Provision of Sensory Opportunities

This section includes articles from the literature on specific sensory processing, and outcomes of enriched environments (both human and animal literature are included).

2009

Bruno RM, Hahn TT, Wallace DJ, de Kock CP, Sakmann B. (2009). Sensory experience alters specific branches of individual corticocortical axons during development. J Neurosci. 29(10):3172-81.

> Sensory experience can, over the course of days to weeks, produce long-lasting changes in brain function. Recent studies suggest that functional plasticity is mediated by alterations of the strengths of existing synapses or dynamics of dendritic spines. Alterations of cortical axons could also contribute to functional changes, but little is known about the effects of experience at the level of individual corticocortical axons. We reconstructed individual layer (L) 2/3 pyramidal neurons filled in vivo in developing barrel cortex of control and partially sensory-deprived rats. L2 axons had larger field spans than L3 axons but were otherwise equivalently affected by deprivation. Whisker trimming over approximately 2 weeks markedly reduced overall length of axonal branches in L2/3, but individual horizontal axons were as likely to innervate deprived areas as spared ones. The largest effect of deprivation was instead to reduce the length of those axonal branches in L2/3 oriented toward deprived regions. Thus, the location of a branch relative to its originating soma, rather than its own location within any specific cortical column, was the strongest determinant of axonal organization. Individual axons from L2/3 into L5/6 were similarly altered by whisker trimming although to a lesser extent. Thus, sensory experience over relatively short timescales may change the patterning of specific axonal branches within as well as between cortical columns during development.

Scholey, Andrew; Haskell, Crystal; Robertson, Bernadette; Kennedy, David; Milne, Anthea; Wetherell, Mark (2009). Chewing gum alleviates negative mood and reduces cortisol during acute laboratory psychological stress. Physiology & Behavior, 97(3-4), 304-312. [Journal Article]

> Abstract: The notion that chewing gum may relieve stress was investigated in a controlled setting. A multi-tasking framework which reliably evokes stress and also includes performance measures was used to induce acute stress in the laboratory. Using a randomised crossover design forty participants (mean age 21.98 years) performed on the multi-

tasking framework at two intensities (on separate days) both while chewing and not chewing. Order of workload intensity and chewing conditions were counterbalanced. Before and after undergoing the platform participants completed the state portion of the State-Trait Anxiety Inventory, Bond–Lader visual analogue mood scales, a single Stress Visual Analogue Scale and provided saliva samples for cortisol measurement. Baseline measures showed that both levels of the multi-tasking framework were effective in significantly reducing self-rated alertness, calmness and contentment while increasing self-rated stress and state anxiety. Cortisol levels fell during both levels of the stressor during the morning, reflecting the predominance of a.m. diurnal changes, but this effect was reversed in the afternoon which may reflect a measurable stress response. Pre–post stressor changes (Δ) for each measure at baseline were subtracted from Δ scores under chewing and no chewing conditions. During both levels of stress the chewing gum condition was associated with significantly better alertness and reduced state anxiety, stress and salivary cortisol. Overall performance on the framework was also significantly better in the chewing condition. The mechanisms underlying these effects are unknown but may involve improved cerebral blood flow and/or effects secondary to performance improvement during gum chewing. (PsycINFO Database Record (c) 2009 APA, all rights reserved)

Ali, Ata E. A.; Wilson, Yvette M.; Murphy, Mark;(2009). A single exposure to an enriched environment stimulates the activation of discrete neuronal populations in the brain of the fos-tau-lacZ mouse. Neurobiology of Learning and Memory, Vol 92(3), 381-390. [Journal Article]

Abstract: Storage of experience, including learning and memory, is thought to involve plasticity within pre-existing brain circuits. One model for looking at experience-dependent changes is environmental enrichment (EE), which involves exposing animals to a complex novel environment. Animals exposed to EE have previously been shown to exhibit a variety of behavioral and structural alterations in the brain, including decreased stress, improved learning and memory, altered levels of immediate early genes and synaptic change in the visual cortex. We were interested in understanding what regions of the brain are activated during the initial stages of EE. We used fos-tau-lacZ (FTL) transgenic mice to examine changes in functional activation throughout the brain after a single exposure to EE. We found that there was a significant increase in FTL expression within particular morphologically identified neurons in a series of brain regions in the enriched group compared to control groups, indicating that multiple circuits were activated. These regions include the claustrum, infralimbic cortex,

hippocampus, amygdala and the hypothalamus. The data suggest that EE stimulates an initial strong increase in activation of multiple functional circuits. These circuits are presumably involved in the initial response of the animal to the enriched environment.

Pawlowicz, Artur; Demner, Adam; Lewis, Mark H (2009). Effects of access to voluntary wheel running on the development of stereotypy. Behavioural Processes, Nov 26, 2009.

Abstract: Stereotyped motor behaviors are a common consequence of environmental restriction in a wide variety of species. Although environmental enrichment has been shown to substantially reduce stereotypy levels, the various components of enrichment have not been evaluated independently to determine which is responsible for this effect. Exercise, particularly voluntary wheel running, is a promising candidate based on several lines of behavioral and neurobiological evidence. To test the hypothesis that access to wheel running will reduce stereotyped motor behavior, we reared deer mice from weaning with continuous access to either a functional running wheel or a locked wheel. We assessed running behavior throughout this time period and stereotypy levels in a test context at 30 and 45 days post-weaning. We found that exercise did not significantly affect stereotypy level nor was there an association between wheel running and stereotypy. Thus, exercise alone, unlike environmental enrichment, does not prevent the development of stereotypy. These results have important implications for animal welfare. (PsycINFO Database Record (c) 2009 APA, all rights reserved)

Catlow, Briony J.; Rowe, Amanda R.; Clearwater, Courtney R.; Mamcarz, Maggie; Arendash, Gary W.; Sanchez-Ramos, Juan (2009). Effects of environmental enrichment and physical activity on neurogenesis in transgenic PS1/APP mice. Brain Research, Vol 1256, 173-179. [Journal Article]

Abstract: Rodents exposed to environmental enrichment show many differences, including improved cognitive performance, when compared to those living in standard (impoverished) housing. The purpose of the present study was to determine if a selective increase in neurogenesis occurred in cognitively-protected Tg mice raised in an enriched environment compared to those reared in physical activity housing. At weaning, double Tg APP+PS1 mice were placed into one of three environments: complete environmental enrichment (CE), enhanced physical activity (PA), or individual, impoverished housing (IMP). At 9–10 months of age, Tg mice were injected with BrdU (100 mg/kg BID)

followed by euthanasia either 24 h or 2 weeks after the last injection. Unbiased estimates of BrdU positive cells in the hippocampal subgranular zone revealed a significant increase in cellular proliferation in Tg mice raised in CE or PA compared to Tg mice reared in IMP housing. However, counts of BrdU birth-dated cells 2 weeks after labeling showed no difference among the three groups, indicating decreased survival of cells in those groups (CE and PA) with higher cellular proliferation rates in the neurogenic niche. Counts of calretinin-expressing cells, a marker of immature neurons, also indicated no difference among the three groups of mice. In view of our prior study showing that enhanced cognitive activity (but not enhanced physical activity) protects Tg mice against cognitive impairment, the present results indicate that increased generation and survival of new neurons in the hippocampal dentate gyrus is not involved with the cognitively-protective effects of complete CE in Alzheimer's transgenic mice.

Hughes, Robert N.; Collins, Michelle A.(2009). Enhanced habituation and decreased anxiety by environmental enrichment and possible attenuation of these effects by chronic α-tocopherol (vitamin e) in aging male and female rats. Pharmacology, Biochemistry and Behavior, Nov 24.

