comprise the organ system involved in attention (Posner, 2012).

During early development, attentional orienting operates in conjunction with the actions of caregivers to provide regulation of behavior. This association underlies the frequent observation that infants and young children are largely controlled by their environment including caregivers. Later the executive attention network comes to dominate self regulation allowing internal goals to guide behavior. In this paper we trace the development of the mechanisms through which volition operates. We consider both the common networks that serve as mechanisms of voluntary control for all people and individual differences in the efficiency of these networks. We stress the joint role of genes and experience, including parenting, in the development of the will and in the ability to modify it through training. Finding the mechanisms of will may further our understanding of the extent to which will is constrained as well as free.

Self Regulation and Attention

Imaging the human brain by use of functional magnetic resonance (fMRI) has revealed brain networks related to specific aspects of attention including obtaining and maintaining the alert state, orienting to sensory stimuli and resolving conflict among competing responses (Posner & Petersen, 1990; Petersen & Posner, 2012).

[1] This paper is based on a lecture at the Vatican Nov. 8, 2012 by the first author. This research was supported by NICHD Grant HD 060563 and Office of Naval Research grant N000141110034 to the University of Oregon.

[2] University of Oregon, Eugene OR USA.

[3] Texas Tech University, Lubbock TX USA.

The alerting network is modulated by the brain's norepinephrine system and involves major nodes in frontal and parietal cortex. The alert state is critical to high-level performance. Phasic changes in alertness can be produced by the presentation of a warning of an impending target. This leads to a rapid change from a resting state to one of increased receptivity to the target.

The orienting network interacts with sensory systems to amplify information relevant to task performance. The orienting network exerts much of the regulatory control present during infancy and early childhood (Posner, Rothbart, Sheese & Voelker, 2012; Rothbart, Sheese, Rueda & Posner, 2011).

The executive network is involved in resolving competing actions in tasks where there is conflict. This is done both by enhancing activity in networks related to our goals and inhibiting activity in conflicting networks. These controls are effected by long connections between the nodes of the executive network and cognitive and emotional areas of the frontal and posterior brain. In this way the executive network is important for voluntary control and self regulation (Bush, Luu & Posner, 2000; Sheth *et al.,* 2012). Effortful control is a higher order temperament factor assessing self regulation that is obtained from parent report questionnaires (Rothbart, 2011). In childhood, performance on conflict related cognitive tasks is positively related to measures of children's effortful control (Rothbart, 2011). During childhood and in adulthood effortful control is correlated with school performance and with indices of life success, including health, income and successful human relationships (Checa & Rueda, 2011; Moffitt *et al.,* 2011).

There are individual differences in the efficiency of each of the three networks. The Attention Network Test (ANT) was devised as a means of measuring these differences (Fan *et al.,* 2002). The task requires the person to press one key if a central arrow points to the left and another if it points to the right. Conflict is introduced by having surrounding flanker arrows point in either the same (congruent) or the opposite (incongruent) direction. Cues presented prior to the target provide information on where or when the target will occur. Three scores are computed that are related to the performance of each individual in alerting, orienting and executive control. In our work we have used the Attention Network Test (ANT) to examine the efficiency of brain networks underlying attention (Fan *et al.,* 2002). A children's version of this test is very similar to the adult test, but replaces the arrows with fish (Rueda *et al.,* 2004).

Studies have shown moderate reliability of conflict scores, but much lower reliability for the orienting and alerting scores (MacLeod *et al.,* 2010) and recent revisions of the ANT provide better measures of orienting and alerting that may improve these results (Fan *et al.,* 2010). The attentional networks involve different cortical brain areas (Fan *et al.,* 2005), and scores on the ANT are related to distinct white matter pathways (Niogi & McCandliss, 2009) and structural differences in cortical thickness (grey matter) (Westlye, Grydland, Walhove, Fjell, 2011). The ANT and its various revisions show significant interaction between networks (Callejas, Lupianex & Tudela, 2004; Fan *et al.,* 2010). It is clear that the networks communicate and work together in many situations, even though their anatomy is distinct.