Abstract: Middle-aged 330-day-old male and female hooded rats were group-housed for nearly 5months in either standard cages, or in cages containing objects. Each cage also provided either pure water, or a solution of vitamin E (DL-α-tocopherol acetate) for drinking. Records were kept of averages for each cage of the rats' body weights and the volume of fluid/100g average body weight drunk. The average daily dose of tocopherol was approximately 162 and 173mg/kg for males and females respectively. Males (but not females) kept in enriched cages weighed less than those from standard cages. They also drank less fluid than females who also drank more tocopherol solution than males. When 490+days old, for rats provided with water, enrichment led to decreased open-field ambulation and increased within-session decrements in the response (habituation). Enrichment also led to decreased occupancy of the center of the apparatus for males only and, for all rats combined, increased grooming behavior. It was concluded that the effects of enrichment on aged rats were due to increased within-session habituation to novelty and decreased anxiety similar to what has been suggested for younger animals. Tocopherol appeared to interfere with effects of enrichment possibly because of pro-oxidant-related increased anxiety. (PsycINFO Database Record (c) 2009 APA, all rights reserved)

Sale, Alessandro; Berardi, Nicoletta; Maffei, Lamberto (2009). Enrich the environment to empower the brain. Trends in Neurosciences, 32(4), 233-239. [Journal Article]

Abstract: Environmental enrichment (EE) has long been exploited to investigate the influence of the environment on brain structure and function. Robust morphological and functional effects elicited by EE at the neuronal level have been reported to be accompanied by improvements in cognitive performance. Recently, EE has been shown to accelerate the development of the visual system and to enhance visual-cortex plasticity in adulthood. These new findings highlight the potential of EE as a promising noninvasive strategy to ameliorate deficits in the maturation of the nervous system and to promote recovery of normal sensory functions in pathological conditions affecting the adult brain. (PsycINFO Database Record (c) 2009 APA, all rights reserved)

Nag, Nupur; Moriuchi, Jennifer M.; Peitzman, Cassandra G. K.; Ward, Bonnie C.; Kolodny, Nancy H.; Berger-Sweeney, Joanne E.(2009). Environmental enrichment alters locomotor behaviour and ventricular volume in Mecp2<xh:sup>1lox</xh:sup> mice. Behavioural Brain Research, 196(1), 44-48. [Journal Article]

Abstract: Rett syndrome (RTT) is an autistic spectrum developmental disorder associated with mutations in the X-linked Mecp2 gene, and severe behavioural and neuropathological deficits. In a mouse model of RTT (Mecp2[sup] <xh:i>1lox[/sup]1lox), we examined whether environmental enrichment (EE) alters behavioural performance and regional brain volume. At weaning, Mecp2[sup] <xh:i>1lox[/sup]1lox and control mice were assigned to enriched or standard housing. From postnatal day 29 to 43, mice were subjected to behavioural tasks measuring motor and cognitive performance. At postnatal day 44, volumes of whole brain, cerebellum, ventricles, and motor cortex were measured using magnetic resonance imaging. EE provided subtle improvements to locomotor activity and contextual fear conditioning in Mecp2[sup] <xh:i>1lox[/sup]1lox mice. Additionally, EE reduced ventricular volumes, which correlated with improved locomotor activity, suggesting that neuroanatomical changes contribute to improved behaviour. Our results suggest that post-weaning EE may provide a non-invasive palliative treatment for RTT. (PsycINFO Database Record (c) 2009 APA, all rights reserved)

de Carvalho, Cristiane Ribeiro; Pandolfo, Pablo; Pamplona, Fabrício Alano; Takahashi, Reinaldo Naoto (2009). Environmental enrichment reduces the impact of novelty and motivational properties of ethanol in spontaneously hypertensive rats. Behavioural Brain Research, Dec 3, 2009.

Abstract: The present study investigated the consequences of environmental enrichment on the impact of novelty and motivational properties of ethanol in spontaneously hypertensive rats (SHR), a validated model of attention deficit hyperactivity disorder (ADHD). This rat strain displays increased sensitivity to distinct classes of abused drugs, which makes it an interesting model for the study of the association between ADHD and drug abuse. Female SHR reared from weaning to adulthood in standard (SE) or enriched (EE) environment were tested on novelty-induced locomotion, saccharin consumption, ethanol consumption (forced and free-choice schedules) and ethanol-induced conditioned place preference (CPP). SHR reared in an EE showed reduced novelty-induced locomotion, consumed less saccharin and ethanol in a forced schedule and showed less ethanol preference in a free-choice schedule compared to SE rats. Moreover, EE rats did not develop CPP, whereas SE rats developed preference for ethanol (1.2g/kg). These results show that exposure to stimuli mimicking positive life experiences (environmental enrichment) induces persistent changes in the reward/motivational system of female SHR, suggesting an important role of the familiar environment during early stages of the neurodevelopment on the co-morbidity of ADHD and drug abuse. (PsycINFO Database Record (c) 2009 APA, all rights reserved)

Harrar, Vanessa; Harris, Laurence R.(2009). Eye position affects the perceived location of touch. Experimental Brain Research, 198(2-3), 403-410. [Journal Article]

Abstract: Here, we demonstrate a systematic shift in the perceived location of a tactile stimulus on the arm toward where the eye is looking. Participants reported the perceived position of touches presented between the elbow and the wrist while maintaining eye positions at various eccentricities. The perceived location of the touch was shifted by between 1 and 5 cm (1.9°–9.5° visual angle) by a change in eye position of ±25° from straight ahead. In a control condition, we repeat the protocol with the eyes fixating straight ahead. Changes in attention accounted for only 17% of the shift due to eye position. The pattern of tactile shifts due to eye position was comparable whether or not the arm was visible. However, touches at locations along the forearm were perceived as being farther apart when the arm was visible compared to when it was covered. These results are discussed in terms

of the coding of tactile space, which seems to require integration of tactile, visual and eye position information. (PsycINFO Database Record (c) 2009 APA, all rights reserved)

Tall JM.(2009). Housing supplementation decreases the magnitude of inflammation-induced nociception in rats. Behav Brain Res. 197(1):230-3. Epub 2008 Aug 19.

Previous reports have demonstrated that pain is influenced by environmental factors. This investigation examined the effects of housing supplementation, via the inclusion of objects to the home cage environment, on inflammation-induced nociceptive behaviors. The degree of thermal hyperalgesia was significantly lower in rats housed in a supplemented home cage environment, as compared to rats housed in basic cages. These data indicate that environmental enrichment significantly affects nociceptive responses.

Lewis CM, Baldassarre A, Committeri G, Romani GL, Corbetta M. (2009). Learning sculpts the spontaneous activity of the resting human brain. Proc Natl Acad Sci U S A. 106(41):17558-63. Epub 2009 Oct 5.

The brain is not a passive sensory-motor analyzer driven by environmental stimuli, but actively maintains ongoing representations that may be involved in the coding of expected sensory stimuli, prospective motor responses, and prior experience. Spontaneous cortical activity has been proposed to play an important part in maintaining these ongoing, internal representations, although its functional role is not well understood. One spontaneous signal being intensely investigated in the human brain is the interregional temporal correlation of the blood-oxygen level-dependent (BOLD) signal recorded at rest by functional MRI (functional connectivity-by-MRI, fcMRI, or BOLD connectivity). This signal is intrinsic and coherent within a number of distributed networks whose topography closely resembles that of functional networks recruited during tasks. While it is apparent that fcMRI networks reflect anatomical connectivity, it is less clear whether they have any dynamic functional importance. Here, we demonstrate that visual perceptual learning, an example of adult neural plasticity, modifies the resting covariance structure of spontaneous activity between networks engaged by the task. Specifically, after intense training on a shape-identification task constrained to one visual

quadrant, resting BOLD functional connectivity and directed mutual interaction between trained visual cortex and frontal-parietal areas involved in the control of spatial attention were significantly modified. Critically, these changes correlated with the degree of perceptual learning. We conclude that functional connectivity serves a dynamic role in brain function, supporting the consolidation of previous experience.

Viel S, Vaugoyeau M, Assaiante C. (2009). Adolescence: a transient period of proprioceptive neglect in sensory integration of postural control. Motor Control. 13(1):25-42.

In the current study, we adopted the hypothesis that the body scheme disturbances occurring during adolescence might lead subjects to transiently neglect proprioceptive information and that adolescents might rely more strongly on vision to control their orientation and stabilize their body. To check this point, we asked adolescents 14-15 years to maintain vertical stance while very slow sinusoidal oscillations in the frontal plane were applied to the supporting platform at 0.01 Hz (below the detection threshold of the semicircular canal system) and at 0.06 Hz (above) with the eyes open and closed. Two postural components, orientation and segmental stabilization, were analyzed at the head, shoulder, trunk, and pelvis levels. At the lowest frequency without vision, the performances of adolescents were much less efficient than those of adults. Moreover, this study showed that vision plays a predominant role in adolescents' control of orientation and body stabilization. At 0.06 Hz without vision, a clearcut difference was observed between the strategies used by girls and boys; specifically, the maturation of the segmental stabilization processes was found to be more advanced in girls than in boys. However, no such difference was observed at 0.01 Hz. Lastly, comparisons between the data obtained in adolescents and those previously obtained in young adults (Vaugoyeau, Viel, Amblard, Azulay, & Assaiante, 2008) clearly show that adolescents use different postural strategies and that they are not yet capable of reaching comparable postural performance levels to those observed in adults. Because adolescents were not able to use the proprioceptive information available to improve their postural control, we concluded that they showed a maturational lag in comparison with adults. This suggests that the mechanisms underlying postural control are still maturing during adolescence, which might constitute a transient period of proprioceptive neglect in sensory integration of postural control.