The dorsal part of the anterior cingulate cortex (ACC) is involved in the regulation of conflict in cognitive tasks, while the more ventral part of the cingulate is involved in regulation of emotion (Bush, Luu & Posner, 2000). One way to examine this issue is to image the structural connections of different parts of the cingulate using diffusion tensor imaging (DTI). This form of imaging traces the diffusion of water molecules in along myelinated fibers, and provides a means of examining the physical connections present in the brain. DTI studies have shown that the dorsal part of the ACC is connected primarily to parietal and frontal lobes, while the ventral part of the ACC has strong connections to subcortical limbic areas (Posner, Sheese, Odulas and Tang 2006).

The executive attention network also includes the underlying basal ganglia and adjacent areas of the prefrontal cortex. There is evidence that the anterior insula is involved particularly when switching between tasks (Supekar & Menon, 2012), while adjacent midprefrontal cortex is important during complex decision making (Behrens, 2012). Comparative anatomical studies point to important differences in the evolution of cingulate connectivity between non-human primates and humans. Anatomical studies show the great expansion of white matter, which has increased more in recent evolution than has the neocortex itself (Zilles, 2005). One type of projection cell called the Von Economo neuron is found only in the anterior cingulate and a related area of the anterior insula, two brain areas that are active together even when the person is resting and not performing a task (Allman, Watson, Tetreault, and Hakeem, 2005; Dosenbach *et al.,* 2007)**.** It is thought that von Economo neurons are important in communication between the cingulate and other brain areas. This neuron is not present at all in macaques and its frequency increases between the great apes and adult humans. Moreover, there is some evidence that the frequency of the neuron increases in development between infancy and later childhood (Allman, *et al.,* 2005).

Development of Self Regulation

Resting State Studies

It has recently become common to study the brains of children and adults while they are resting (resting state rsMRI; Raichle, 2009). One of the brain networks active during rest is the executive attention network involved in resolving conflict and related to parent reports of effortful control (Dosenbach *et al.,* 2007; Fair *et al.,* 2009). Resting state methods can be applied at any age because they do not require a task. Studies have examined how brain networks change with age (Fair *et al.,* 2009; Gao, *et al.,* 2009). Resting state studies have found that during infancy and early childhood most brain networks involve short connections between adjacent areas, but the long connections important for self regulation develop slowly over childhood (Fair *et al.,* 2009; Gao *et al.,* 2009). Development of this system may relate to the achievements in self regulation that we have documented between infancy and 7-8 years of age (Rueda *et al.,* 2004). A study using fMRI for 725 children from 4 to 21 years showed a relationship between the ability to resolve conflict in a flanker task and the size of the right dorsal anterior cingulate in the early years of childhood as well as the connectivity of the cingulate in later years (Fjell *et al.,* 2012).

Longitudinal Study

In our work we found that 7-month-old infants activated the anterior cingulate when they detected an error (Berger, Tzur & Posner, 2006; Wynne, 1994), showing that they have rudimentary executive attention in place, even though parents are not yet able to report on effortful control and infants do not carry out instructed behaviors. It was not until age three that children began to show regulation of their behavior by slowing their next response following an error as adults do (Jones, Rothbart & Posner, 2003).

We conducted a longitudinal study on the development of self regulation during infancy and childhood. The testing began when the infants were 7 months old. Because infants are not able to carry out voluntary attention tasks, we used a visual task in which a series of attractive stimuli are put on the screen in a repetitive sequence (Clohessy, Posner & Rothbart, 2001; Haith, Hazan & Goodman, 1988). Infants orient to them by moving their eyes (and head) to the location. On some trials infants showed they anticipated what was coming by orienting prior to the stimulus. We found (Sheese *et al.,* 2008) that infants who made the most anticipatory eye movements also exhibited a pattern of cautious reaching toward novel objects that predicts effortful control in older children (Rothbart, 2011). In addition, infants with more anticipatory looks showed more spontaneous attempts at self regulation when presented with somewhat frightening objects.

We retested and genotyped the children at age 18 to 20 months and tested them again at about age 4 when they were able perform the ANT as a measure of executive attention. We found that the early regulatory effects in infancy and at age 2 were correlated with their later orienting network scores rather than their executive network performance in the ANT. In addition, we found that in infancy orienting of attention was related to lower negative and higher positive affect. By age two, orienting was no longer related to affect, but later in childhood and for adults, effortful control is related to lower negative affect (Rothbart, 2011).

These findings led us to the view that the orienting network provides the primary regulatory function during infancy. The orienting network continues to serve as a control system, but starting in childhood the executive attention appears to dominate in regulating emotions and thoughts (Isaacowitz, 2012; Posner *et al.,* 2012; Rothbart *et al.,* 2011). This parallel use of the two networks fits with the findings of Dosenbach *et al.* (2007) that in adults the frontal-parietal network controls task behavior at short time intervals whereas the cingulo-opercular network exercises strategic control over long intervals.

Our general view is that cognitive and emotional control systems arise as part of attentional networks. Our view contrasts with some general views of cognitive development that see self control as arising out of the child's ability to employ language to implement control (Luria, 1973; Vygosky, 1934). While we do not deny that language plays an important role in development, we have observed young children when they attempt to exercise control of dominant responses in Simple Simon type games (Jones *et al.,* 2005). In general, self regulation involved physical actions such as children sitting on their hands or holding one hand with the other, rather than self instruction by language. In addition, the importance of the growth of the right rather than the left ACC in self regulation (Fjell *et al.,* 2012) and association of self regulation with attentional orienting support a separation of control from language. It seems to us that previous work has failed to recognize the separate evolutionary development of attention systems as a basis for control, placing too much emphasis on language as a uniquely human control system.

Physical changes in connectivity

The changes in connectivity during development reported in resting state MRI studies involve functional connectivity based upon correlations between BOLD activity in separated brain areas. Is there evidence of the actual physical changes in the white matter thought to underlie these correlations? Our recent work with adults using DTI has uncovered white matter changes that have similarities to those found in development. Training adults might thus allow us to uncover how the connections developing during childhood support the changes in self control between infancy and adults.

During development there is a large change in the physical connections between brain areas. The number of axons connecting brain areas increases followed by an increase in the myelin sheath that surrounds the axon and provides insulation. Together these changes result in more efficient connections (Lebel *et al.,* 2012). Fractional anisotropy (FA) is the main index for measuring the integrity of white matter fibers when using DTI.

In our work we studied FA in college students before and after a form of mindfulness meditation called Integrated Body Mind Training (IBMT) in comparison to a control group given the same amount of relaxation training. We found clear improvement in the executive attention network after only five days of training. After two to four weeks of training we found significantly greater change in FA following meditation training than following the relaxation training control in all areas of connectivity of the ACC, but not in other brain areas (Tang *et al.,* 2010).

These alterations in FA could originate from several factors such as changes in myelination, axon density, axonal membrane integrity, axon diameter and intravoxel coherence of fiber orientation and others. Several DTI studies have examined axial diffusivity (AD) and radial diffusivity (RD), the most important indices associated with FA, to understand the mechanisms of FA change (Bennett *et al.,* 2010; Burzynska *et al.,* 2010). Changes in AD are associated with axon morphological changes, with lower AD value indicating higher axonal density. In contrast, RD implicates the character of the myelin. Decreases in RD imply increased myelination, while increases represents demyelination.

In our study (Tang *et al.,* 2012) – we investigated AD and RD where FA indicated that integrity of white matter fibers was enhanced in the IBMT group more than control group. We found that after two weeks there were changes in axonal density but not in myelination. In some areas these changes in axonal density were correlated with improved mood and affect as measured by self report. After 4 weeks of training we found evidence of myelination changes. Since the developmental changes in childhood first involve changes in axonal density and only later myelination, our training may provide changes that are somewhat similar to those found in development. If so, it might be possible to use training to study how physical changes in connectivity alter aspects of control including reaction time, control of affect, stress reduction and other changes found with meditation training.

Genes and Environment

We have pursued two strategies to help understand how genes are related to the individual efficiency of attention networks. One approach involves adults and uses the association of attentional networks with particular neuromodulators (Green *et al.,* 2009; see also Table 1). These associations have led to identification of candidate genes that are expected to relate to each network. The results were summarized by Green *et al.,* (2009) and are shown in Table 1. Since 2009 a number of other results have qualified the view somewhat. It seems clear that serotonin as well as dopamine can influence the executive attention network (Reuter *et al.,* 2007), and that there are interactions between dopaminergic and cholinergic genes at the molecular level that modify the degree of independence between them (Market *et al.,* 2010). Nonetheless the scheme in Table 1 provides a degree of organization and prediction that is often lacking in studies of genetic influence on cognition and behavior.