Gottfried JA, Wu KN.(2009). Perceptual and neural pliability of odor objects. Ann N Y Acad Sci. 1170:324-32.

A key function of the sense of smell is to guide organisms towards rewards and away from dangers. However, because relatively few volatile chemicals in the environment carry intrinsic biological value, the meaning of an odor often needs to be acquired through learning and experience. The tremendous perceptual and neural plasticity of the olfactory system provides a design that is ideal for the establishment of links between odor cues and behaviorally relevant events, promoting appropriate adaptive responses to foods, friends, foes, and mates. This article describes recent human neuroimaging data showing the dynamic effects of olfactory perceptual learning and aversive conditioning on the behavioral discrimination of odor objects, with parallel plasticity and reorganization in the posterior piriform and orbitofrontal cortices. The findings presented here highlight the important role of experience in shaping odor object perception and in ensuring the human sense of smell achieves its full perceptual potential.

Nithianantharajah J, Hannan AJ. (2009). The neurobiology of brain and cognitive reserve: mental and physical activity as modulators of brain disorders. Prog Neurobiol. 89(4),369-82. Epub 2009 Oct 9.

The concept of 'cognitive reserve', and a broader theory of 'brain reserve', were originally proposed to help explain epidemiological data indicating that individuals who engaged in higher levels of mental and physical activity via education, occupation and recreation, were at lower risk of developing Alzheimer's disease and other forms of dementia. Subsequently, behavioral, cellular and molecular studies in animals (predominantly mice and rats) have revealed dramatic effects of environmental enrichment, which involves enhanced levels of sensory, cognitive and motor stimulation via housing in novel, complex environments. Furthermore, increasing levels of voluntary physical exercise, via ad libitum access to running wheels, can have significant effects on brain and behavior, thus informing the relative effects of mental and physical activity. More recently, animal models of brain disorders have been compared under environmentally stimulating and standard housing conditions, and this has provided new insights into environmental modulators and gene-environment interactions involved in pathogenesis. Here, we review animal studies that have investigated the effects of modifying mental and physical activity via experimental manipulations, and discuss their relevance to brain and cognitive reserve

(BCR). Recent evidence suggests that the concept of BCR is not only relevant to brain aging, neurodegenerative diseases and dementia, but also to other neurological and psychiatric disorders. Understanding the cellular and molecular mechanisms mediating BCR may not only facilitate future strategies aimed at optimising healthy brain aging, but could also identify molecular targets for novel pharmacological approaches aimed at boosting BCR in 'at risk' and symptomatic individuals with various brain disorders.

Catlow BJ, Rowe AR, Clearwater CR, Mamcarz M, Arendash GW, Sanchez-Ramos J.(2009). Effects of environmental enrichment and physical activity on neurogenesis in transgenic PS1/APP mice. Brain Res. 1256:173-9. Epub 2008 Dec 24.

Rodents exposed to environmental enrichment show many differences, including improved cognitive performance, when compared to those living in standard (impoverished) housing. The purpose of the present study was to determine if a selective increase in neurogenesis occurred in cognitively-protected Tg mice raised in an enriched environment compared to those reared in physical activity housing. At weaning, double Tg APP+PS1 mice were placed into one of three environments: complete environmental enrichment (CE), enhanced physical activity (PA), or individual, impoverished housing (IMP). At 9-10 months of age, Tg mice were injected with BrdU (100 mg/kg BID) followed by euthanasia either 24 h or 2 weeks after the last injection. Unbiased estimates of BrdU positive cells in the hippocampal subgranular zone revealed a significant increase in cellular proliferation in Tg mice raised in CE or PA compared to Tg mice reared in IMP housing. However, counts of BrdU birth-dated cells 2 weeks after labeling showed no difference among the three groups, indicating decreased survival of cells in those groups (CE and PA) with higher cellular proliferation rates in the neurogenic niche. Counts of calretinin-expressing cells, a marker of immature neurons, also indicated no difference among the three groups of mice. In view of our prior study showing that enhanced cognitive activity (but not enhanced physical activity) protects Tg mice against cognitive impairment, the present results indicate that increased generation and survival of new neurons in the hippocampal dentate gyrus is not involved with the cognitively-protective effects of complete CE in Alzheimer's transgenic mice.

Trickett, Sarah L.; Guy, Jonathan H.; Edwards, Sandra A.(2009) The role of novelty in environmental enrichment for the weaned pig. Applied Animal Behaviour Science, Vol 116(1-2), 45-51. [Journal Article]

Abstract: Habituation to environmental enrichment objects can occur rapidly. Novelty of an object is an important property involved in initiating and maintaining exploration, and this can be achieved by renewing objects. The aims of this study were to assess whether alternation of two contrasting objects increased enrichment value, and whether simultaneous access increased overall object-directed behaviour in comparison with single presentation of each object. The experiment was designed as a 2 × 2 factorial, with 2 enrichment objects (suspended rope and loose wood block) and 2 presentation methods (continuous access, or weekly alternation). An additional treatment examined object use when both objects were presented simultaneously. Five replicate pens, each of 10 weaned pigs, were allocated to each treatment: R, continuous rope; W, continuous wood; R/W, alternation rope-wood; W/R, alternation wood-rope; R + W, simultaneous rope and wood. Observations of behaviour were made for two 1-h periods, three times a week for a 4-week period. Direct scan samples at 5-min intervals measured use of the enrichment object(s), penmate and pen manipulation, and general activity. These were supplemented by two 24 h time-lapse video recordings made in the first and last experimental weeks. Object interaction was significantly affected by treatment, with W spending a lower overall proportion of observations in contact with the object than the other treatments (in order 0.102, 0.037, 0.093, 0.110, 0.134, s.e.d. 0.007; $P < 0.001$). In R, week had a significant effect on rope interaction, which decreased in week 2 and increased again in week 3 when new rope was added, although rope interaction was still lower in week 3 than in week 1 (0.106 vs. 0.151, respectively, s.e.d. 0.017; $P < 0.01$). When R/W and W/R received rope for a second time, rope interaction was lower than in the first presentation week (R/W, 0.166 vs. 0.129, s.e.d. 0.017; $P < 0.05$). Interaction with wood was always lower than with rope (in R + W, 0.03 vs. 0.19, respectively, s.e.d. 0.027; $P < 0.001$). Object interaction was additive in R + W when compared to R and W. To conclude, the rotation of enrichment objects did increase novelty, although habituation still occurred. Rope was extremely effective at occupying the pigs' time, with interaction levels comparable to those previously reported for straw. (PsycINFO Database Record (c) 2009 APA, all rights reserved)

Simonetti T, Lee H, Bourke M, Leamey CA, Sawatari A.(2009). Enrichment from birth accelerates the functional and cellular development of a motor control area in the mouse. PLoS One. 4(8):e6780.

BACKGROUND: There is strong evidence that sensory experience in early life has a profound influence on the development of sensory circuits. Very little is known, however, about the role of experience in the early development of striatal networks which regulate both motor and cognitive function. To address this, we have investigated the influence of early environmental enrichment on motor development. METHODOLOGY/PRINCIPAL FINDINGS: Mice were raised in standard or enriched housing from birth. For animals assessed as adults, half of the mice had their rearing condition reversed at weaning to enable the examination of the effects of pre- versus post-weaning enrichment. We found that exclusively pre-weaning enrichment significantly improved performance on the Morris water maze compared to non-enriched mice. The effects of early enrichment on the emergence of motor programs were assessed by performing behavioural tests at postnatal day 10. Enriched mice traversed a significantly larger region of the test arena in an open-field test and had improved swimming ability compared to non-enriched cohorts. A potential cellular correlate of these changes was investigated using Wisteria-floribunda agglutinin (WFA) staining to mark chondroitin-sulfate proteoglycans (CSPGs). We found that the previously reported transition of CSPG staining from striosome-associated clouds to matrix-associated perineuronal nets (PNNs) is accelerated in enriched mice. CONCLUSIONS/SIGNIFICANCE: This is the first demonstration that the early emergence of exploratory as well as coordinated movement is sensitive to experience. These behavioural changes are correlated with an acceleration of the emergence of striatal PNNs suggesting that they may consolidate the neural circuits underlying these behaviours. Finally, we confirm that pre-weaning experience can lead to life long changes in the learning ability of mice.

Zajac MS, Pang TY, Wong N, Weinrich B, Leang LS, Craig JM, Saffery R, Hannan AJ. (2009). Wheel running and environmental enrichment differentially modify exon-specific BDNF expression in the hippocampus of wild-type and pre-motor symptomatic male and female Huntington's disease mice. Hippocampus. Jun 4. [Epub ahead of print]

Brain-derived neurotrophic factor (BDNF) is an essential neurotrophin and regulation of its expression is complex due to multiple 5' untranslated exons which are separately spliced to a common coding exon to form unique mRNA transcripts. Disruption of BDNF gene expression is a key to the development of symptoms in Huntington's disease (HD), a fatal neurodegenerative condition. Abnormal epigenetic modifications are associated with reduced gene expression in late-stage HD but such regulation of BDNF gene expression has yet to be investigated. We hypothesized that BDNF gene expression is altered in the HD hippocampus of pre-motor symptomatic R6/1 transgenic HD mice, correlating with a change in the DNA methylation profile. The effects of wheel-running and environmental enrichment on wild-type mice, in association with a proposed environment-mediated correction of BDNF gene expression deficits in HD mice, were also investigated. Using real-time PCR, levels of total BDNF mRNA were found to be reduced in the hippocampus of both male and female HD mice. Wheel-running significantly increased total BDNF gene expression in all groups of mice except male HD mice. In contrast, environmental enrichment significantly increased expression only in male wild-type animals. Further quantification of BDNF exon-specific transcripts revealed sex-specific changes in relation to the effect of the HD mutation and differential effects on gene expression by wheel-running and environmental enrichment. The HD-associated reduction of BDNF gene expression was not due to increased methylation of the gene sequence. Furthermore, environment-induced changes in BDNF gene expression in the wild-type hippocampus were independent of the extent of DNA methylation. Overall, the results of this study provide new insight into the role of BDNF in HD pathogenesis in addition to the mechanisms regulating normal BDNF gene expression.

Peña Y, Prunell M, Rotllant D, Armario A, Escorihuela RM.(2009). Enduring effects of environmental enrichment from weaning to adulthood on pituitary-adrenal function, pre-pulse inhibition and learning in male and female rats. Psychoneuroendocrinology. 34(9):1390-404. Epub 2009 May 29.

Environmental enrichment (EE) increases stimulation and provides richer sensory, cognitive and motor opportunities through the interaction with the social and physical environment. EE produces a wide range of neuroanatomical, neurochemical and behavioural effects in several animal species. However, the effects of EE have mainly been studied shortly after the treatment, so its long-lasting effects remain to be

elucidated. Thus, we studied in male and female Sprague-Dawley rats the enduring effects of EE on tasks that measured emotional reactivity, social exploration and memory, sensorimotor gating and learning. After weaning, rats reared in EE were housed in single-sex groups of 12-14 in enriched cages during 12 weeks, whereas control rats were housed in single-sex groups of 2-3 animals in standard cages. Then, all rats were housed in pairs and successively exposed to different tests between 4 and 60 weeks post-EE. The results indicated that animals of both sexes reared in EE gained less weight during the enrichment period; differences disappeared in females during the post-EE period, but were maintained intact in males. Rats reared in EE showed an altered daily pattern of corticosterone and a lower hormone response to a novel environment (hole board, HB), although no differences in ACTH were found. EE resulted in more exploratory behaviour in the HB and higher number of entries in the open arms of the elevated plus maze (with no changes in the time spent in the open arms), suggesting a greater motivation to explore. Unexpectedly, rats reared in EE showed reduced pre-pulse inhibition (PPI), a measure of sensorimotor gating, suggesting lower capability to filter non-relevant information compared with control rats. EE increased social exploratory behaviour towards juvenile rats and social discrimination in males, but decreased social discrimination in females. Finally, in the Hebb-Williams maze, rats reared in EE showed better performance in terms of reduced number of errors and shorter distances travelled in the mazes. It is concluded that EE exposure from weaning to adulthood has important and long-lasting consequences on physiological and behavioural variables, most of them similar in both sexes, although sex differences in response to the EE are also reported.

Mégevand P, Troncoso E, Quairiaux C, Muller D, Michel CM, Kiss JZ. (2009). Long-term plasticity in mouse sensorimotor circuits after rhythmic whisker stimulation. J Neurosci. 29(16):5326-35.

Mice actively explore their environment by rhythmically sweeping their whiskers. As a consequence, neuronal activity in somatosensory pathways is modulated by the frequency of whisker movement. The potential role of rhythmic neuronal activity for the integration and consolidation of sensory signals, however, remains unexplored. Here, we show that a brief period of rhythmic whisker stimulation in anesthetized mice resulted in a frequency-specific long-lasting increase in the amplitude of somatosensory-evoked potentials in the contralateral primary somatosensory (barrel) cortex. Mapping of evoked potentials and

intracortical recordings revealed that, in addition to potentiation in layers IV and II/III of the barrel cortex, rhythmic whisker stimulation induced a decrease of somatosensory-evoked responses in the supragranular layers of the motor cortex. To assess whether rhythmic sensory input-based plasticity might arise in natural settings, we exposed mice to environmental enrichment. We found that it resulted in somatosensory-evoked responses of increased amplitude, highlighting the influence of previous sensory experience in shaping sensory responses. Importantly, environmental enrichment-induced plasticity occluded further potentiation by rhythmic stimulation, indicating that both phenomena share common mechanisms. Overall, our results suggest that natural, rhythmic patterns of whisker activity can modify the cerebral processing of sensory information, providing a possible mechanism for learning during sensory perception.

Pawlowicz A, Demner A, Lewis MH. (2009). Effects of access to voluntary wheel running on the development of stereotypy. Behav Processes. Nov 26. [Epub ahead of print]

Stereotyped motor behaviors are a common consequence of environmental restriction in a wide variety of species. Although environmental enrichment has been shown to substantially reduce stereotypy levels, the various components of enrichment have not been evaluated independently to determine which is responsible for this effect. Exercise, particularly voluntary wheel running, is a promising candidate based on several lines of behavioral and neurobiological evidence. To test the hypothesis that access to wheel running will reduce stereotyped motor behavior, we reared deer mice from weaning with continuous access to either a functional running wheel or a locked wheel. We assessed running behavior throughout this time period and stereotypy levels in a test context at 30 and 45 days post-weaning. We found that exercise did not significantly affect stereotypy level nor was there an association between wheel running and stereotypy. Thus, exercise alone, unlike environmental enrichment, does not prevent the development of stereotypy. These results have important implications for animal welfare.

Hyde KL, Lerch J, Norton A, Forgeard M, Winner E, Evans AC, Schlaug G. (2009). Musical training shapes structural brain development. J Neurosci. 2009 Mar 11;29(10):3019-25.

The human brain has the remarkable capacity to alter in response to environmental demands. Training-induced structural brain changes have been demonstrated in the healthy adult human brain. However, no study has yet directly related structural brain changes to behavioral changes in the developing brain, addressing the question of whether structural brain differences seen in adults (comparing experts with matched controls) are a product of "nature" (via biological brain predispositions) or "nurture" (via early training). Long-term instrumental music training is an intense, multisensory, and motor experience and offers an ideal opportunity to study structural brain plasticity in the developing brain in correlation with behavioral changes induced by training. Here we demonstrate structural brain changes after only 15 months of musical training in early childhood, which were correlated with improvements in musically relevant motor and auditory skills. These findings shed light on brain plasticity and suggest that structural brain differences in adult experts (whether musicians or experts in other areas) are likely due to training-induced brain plasticity.

Guzzetta A, Baldini S, Bancale A, Baroncelli L, Ciucci F, Ghirri P, Putignano E, Sale A, Viegi A, Berardi N, Boldrini A, Cioni G, Maffei L. (2009). Massage accelerates brain development and the maturation of visual function. J Neurosci. 29(18):6042-51.