Table 1. Relating Attention Networks to Dominant Modulators and Genetic Alleles

NETWORK	MODULATOR	GENES
ALERTING	NOREPINEPHRINE	ADRA2A NET
ORIENTING	ACETYCHOLINE	CHRNA4 APOE
EXECUTIVE	DOPAMINE	DRD4, DAT1, COMT MAOA, DBH
	SEROTONIN	TPH2, 5HTT

This table adapted from Green *et al.,* 2008

Some individuals have stronger activations and connectivity than others and are thus better able to exercise the various functions of self regulation. Moreover childhood assessments of effortful control (Moffitt *et al.,* 2011) and self regulation (Casey, *et al.,* 2011) predict performance as adults. How do these differences arise? In part they are due to genetic variations. However, environmental influences and learning can also lead to differences in efficiency; so experience and genetics are not separate influences but frequently interact. Gene expression, for example, can be altered by the environment in which the genes operate. Genetic differences can also influence the degree to which specific experience is effective in leading to learning (Belsky & Pluess, 2009). Our genes thus influence the degree to which our behavior is altered by experience. This is a far cry from the view of immutability of genes that might underlie the idea that our weaknesses are unchangeable (see also Spector, 2012).

We illustrate the complex interaction between genetic variation and environmental influence with results obtained in our longitudinal study that involve the 7-repeat allele of the DRD4 gene. This allele has been associated with attention-deficit/hyperactivity disorder (ADHD) and the temperamental quality of sensation seeking. Evidence that environment and/or experience can have a stronger influence in individuals with the 7-repeat allele has been reported (Bakermans-Kranenburg and van Ijzendoorn, 2006; van Ijzendoorn & Bakermans-Kranenburg, 2006). Moreover, in one study an intervention that increased parent use of positive discipline reduced externalizing behavior in toddlers with the 7-repeat allele of the DRD4 gene significantly more than for those without this allele (Bakersman-Krannenburg, Ijzendoorn, Pijlman, Mesman, & Juffer, 2008). This finding is important because assignment to the intervention group was random, thus ensuring that the result is not due to something about the parents other than the training.

In our longitudinal study conducted at the University of Oregon, cheek swabs were used to collect DNA samples and genetic variation was identified in twelve genes that had been related to attention in adult studies (Sheese, Voelker, Rothbart, & Posner, 2007). The children had been evaluated when they were 7 months old, and genotyping took place when they returned to the laboratory at about 2 years of age. In addition, parenting quality was examined through observation of caregiver–child interactions in which the children played with toys in the presence of one of their caregivers. Raters reviewed videotapes of the caregiver–child interaction and rated the parents on five dimensions of parenting quality according to a schedule developed by NICHD (1993): support, autonomy, stimulation, lack of hostility, and confidence in the child. According to their scores, parents were divided at the mean into two groups: one showing a higher quality of parenting, and the other a lower quality. Results showed an interaction between parenting quality and variation of the DRD4 gene. For children with the 7-repeat allele, there was a strong influence of parenting quality. Children with the 7-repeat allele and lower quality parenting were high in impulsivity while those with higher quality parenting were normal in impulsivity. Children without the 7 repeat allele showed normal levels of impulsivity regardless of parent quality. Similar results were obtained for activity level and high-intensity stimulation seeking, which can be combined with impulsivity into one aggregate measure of sensation seeking.

Some evidence suggests that the 7-repeat allele is under positive selective pressure in recent human evolution (Ding, Chi, Grady, Morishima, Kidd, *et al.,* 2002). Why should an allele that has been found to be over represented in Attention Deficit Disorder (ADHD) be undergoing positive selection? We think that positive selection of the 7-repeat allele could well arise from its sensitivity to environmental influences. Parenting provides training for children in the values favored by the culture in which they live. For example, Rothbart and colleagues (Ahadi, Rothbart, & Ye, 1993) found that in Western culture, effortful control appears to regulate negative affect (sadness and anger), while in China (at least in the 1980s) it was found to regulate positive affect (outgoingness and enthusiasm). In recent years, the genetic part of the nature-by-nurture interaction has been given a lot of emphasis. Theories of positive selection in the DRD4 gene have stressed the role of sensation seeking in human evolution (Harpending & Cochran, 2002; Wang, Kodama, Baldi, & Moyzis, 2006). The finding that individual differences in impulsivity may be influenced by the interaction between genetics and parenting style do not contradict this evolutionary emphasis, but suggest a form of explanation that could have even wider significance. If genetic variations are selected according to their sensitivity to cultural influence, this could fit with evidence that the 7 repeat allele is under positive selective pressure and is over represented among the elderly (Grady *et al.,* 2013). It remains to be seen whether the other 300 genes estimated to show positive selection would also increase an individual's sensitivity to variations in rearing environments.

How could variation in genetic alleles lead to enhanced influence of cultural factors such as parenting? The anterior cingulate receives input pertaining to both reward value and pain or punishment, and this information is clearly important in regulating thoughts and feelings. Dopamine is the most important neuromodulator in these reward and punishment pathways. Thus, changes in the response to dopamine could enhance the influence of signals from parents related to reward and punishment. Because the ACC is important in executive attention, we expected that the 7 repeat influence on behavior was mediated by executive attention. However, in the study by Sheese and colleagues (2007), data showed that at two years there was no influence of the 7-repeat allele on executive attention; rather, the gene and environment interacted to influence the child's behavior as observed by the caregiver. However, the same children at age 4 did show an interaction between the presence of the DRD4 7-repeat allele and parenting quality in determining effortful control and this effect has been replicated in another study (Sheese *et al.,* 2012; Smith *et al.,* 2012). Since effortful control is linked to executive attention, this finding suggests that the executive network could be a mechanism for the widespread effects of Gene x Environment interactions, at least in older children and adults. Thus the DRD4 7 repeat allele may operate through executive attention after age 4 but through some other mechanism before executive attention is sufficiently developed.

There is other evidence that despite changes in the brain and behavior, the DRD4 7 repeat allele may play the same role in adults as in children. This study (Larson, *et al.,* 2010) exposed young adolescents to either high or low levels of alcohol consumption by peers. Adolescents with the 7 repeat allele were more influenced in their drinking by peer behavior than those without the 7 repeat.

We have illustrated the way parenting and other environmental influences may show continuity, despite changes in the underlying control networks, with the story of only one genetic allele. However, a recent selective review of the longitudinal literature (Ronald, 2011) reaches a similar conclusion over a larger number of genes and studies. More data in this area are needed to better understand the mechanisms by which genes operate over the lifespan.

This paper has examined attention and the mechanisms supporting will. We view will as involving regulation of cognitive and emotional systems, and argue that such self regulation is carried out in older children and adults by the executive attention network. We have traced the early reliance of control on the orienting network and seen how during development control shifts to the executive network. We have examined methods of changing the efficiency of self regulation through training as a model for what might happen in development. Finally we examined how genes influence the degree to which training can shape self regulation. We hope that this approach will eventually provide a more complete picture of the origins and neural systems of voluntary control and provide scientific data on the constraints that operate on *will.*

References

Ahadi, S.A., Rothbart, M.K., & Ye, R. (1993). Children's Temperament in the U.S. and China: Similarities and differences. *European Journal of Personality,* 7, 359-378.

Allman, J., Watson, K.K., Tetreault, N.A., & Hakeem, A.Y. (2005). Intuition and autism: A possible role for von Economo neurons. *Trends in Cognitive Science,* 9:367-373.

Bakermans-Kranenburg, M.J., & van Ijzendoorn, M.H. (2006). Gene-environment interaction of the dopamine D4 receptor (DRD4) and observed maternal insensitivity predicting externalizing behavior in preschoolers. *Developmental Psychobiology*, *48*, 406-409.

Bakersmans-Kranenburg, M.J., van Ijzendoorn, M.H., Pijlman, F.T.A., Mesman, J., & Juffer, F. (2008). Experimental evidence for differential susceptibility: Dopamine D4 receptor polymorphism (DRD4VNTR) moderates intervention effects on toddlers externalizing behavior in a randomized controlled trial. *Developmental Psychology, 44*, 293-300, doi:10.1037/0012-1649.44.1.293

Behrens, T.E. (2013). Neural mechanisms underlying human choice in frontal cortex. In Pontifical Academy of Sciences, *Neurosciences and the Human Person*, Proceedings of the Working Group of 8-10 November 2012, *Scripta Varia* 121, Vatican City.