Environmental enrichment (EE) was shown recently to accelerate brain development in rodents. Increased levels of maternal care, and particularly tactile stimulation through licking and grooming, may represent a key component in the early phases of EE. We hypothesized that enriching the environment in terms of body massage may thus accelerate brain development in infants. We explored the effects of body massage in preterm infants and found that massage accelerates the maturation of electroencephalographic activity and of visual function, in particular visual acuity. In massaged infants, we found higher levels of blood IGF-1. Massage accelerated the maturation of visual function also in rat pups and increased the level of IGF-1 in the cortex. Antagonizing

IGF-1 action by means of systemic injections of the IGF-1 antagonist JB1 blocked the effects of massage in rat pups. These results demonstrate that massage has an influence on brain development and in particular on visual development and suggest that its effects are mediated by specific endogenous factors such as IGF-1.

Zhu SW, Codita A, Bogdanovic N, Hjerling-Leffler J, Ernfors P, Winblad B, Dickins DW, Mohammed AH. (2009). Influence of environmental manipulation on exploratory behaviour in male BDNF knockout mice. Behav Brain Res. 197(2):339-46. Epub 2008 Oct 5.

It is widely accepted that brain derived neurotrophic factor (BDNF) plays a crucial role in mediating changes in learning and memory performance induced by environmental conditions. In order to ascertain whether BDNF modulates environmentally induced changes in exploratory behaviour, we examined mice carrying a deletion in one copy of the BDNF gene. Young heterozygous male BDNF knockout mice (BDNF+/-) and their wild-type (WT) controls were exposed to the enriched environment condition (EC) or the standard condition (SC) for 8 weeks. Exploratory behaviour was assessed in the open-field (OF) and hole-board (HB) test. Brains from EC and SC reared animals were processed for Golgi-Cox staining and the dendritic spine density in the dentate gyrus (DG) and CA1 hippocampal regions were examined. We found behavioural differences both due to the genetic modification and the environmental manipulation, with the BDNF+/- mice being more active in the OF whereas the EC mice had increased exploratory behaviour in the HB test. Environmental enrichment also led to an increase in dendritic spines in the hippocampal CA1 region and DG of the wild-type mice. This effect was also found in the enriched BDNF+/- mice, but was less pronounced. Our findings support the critical role of BDNF in behavioural and neural plasticity associated with environmental enrichment and suggest that besides maze learning performance, BDNF dependent mechanisms are also involved in other aspects of behaviour. Here we provide additional evidence that exploratory activity is influenced by BDNF.

Veyrac A, Sacquet J, Nguyen V, Marien M, Jourdan F, Didier A. (2009). Novelty determines the effects of olfactory enrichment on memory and neurogenesis through noradrenergic mechanisms. Neuropsychopharmacology. 2009 Feb;34(3):786-95. Epub 2008 Oct 22.

Commonly used experimental paradigms of environmental enrichment combine increased social interactions and sensory inputs and renewal of the objects present in the environment. However, the specific contribution of novelty to the effects of enrichment is unclear. Here, we show that repeated daily exposure to single novel odorants and not to an enriched but stable olfactory environment improves short-term olfactory memory and neurogenesis in the mouse olfactory bulb. In addition, these positive effects are mediated by noradrenalin as they are blocked by a noradrenergic receptor antagonist. These data suggest that novelty recognition and noradrenergic mechanisms are crucial in mediating neural plasticity induced by olfactory enrichment.

Kelsch W, Lin CW, Mosley CP, Lois C. (2009). A critical period for activity-dependent synaptic development during olfactory bulb adult neurogenesis. J Neurosci. 2009 Sep 23;29(38):11852-8.

New neurons integrate in large numbers into the mature olfactory bulb circuit throughout life. The factors controlling the synaptic development of adult-born neurons and their connectivity remain essentially unknown. We examined the role of activity-dependent mechanisms in the synaptic development of adult-born neurons by genetic labeling of synapses while manipulating sensory input or cell-intrinsic excitability. Sensory deprivation induced marked changes in the density of input and output synapses during the period when new neurons develop most of their synapses. In contrast, when sensory deprivation started after synaptic formation was complete, input synapses increased in one domain without detectable changes in the other dendritic domains. We then investigated the effects of genetically raising the intrinsic excitability of new neurons on their synaptic development by delivering a voltage-gated sodium channel that triggers long depolarizations. Surprisingly, genetically increasing excitability did not affect synaptic

development but rescued the changes in glutamatergic input synapses caused by sensory deprivation. These experiments show that, during adult neurogenesis in the olfactory bulb, synaptic plasticity is primarily restricted to an early period during the maturation of new neurons when they are still forming synapses. The addition of cells endowed with such an initial short-lived flexibility and long-term stability may enable the processing of information by the olfactory bulb to be both versatile and reliable in the face of changing behavioral demands.

Benedetti BL, Glazewski S, Barth AL. (2009). Reliable and precise neuronal firing during sensory plasticity in superficial layers of primary somatosensory cortex. J Neurosci. 29(38):11817-27.

Neocortical neurons show astonishing variation in the presence and timing of action potentials across stimulus trials, a phenomenon whose function and significance has been the subject of great interest. Here we present data showing that this response variability can be significantly reduced by altered sensory experience. Removal of all but one whisker from the side of the mouse face results in the rapid (within 24 h) potentiation of mean firing rates within the cortical representation of the spared whisker in young postnatal animals (postnatal days 13-16). Analysis of single-unit responses from whisker-spared animals shows that this potentiation can be attributed to an enhancement of trial-to-trial reliability (i.e., reduced response failures), as well as an increase in the mean number of spikes evoked within a successful trial. Changes were confined to superficial layers 2/3 and were not observed in the input layer of the cortex, layer 4. In addition to these changes in firing rates, we also observed profound changes in the precise timing of sensory-evoked responses. Trial-to-trial temporal precision was enhanced and the absolute latency of responses was reduced after single-whisker experience. Enhanced spike-timing precision and trial-to-trial reliability could also be triggered in adolescent animals with longer periods (7 d) of single-whisker experience. These experiments provide a quantitative analysis of how sensory experience can enhance both reliability and temporal precision in neocortical neurons and provide a framework for testing specific hypotheses about the role of response variability in cortical function and the molecular mechanisms underlying this phenomenon.

Prior to 2009

Matthew S Grubb and Ian D Thompson (2004). The influence of early experience on the development of sensory systems. Current Opinion in Neurobiology 2004, 14:503–512

> Once sensory stimuli become able to alter firing patterns in the developing brain, they can influence the maturation of neuronal circuits. Recent experimental studies add to our understanding of precisely which developmental events are affected by early experience. In particular, it appears that experience of the external environment can affect the brain earlier in development and at earlier stages of sensory processing than previously thought. These studies emphasise the developmental importance of the patterning of neuronal firing produced either by sensory stimuli or by spontaneous activity. The timing of action potentials is also an important aspect of several exciting studies describing the mechanisms — anatomical, synaptic, and molecular — by which early experience brings about alterations in the maturation of sensory circuitry. Importantly, this kind of approach can lead to predictions concerning the nature of sensory stimulation
>
> that is most effective in instructing brain development

S. Lores-Arnaiz, J. Bustamante, A. Czernizyniec, P. Galeano, M. González Gervasoni, A. Rodil Martínez, N. Paglia, V. Cores, & M.R. Lores-Arnaiz (2007). Exposure to enriched environments increases brain nitric oxide synthase and improves cognitive performance in prepubertal but not in young rats. *Behavioural Brain Research*, *184*, 117-123.

> Rats were randomly assigned to enriched (EE) or standard environments (SE) at 21 or 73 days of age, for 17 days. Half of the rats of each rearing condition were trained in a radial maze (RM). At 38 days (pre-pubertal) or 90 days (young), rats were sacrificed and brain cytosolic and mitochondrial nitric oxide synthase (mtNOS) activity was assayed. Western blot analysis of brain mtNOS was conducted. In the pre-pubertal group, EE rats improved their performance in the RM while SE rats did not. In the young group, SE and EE rats showed a random performance in the RM. In SE pre-pubertal rats, training increased brain cytosolic NOS and mtNOS activity by 68% and 82%. In EE non-trained pre-pubertal rats,

brain cytosolic NOS and mtNOS activity increased by 80% and 60%, as compared with SE non-trained pre-pubertal rats. In EE pre-pubertal rats that were trained, brain cytosolic NOS and mtNOS activity increased by 70% and 90%, as compared with SE pre-pubertal rats that were not trained. A higher protein expression of brain mtNOS was found in EE rats, as compared with SE animals. Mitochondrial complex I activity was higher in EE than in SE rats. Training had no effect on complex I activity neither in SE nor in EE rats. In young rats, no significant differences in enzyme activities were found between EE and SE rats. These results support the hypothesis that brief exposure to EE and training produce effects on behavioral performance and on biochemical parameters in an age-dependent manner.

Bark, K. Wheeler, J.W. Premakumar, S. & Cutkosky, M.R (2008). Comparison of Skin Stretch and Vibrotactile Stimulation for Feedback of Proprioceptive Information. This paper appears in: Haptic interfaces for virtual environment and teleoperator systems, 2008. haptics 2008. symposium 71-78.

We present the results of experiments to compare vibration and skin stretch in a virtual proprioception task in which subjects used a force sensor to control the movement of a virtual aim. Pilot experiments pointed to the need to provide the arm with varying dynamics (like a real arm) and to scale the feedback from vibratory and skin stretch displays to demonstrate a clear improvement in the accuracy of movement. For the final experiments, ten subjects were first trained on the system with visual feedback and then tested with vibratory feedback, skin stretch feedback and no feedback. Both vibration and skin stretch improved the subjects' performance. For some subjects, a second no-feedback case showed improvement over the initial case, indicating learning; in other cases, the no- feedback performance deteriorated and subjects reported that they had become used to relying on feedback. Overall, skin stretch provided superior results, particularly when the virtual arm was in a low-inertia configuration and at low velocity. The results suggest that small skin-stretch devices could be worn on the body to provide useful proprioceptive information when interacting with virtual environments and in motion training for rehabilitation or sports.

Alessandro Sale,[1*] Maria Cristina Cenni,[2] Francesca Ciucci,[1] Elena Putignano,[1] Sabrina Chierzi,[1] & Lamberto Maffei[.] (2007). Maternal Enrichment during Pregnancy Accelerates Retinal Development of the Fetus *PLoS ONE*, *2*, e1160.

The influence of maternal environment on fetal development is largely unexplored, the available evidence concerns only the deleterious effects elicited by prenatal stress. Here we investigated the influence of prenatal enrichment on the early development of the visual system in the fetus. We studied the anatomical development of the rat retina, by analyzing the migration of neural progenitors and the process of retinal ganglion cell death, which exerts a key role in sculpturing the developing retinal system at perinatal ages. The number of apoptotic cells in the retinal ganglion cell layer was analyzed using two distinct methods: the presence of pyknotic nuclei stained for cresyl violet and the appearance of DNA fragmentation (Tunel method). We report that environmental enrichment of the mother during pregnancy affects the structural maturation of the retina, accelerating the migration of neural progenitors and the dynamics of natural cell death. These effects seem to be under the control of insulin-like growth factor-I: its levels, higher in enriched pregnant rats and in their milk, are increased also in their offspring, its neutralization abolishes the action of maternal enrichment on retinal development and chronic insulin-like growth factor-I injection to standard-reared females mimics the effects of enrichment in the fetuses. Thus, the development of the visual system is sensitive to environmental stimulation during prenatal life. These findings could have a bearing in orienting clinical research in the field of prenatal therapy.

Percaccio, C.R., Pruette, A.L., Mistry, S.T., Chen, Y.H. & Kilgard, M.P. (2007). Sensory experience determines enrichment-induced plasticity in rat auditory cortex *Brain Research*, *1174*, 76-91.

Our previous studies demonstrated that only a few days of housing in an enriched environment increases response strength and paired-pulse depression in the auditory cortex of awake and anesthetized rats [Engineer, N.D., Percaccio, C.R., Pandya, P.K., Moucha, R., Rathbun, D.L., Kilgard, M.P., 2004. Environmental enrichment improves response strength, threshold, selectivity, and latency of auditory cortex neurons. J Neurophysiol. 92, 73–82 and Percaccio, C.R., Engineer, N.D., Pruette, A.L., Pandya, P.K., Moucha, R., Rathbun, D.L., Kilgard, M.P., 2005. Environmental enrichment increases paired-pulse depression in rat auditory cortex. J Neurophysiol. 94, 3590–3600]. Multiple environmental

and neurochemical factors likely contribute to the expression of this plasticity. In the current study, we examined the contribution of social stimulation, exercise, auditory exposure, and cholinergic modulation to enrichment-induced plasticity. We recorded epidural evoked potentials from awake rats in response to tone pairs and noise bursts. Auditory evoked responses were not altered by social stimulation or exercise. Rats that could hear the enriched environment, but not interact with it, exhibited enhanced responses to tones and increased paired-pulse depression. The degree to which enrichment increased response strength and forward masking was not reduced after a ventricular injection of 192 IgG-saporin. These results indicate that rich auditory experience stimulates physiological plasticity in the auditory cortex, despite persistent deficits in cholinergic activity. This conclusion may be beneficial to clinical populations with sensory gating and cholinergic abnormalities, including individuals with autism, schizophrenia, and Alzheimer's disease.

Schmuckler MA, & Jewell DT. (2007). Infants' visual-proprioceptive intermodal perception with imperfect contingency information. *Developmental Psychobiology*, *49*, 387-98.

Two experiments explored 5-month-old infants' recognition of self-movement in the context of imperfect contingencies between felt and seen movement. Previous work has shown that infants can discriminate a display of another child's movements from an on-line video display of their own movements, even when featural information is removed. These earlier findings were extended by demonstrating self versus other discrimination when the visual information for movement was an unrelated object (a fluorescent mobile) directly attached to the child's leg, thus producing imperfect spatial and temporal contingency information. In contrast, intermodal recognition failed when the mobile was indirectly attached to infants' legs, thus eliminating spatial contingencies altogether and further weakening temporal contingencies. Together, these studies reveal that even imperfect contingency information can drive intermodal perception, given appropriate levels of spatial and temporal contingency information. (c) 2007 Wiley Periodicals, Inc.

Kreppner, J. M.; Rutter, M., Beckett, C., Castle, J., Colvert, E., Groothues, C., Hawkins, A., O'Connor, T.G., Stevens, S., Sonuga-Barke, & Edmund J. S. (2007). Normality and Impairment following Profound Early Institutional Deprivation: A Longitudinal follow-up into Early Adolescence. ***Developmental Psychology*****, *43* , 931-946.**

Longitudinal analyses on normal versus impaired functioning across 7 domains were conducted in children who had experienced profound institutional deprivation up to the age of 42 months and were adopted from Romania into U.K. families. Comparisons were made with noninstitutionalized children adopted from Romania and with nondeprived within-U.K. adoptees placed before the age of 6 months. Specifically, the validity of the assessment, the degree of continuity and change in levels of functioning from 6 to 11 years, and the factors in the pre- and postadoption environment accounting for heterogeneity in outcome were examined. Pervasive impairment was significantly raised in children experiencing institutional deprivation for =6 months of life, with a minority within this group showing no impairment. There was no additional significant effect of duration of deprivation beyond the 6-month cutoff, and few other predictors explained outcome. The pattern of normality/impairment was mainly established by 6 years of age, with considerable continuity at the individual level between 6 and 11 years. The findings are discussed in terms of the possibility of a sensitive period for development.

Jiao, Y.., Zhang, C., Yanagawa,Y., & Sun, Q. (2006). Major Effects of Sensory Experiences on the Neocortical Inhibitory Circuits. ***Journal of Neuroscience****, 26,* 8691-8701

During postnatal development, sensory experiences play critical roles in the refinement of cortical connections. However, both the process of postnatal experience-dependent maturation of neocortical inhibitory networks and its underlying mechanisms remain elusive. Here, we examined the differential properties of intracortical inhibitory networks of layer IV in "sensory-spared" and "sensory-deprived" cortices of glutamate acid decarboxylase 67 (GAD67)–green fluorescent protein (GFP) (Δneo) and wild-type mouse. Our results showed that row D whisker trimming (WT) begun at postnatal day 7 (P7), but not after P15, induced a robust reduction of parvalbumin (PV) expression, measured by the PV/GFP ratio and PV cell densities, in the deprived barrels. WT also induced a robust reduction in the number of inhibitory perisomatic varicosities and synaptic GAD65/67 immunoreactivities in spiny neurons of the deprived barrels. Although the GAD65/67 expressions in interneurons were also downregulated in the deprived barrels, the GFP

expression remained unchanged. Patch-clamp recording from spiny cells showed a 1.5-fold reduction of intracortical evoked IPSCs (eIPSCs) in deprived versus spared cortices. The reduction in eIPSCs occurred via changes in presynaptic properties and unitary IPSC amplitudes. Miniature IPSCs showed subtle but significant differences between the two experimental conditions. In addition, properties of the IPSCs in deprived barrels resemble those of IPSCs recorded in immature brains (P7). Together, these results suggest that the properties of local intracortical inhibitory networks are modified by sensory experiences. Perisomatic inhibition mediated by PV-positive basket cells is pruned by sensory deprivation.