Belsky, J., & Pluess, M. (2009). Beyond diathesis stress: Differential susceptibility to environmental stress. *Psychological Bulletin*, 135:895-908.

Bennett I.J., Madden D.J., Vaidya C.J., Howard D.V., Howard J.H., Jr. (2010). Age-related differences in multiple measures of white matter integrity: A diffusion tensor imaging study of healthy aging. *Hum. Brain Mapp.* 31:378-390.

Berger, A., Tzur, G., & Posner, M.I. (2006). Infant brains detect arithmetic errors. *Proceedings of the National Academy of Science of the United States of America*, *103*, 12649-12653, doi:10.1073/pnas.0605350103

Burzynska AZ, *et al.,* (2010). Age-related differences in white matter microstructure: region-specific patterns of diffusivity. *Neuroimage* 49: 2104-2112.

Bush, G., Luu, P. & Posner, M.I. (2000). Cognitive and emotional influences in the anterior cingulate cortex. *Trends in Cognitive Science*, 4/6:215-222.

Callejas, A. Lupianez, J. & Tudela, P. (2004). The three attentional networks: on their independence and interactions. *Brain and Cognition* 54(3) 225-227.

Casey, B.J. *et al.,* (2011). Behavioral and neural correlates of delay of gratification 40 years later. Proceedings of the National Academy of Sciences USA 108/36, 14998-1503.

Checa, P. & Rueda, M.R. (2011). Behavior and brain measures of executive attention and school competence in late childhood *Developmental Neuropsychology* 36/8, 1018-1032, doi:10.1080/87565641.2011.591857

Clohessy, A.B., Posner, M.I., & Rothbart, M.K. (2001). Development of the functional visual field. *Acta Psychologica*, 106:51-68.

Ding, Y.C., Chi, H.C., Grady, D.L., Morishima, A., Kidd, J.R., Kidd, K.K. *et al.,* (2002). Evidence of positive selection acting at the human dopamine receptor D4 gene locus. *Proceedings of the National Academy of Sciences of the USA, 99*(1), 309-314.

Dosenbach, N.U.F. Fair, D.A. Miezin, F.M. Cohen, A.L. Wenger, K.K. R. Dosenbach, A.T. Fox, M.D. Snyder, A.Z. Vincent, J.L. Raichle, M.E, Schlaggar, B.L.and Petersen, S.E. (2007). Distinct brain networks for adaptive and stable task control in humans, *Proceedings of the National Academy of Sciences of the USA* 104, 1073-1978.

Fair, D.A., Cohen, A.L., Power, J.D., Dosenbach, N.U.F., Church, J.A., Miezin, F.M., Schlaggar, B.L., & Petersen, S.E. (2009). Functional brain networks develop from a "local to distributed" organization. *PLoS Computational Biology, 5*, e1000381, doi:10.1371/journal.pcbi.1000381

Fan, J., Gu, X., Guise, K.G., Liu, X., Fossella, J., Wang, H., & Posner, M.I. (2009). Testing the behavior interaction and integration of attentional networks. *Brain and Cog.* 70, 209-220.

Fan, J., McCandliss, B.D., Sommer, T., Raz, M. & Posner, M.I. (2002). Testing the efficiency and independence of attentional networks. *Journal of Cognitive Neuroscience*, 3(14):340-347.

Fjell, A.M. *et al.,* (2012). Multi modal imaging of the self-regulating brain. *Proceedings of the National Academy of Sciences USA published ahead of print, November 12, 2012,* doi:10.1073/pnas.1208243109

Gao, W., Zhu, H., Giovanello, K.S., Smith, J. K., Shen, D., Gilmore, J.H., & Lin, W. (2009). Evidence on the emergence of the brain's default network from 2-week-old to 2-year-old healthy pediatric subjects. *Proceedings of the National Academy of Sciences USA, 106*, 6790-6795, doi:10.1073/pnas.0811221106

Green A.E., Munafo M.R., DeYoung C.G., Fossella J.A., Fan J., Gray J.R. (2008). Using genetic data in cognitive neuroscience: from growing pains to genuine insights. *Nat. Rev. Neurosci.* 9: 710-20.