Hay, L, Bard, C., Ferrel, C., Olivier, I., & Fleury, M. (2005). Role of proprioceptive information in movement programming and control in 5 to 11-year old children. *Human Science Movement*, 24, 139-154.

This study investigated the role of proprioceptive sensations in the control of hand movements towards specific targets. The subjects consisted of four groups of boys and girls: fifteen 5-year olds, thirteen 7-year olds, twelve 9-year olds, and twelve 11-year olds. They performed a serial pointing task by alternating wrist flexion and extension. They made movements of various amplitudes and various positions using a pointer. Under the experimental conditions, the subjects received tendon vibration to the wrist flexors and extensors either while stopped at the targets or while moving towards the targets. The vibration altered the proprioceptive information. Additionally during the experimental phases the children did not receive visual feedback of their movements or pointing errors. The application of vibration during motion led to an increased constant error of reduced movement amplitude in all age groups and position error in the direction of the movement starting point. The distortion of proprioceptive input during the static phases before movement increased the variable amplitude error, with the greatest negative effect on 5-year old children performing extension movements. The conclusions were that: there are 1) developmental trends in the weighted use of proprioceptive input in the feedforward and feedback based components of movement control in children, 2) changes that include an improved ability to shift from one strategy to another, dependent upon the incoming sensory information, and 3) developmental trends indicating alternating mastery of different approaches to control of amplitude and position leading to eventual integrated use of the approaches. More specifically, the 5-year old children relied primarily on a ballistic-like type of movement control governed by the spatial reference of the hand starting position; the 7- and 9-year old children depend more on vision to direct their hand

movements and spatial calibration of hand position during movement; and the 11-year old children were best at congruently controlling for both amplitude and spatial movement parameters.

SIGN note: This study provides information about the developmental trends in typical children relative to the use of proprioceptive sensations to direct hand movements. The findings could expand Ayres' SI theory on the effects of vision and proprioception on praxis.

Reviewed by Katherine Inamura, 11/18/2005

Restivo, L., Ferrari, F., Passino, E., Sgobio, C., Bock, J., Oostra, B.A., Bagni, C., & Ammassari-Teule, M., (2005). Enriched environment promotes behavioral and morphological recovery in a mouse model for the fragile X syndrome. N*euroscience*, *102,* 11557-11562.

Fragile X syndrome, the most frequent form of hereditary mental retardation, is due to a mutation of the fragile X mental retardation 1 (*FMR1*) gene on the X chromosome. Like fragile X patients, *FMR1*-knockout (*FMR1*-KO) **mice** lack the normal fragile X mental retardation protein (FMRP) and show both cognitive alterations and an immature neuronal morphology. We reared *FMR1*-KO **mice** in a C57BL/6 background in enriched **environmental** conditions to examine the possibility that experience-dependent stimulation alleviates their behavioral and neuronal abnormalities. *FMR1*-KO **mice** kept in standard cages were hyperactive, displayed an altered pattern of open field exploration, and did not show habituation. Quantitative morphological analyses revealed a reduction in basal dendrite length and branching together with more immature-appearing spines along apical dendrites of layer five pyramidal neurons in the visual cortex. **Enrichment** largely rescued these behavioral and neuronal abnormalities while increasing α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) glutamate receptor subunit 1 (GluR1) levels in both genotypes. **Enrichment** did not, however, affect FMRP levels in the WT **mice**. These data suggest that FMRP-independent pathways activating glutamatergic signaling are preserved in *FMR1*-KO **mice** and that they can be elicited by **environmental** stimulation.

Sober, S. J. & Sabes, P. N. (2005). Flexible strategies for sensory integration during motor planning. *Nature Neuroscience*, 8(4), 490-497.

This study investigated the process of combining visual and proprioceptive feedback to create two estimates of the arm's position for planning target-directed movements. One estimate is used for movement vector planning and the other is for conversion of the direction into a motor command. The first experiment involved 5 female and 2 male subjects, 18 – 34 years of age. The subjects made planar reaching movements on a horizontal table with virtual visual feedback to either a visual target (spot of light) or a proprioceptive target, (felt position of left index fingertip). The visual feedback was eliminated as the subject began to reach. The second experiment included 5 female and 5 male subjects, 18 – 34 years of age. The subjects made the reaching movements to visual targets and received feedback of either a spot indicating fingertip position or simple virtual image of the arm. The researchers interpreted the results of the experiments to be evidence that the brain weights visual and proprioceptive input according to the sensory modality of the target and the information content of the visual feedback. The planning of the reach direction is more dependent upon visual information and creation of the motor command is more dependent upon proprioceptive information. The researchers postulated that the variability in the weightings was to reduce errors related to the transformation of sensory signals between coordinate frames.

SIGN note: This study provides information about the integration of proprioceptive and visual sensations to direct hand movements in adults. The findings could expand Ayres' SI theory on the effects of vision and proprioception on praxis.

Reviewed by Katherine Inamura, 1/28/2006

Soto-Faraco, S., Ronald, A., & Spence, C. (2004). Tactile selective attention and body posture: assessing the multisensory contributions of vision and proprioception. *Perception & Psychophysics*, 66 (7), 1077-1094.

This study evaluated the effects of proprioceptive and visual cues concerning arm/hand posture on tactile spatial attention. Five experiments were performed utilizing small groups (n = 8-10 male and female college students). In each experiment the subjects were required to speedily report if the continuous vibrotactile stimulus was being received either by the thumb or index finger (either in an up or down position) on one hand while a digit (either thumb or index finger) on the other hand was receiving a pulsed vibrotactile distractor stimulus. The first four experiments were conducted in a darkened room to eliminate

visual cues. The first two experiments indicated that the subjects could not ignore the distractor stimulus to the non-target hand. The interference effect was greatest when the hand to receive the target stimulus was uncertain. The results suggested that people could direct their spatial attention to a particular hand when the target hand was known in advance and that this focusing of attention improved the processing of the target stimulation. The findings also indicated that the shifting of attention across the body surface to orient to a target stimulus requires time. The third experiment involved varying the posture of the hands (i.e., hand/wrist up or down, in different combinations). It was found that the perception of the target stimulus was effected by the position of the target and distractor in external space or relative to some part of the body. The fourth experiment contrasted the effects of the proprioceptive inputs of a hands-near position and hands-far position. The interference effect of the distractor stimulus was greatest when the hands were in the near position. These latter two studies supported the postulate that tactile spatial attention is based on an abstract frame of reference (either based egocentrically or externally). For the final experiment the subjects placed one arm close to the body midline and the other arm extended away from their trunk. For half of the trials for each participant, a mirror was used so that the two arms appeared to be close together although the arms actually were not close. The interference effect from the distractors was higher when the arms visually appeared to be closer together. This result suggests that the integration of the visual information was automatically integrated with the tactile and proprioceptive input. The researchers interpreted the studies' results to suggest that multisensory integration of tactile, visual, and proprioceptive information occurs prior to tactile selective attention. Furthermore, they suggest that as a person assumes different body postures there is a reconfiguration of tactile spatial information based on the information from muscle position and gravitational forces to aid in accurate perception of touch stimuli in space. However, the body representation may not be error-free and time is required to improve its preciseness.

SIGN note: The study's findings contribute to the understanding of how visual, proprioceptive, and tactile input is integrated to assist in attention to and interpretation of localized tactile sensations, important in Ayres' SI theory. This information could be helpful in refining tests of tactile perception. It also seems to lend support for the principle of providing varied, multi-sensory enriched activities to promote better integration of sensory information.