Grady, D.L. *et al.,* (2013). DRD4 genotype predicts longevity in mouse and Human. *Journal of Neuroscience*, doi:10.1523/jneurosci.3515-12.2012

Haith, M.M., Hazan, C., & Goodman, G.S. (1988). Expectations and anticipations of dynamic visual events by 3.5-month-old babies. *Child Development* 59, 467-469.

Harpending, H. & Cochran, G. (2002). In our genes. *Proceedings of the National Academy of Sciences of the USA*, *99*, 10-12.

Isaacowitz, D.M. (2012). Mood regulation in real time: age differences in the role of looking. *Current Direction in Psychological Science* 21/4, 237-242.

Jones, L.B., Rothbart, M.K., & Posner, M.I. (2003). Development of executive attention in preschool children. *Developmental Science, 6*, 498-504, doi:10.1111/1467-7687.00307

Larsen, H., van der Zwaluw, C. S., Overbeek, G., Granic, I., Franke, B., & Engels, R.C. (2010). A variable-number-of-tandem-repeats polymorphism in the dopamine D4 receptor gene affects social adaptation of alcohol use: Investigation of a gene-environment interaction. *Psychological Science*, *21*, 1064-1068.

Lebel, C., Gee, M., Camicioli, R., Wielere, M., Martin, W., & Beaulieu, C (2012). Diffusion tensor imaging of white matter tract evolution over the lifespan. *Neuroimage* 60, 240-352.

Luria, A.R. (1973). *The Working Brain.* New York: Basic Books.

MacLeod, J.W. Lawrence, M.A. McConnell, M.M., Eskes, G.A. (2010). Appraising the ANT: Psychometric and Theoretical Considerations of the Attention Network Test. *Neuropsychology* 24/5, 637-651, doi:10.1037/a0019803

Markett, S.A., Montag, C., & Reuter, M. (2010). The association between Dopamine DRD2 polymorphisms and working memory capacity is modulated by a functional polymorphism on the nicotinic receptor gene CHRNA4. *J. of Cognitive Neuroscience* 22/9, 1944-1954.

Moffitt, T.E., Arseneault, L., Belsky, D., Dickson, N., Hancox, R.J., Harrington, H.L., Houts, R., Poulton, R., Roberts, B.W., Ross, S., Sears, M.R., Thomson, W.M., Caspi, A. (2011). A gradient of childhood self control predicts health, wealth and public safety. Proceedings of the National Acad. of Sci. USA 108/72693-98.

NICHD Early Child Care Research Network (1993). *The NICHD Study of Early Child Care: A comprehensive longitudinal* *study of young children's lives* (ERIC Document Reproduction Service No. ED3530870).

Niogi, S. and McCandliss, B.D. (2009). Individual differences in distinct components of attention are linked to anatomical variations in distinct white matter tracts. *Frontiers in Neuroanatomy*, 3:21.

Petersen, S.E. & Posner, M.I. (2012). The attention system of the human brain: 20 years after. *Annual Review of Neuroscience* 35, 71-89.

Posner, M.I. (2012). *Attention in a Social World*. New York, Oxford University Press.

Posner, M.I. & Petersen, S.E. (1990). The attention system of the human brain. *Annual Review of Neuroscience, 13*, 25-42.

Posner, M.I., Rothbart, M.K., Sheese, B.E., Voelker, P. (2012). Control Networks and Neuromodulators of Early Development. *Developmental Psychology* 48/3, 827-835, doi:10 1037/a0025530

Raichle, M.E. (2009). A paradigm shift in functional imaging. *Journal of Neuroscience* 29, 12729-34.

Posner, M.I., Sheese, B, Odludas, Y., Tang, Y. (2006). Analyzing and shaping neural networks of attention. *Neural Networks* 19, 1422-1429.

Reuter, M., Ott, U., Vaitl, D., Hennig, J. (2007). Impaired executive control is associated with a variation in the promoter region of the tryptophan hydroxylase 2 gene. *Journal of Cognitive Neuroscience* 19/3, 401-408, doi:10.1162/jocn.2007.19.3.401

Ronald, A. (2011). Is the child 'father of the man'? Evaluating the stability of genetic influences across development. *Developmental Science* 14:6, 1471-1478.

Rothbart, M.K. (2011). *Becoming who we are: Temperament, personality and development.* Guilford Press.

Rothbart, M.K., Sheese, B.E., Rueda, M.R., & Posner, M.I. (2011). Developing mechanisms of self regulation in early life. *Emotion Review 3/2,* 207-213.

Rueda, M.R., Fan, J., Halparin, J., Gruber, D., Lercari, L.P., McCandliss B.D. & Posner, M.I. (2004). Development of attention during childhood *Neuropsychologia,* 42:1029-1040.

Sheese, B.E., Rothbart, M.K., Voelker, P., & Posner, M.I. (2012). The dopamine receptor D4 gene 7 repeat allele interacts with parenting quality to predict Effortful Control in four-year-old children. *Child Development Research* vol. 2012, ID 863242, 6 pages, doi:10.1155/2012/863242

Sheese, B.E., Rothbart, M.K, Posner, M.I., White, L.K. & Fraundorf, S.H. (2008). Executive attention and self regulation in infancy. *Infant Behavior and Development* 31, 501-510.

Sheese, B.E., Voelker, P.M., Rothbart, M.K., & Posner, M.I. (2007). Parenting quality interacts with genetic variation in Dopamine Receptor DRD4 to influence temperament in early childhood. *Devel. & Psychopathology* 19**,** 1039-1046.

Sheth, S.A., Mian, M.K., Patel, S.R., Asaad, W.F., Williams, Z.M., Dougherty, D.D., Bush, G., & Eskander, E.N. (2012). Human dorsal anterior cingulate cortex neurons mediate ongoing behavioural adaptation. *Nature* 488, 218, doi:10.1038/nature11239

Smith, H.J., Sheikh, H.I., Dyson, M.W., Olino, T.M., Laptook, R.S., Durbin, C.E., Hayden, E.P., Singh, S.M., & Klein, D.N. (2012). Parenting and Child *DRD4* Genotype Interact to Predict Children's Early Emerging Effortful Control. *Child Development*, 83/6, 1932-1944.

Spector, T. (2012). *Identically different: why you can change your genes*. London: Orion Publishing.

Supekar, K. & Menon, V. (2012), Developmental maturation of a dynamic causal control signals in higher-order cognition: a neurocognitive network model. *PLOS Computational Biology* 8/2 e1002374, doi:10.1371/journal.pcbi.1002374

Tang, Y-Y., Lu, Q., Fan, M., Yang, Y., & Posner, M.I. (2012). Mechanisms of White Matter Changes Induced by Meditation, *Proceedings of the National Academy of Sciences USA* 109 (26), 10570-10574, doi:10.1073/pnas.1207817109

Tang Y., Lu Q., Geng X., Stein E.A., Yang Y., & Posner M.I. (2010). Short-term mental training induces white-matter changes in the anterior cingulate, *PNAS* 107, 16649-16652.

van Ijzendoorn, M.H., & Bakermans-Kranenburg, M.J. (2006). DRD4 7-repeat polymorphism moderates the association between maternal unresolved loss or trauma and infant disorganization. *Attachment and Human Development, 8*, 291-307.

Vygotsky, L.S. (1934/1962). *Thought and language*, E. Hanfmann & G.Vakar (eds), Cambridge MA: MIT Press.

Westlye, L.T., Grydeland, H., Walhovd, K.B. & Fjell, A.M. (2011). Associations between Regional Cortical Thickness and Attentional Networks as Measured by the Attention Network Test. *Cerebral Cortex* 21/2, 345-356, doi:10.1093/cercor/bhq101

Wang, E.T., Kodama, G., Baldi, P., & Moyzis, R.K. (2006). Global landscape of recent inferred Darwinan selection for Homo sapiens. *Proceedings of the National Academy of Science, 103*, 135-140.

Wynn, K. (1994). Addition and subtraction by human infants. *Nature*, 358:749-750.

Zilles, K. (2005). Evolution of the human brain and comparative syto and receptor architecture. In S. Dehaene, J.-R. Duhamel, M.D. Hauser and G. Rizzolatti (eds), *From Monkey Brain to Human Brain*: 41-56. Cambridge Mass: MIT Press, Bradford Books.