Reviewed by Katherine Inamura, 11/18/2005

N. Benaroya-Milshtein, N. Hollander, A. Apter, T. Kukulansky, N. Raz, A. Wilf, I. Yaniv, & C.G. Pick (2004). Environmental enrichment in mice decreases anxiety, attenuates stress responses and enhances natural killer cell activity. *European Journal of Neuroscience 20,* 1341–1347.

The importance of environment in the regulation of brain, behaviour and physiology has long been recognized in biological, social and medical sciences. Animals maintained under enriched conditions have clearly been shown to have better learning abilities than those maintained under standard conditions. However, the effects of environmental enrichment (EE) on immunity and emotionality have been less documented and remain questionable. Therefore, we investigated the effect of EE on natural killer (NK) cell activity, psychological stress responses and behavioural parameters. Male C3H mice were housed either in enriched or standard conditions for 6 weeks. Behaviour was then examined by the grip-strength test, staircase and elevated plus maze, and corticosterone levels and NK cell activity were measured. Furthermore, animals exposed to the stress paradigm, achieved by electric shock with reminders, were tested for freezing time in each reminder. Corticosterone levels were also measured. The EE mice showed decreased anxiety-like behaviour and higher activity compared to standard mice, as revealed by a greater percentage of time spent in the open arms of the elevated plus maze, and a higher rate of climbing the staircase. A shorter freezing time in the stress paradigm and no corticosterone level reactivity were measured in EE mice. In addition, NK cell activity in spleens of EE mice was higher than that demonstrated in those of standard mice. Thus, EE has a beneficial effect on anxiety-like behaviour, stress response and NK cell activity. The effect on NK cell activity is promising, due to the role of NK cells in host resistance.

Engineer, N.D., Percaccio, C.R., Pandya, P.K., Moucha, R., Rathbun D.L. & Kilgard, M.P. (2004). Environmental Enrichment Improves Response Strength, Threshold, Selectivity, and Latency of Auditory Cortex Neurons *Journal of Neurophysiology, 92,* 73-82,

Over the last 50 yr, environmental enrichment has been shown to generate more than a dozen changes in brain anatomy. The consequences of these physical changes on information processing have not been well studied. In this study, rats were housed in enriched or standard conditions either prior to or after reaching sexual maturity. Evoked potentials from awake rats and extracellular recordings from anesthetized rats were used to document responses of auditory cortex neurons. This report details several significant, new findings about the

influence of housing conditions on the responses of rat auditory cortex neurons. First, enrichment dramatically increases the strength of auditory cortex responses. Tone-evoked potentials of enriched rats, for example, were more than twice the amplitude of rats raised in standard laboratory conditions. Second, cortical responses of both young and adult animals benefit from exposure to an enriched environment and are degraded by exposure to an impoverished environment. Third, housing condition resulted in rapid remodeling of cortical responses in <2 wk. Fourth, recordings made under anesthesia indicate that enrichment increases the number of neurons activated by any sound. This finding shows that the evoked potential plasticity documented in awake rats was not due to differences in behavioral state. Finally, enrichment made primary auditory cortex (A1) neurons more sensitive to quiet sounds, more selective for tone frequency, and altered their response latencies. These experiments provide the first evidence of physiologic changes in auditory cortex processing resulting from generalized environmental enrichment.

Cancedda L, Putignano E, Sale A, Viegi A, Berardi N, Maffei L. (2004). Acceleration of visual system development by environmental enrichment. *Journal of Neuroscience*, *24*, 4840-8.

Thus far, the developmental plasticity of the visual system has been studied by altering or reducing visual experience. Here, we investigated whether a complex sensory-motor stimulation, provided by rearing animals in an enriched environment, affects visual system development. We found that raising mice in this condition causes an earlier eye opening, a precocious development of visual acuity, and an accelerated decline of white matter-induced long-term potentiation. These effects are accompanied by a precocious cAMP response element-mediated gene expression and a significant increase of BDNF protein and GAD65/67 expression in enriched pups. In addition, we showed that enriched pups experienced higher levels of licking behavior provided by adult females. Thus, rearing mice from birth in an enriched environment leads to a conspicuous acceleration of visual system development as ascertained at behavioral, electrophysiological, and molecular level.

Morley-Fletcher, S., Rea, M., Maccari, S., & Laviola, G. (2003). Environmental enrichment during adolescence reverses the effects of prenatal stress on play behaviour and HPA axis reactivity in rats. *European Journal of Neuroscience 18*, 3367–3374.

Prenatal stress (PS) can produce profound and long-lasting perturbations of individual adaptive capacities, which in turn can result in an increased proneness to behavioural disorders. Indeed, in PS rats there is evidence of impaired social play behaviour, disturbances in a variety of circadian rhythms, enhanced anxiety and increased hypothalamic–pituitary–adrenal (HPA) axis reactivity. This study was designed to experimentally investigate the degree of reversibility of PS-induced disturbances of social play and HPA reactivity by assessing the effect of the enrichment of the physical environment on PS rats during periadolescence. PS subjects showed a reduced expression of social play behaviour and a prolonged corticosterone secretion in response to restraint stress, but both these effects were markedly reversed following environmental enrichment. Interestingly, the enrichment procedure increased social behaviour but had no effect on corticosterone secretion in nonstressed animals, indicating a differential impact of the postnatal environment as a function of prenatal background. As a whole, results clearly indicate that rats prenatally exposed to stress can benefit during periadolescence from the modulatory effects of an enriched environment. Moreover, they confirm that PS may well represent a suitable animal model for the design and testing of new therapeutic strategies for behavioural disorders produced by early insults

Brown, J., Cooper-Kuhn, C. M., Kempermann, G., Van Praag, H., Winkler, J., Gage, F. H., Kuhn, H. G. (2003). Enriched environment and physical activity stimulate hippocampal but not olfactory bulb neurogenesis. *European Journal of Neuroscience*, *17*, 2042–2046.

Exposure to an enriched environment and physical activity, such as voluntary running, increases neurogenesis of granule cells in the dentate gyrus of adult mice. These stimuli are also known to improve performance in hippocampus-dependent learning tasks, but it is unclear whether their effects on neurogenesis are exclusive to the hippocampal formation. In this study, we housed adult mice under three conditions (enriched environment, voluntary wheel running and standard housing), and analysed proliferation in the lateral ventricle wall and granule cell neurogenesis in the olfactory bulb in comparison to the dentate gyrus. Using bromodeoxyuridine to label dividing cells, we could not detect any

difference in the number of newly generated cells in the ventricle wall. When giving the new cells time to migrate and differentiate in the olfactory bulb, we observed no changes in the number of adult-generated olfactory granule cells; however, voluntary running and enrichment produced a doubling in the amount of new hippocampal granule cells. The discrepancy between the olfactory bulb and the dentate gyrus suggests that these living conditions trigger locally through an as yet unidentified mechanism specific to neurogenic signals in the dentate gyrus.

Francis, D.D. Diorio, J. Plotsky, P.M., & Meaney, M.J. (2002). Environmental Enrichment Reverses the Effects of Maternal Separation on Stress Reactivity. *The Journal of Neuroscience, 22*, 7840-7843.

Postnatal maternal separation increases hypothalamic corticotropin-releasing factor (CRF) gene expression and hypothalamic-pituitary-adrenal (HPA) and behavioral responses to stress. We report here that **environmental enrichment** during the peripubertal period completely **reverse**s the effects of maternal separation on both HPA and behavioral responses to stress, with no effect on CRF mRNA expression. We conclude that **environmental enrichment** leads to a functional reversal of the effects of maternal separation through compensation for, rather than reversal of, the neural effects of early life adversity.

Florence , S.L., Boydston, T.A., Hackett, H., Lachoff, Taub, Strata, F., & Niblock, M.M. (2001). Sensory enrichment after peripheral nerve injury restores cortical, not thalamic, receptive field organization. European Journal of Neuroscience, 13, 1755-1766.

These authors examined the effect of providing sensory enrichment experiences to 6 macaque monkeys after inducing a median nerve cut and repair early in life. One of these macque monkeys received a nerve cut, however, was restrained from using the hand, therefore resulting in not receiving any enriched sensory experiences. Multiunit microelectrodes were used to map the sensory representation of the hand in the primary somatosensory cortex. The somatosensory relay in the thalamus and the ventroposterior nucleus was also studied to

determine if the sensory enrichment experience was initiated subcortically or cortically. It was found that rehabilitation involving sensory retraining could improve perceptual function, most probably through plasticity in the somatosensory processing network in the brain. The effect of sensory enrichment was found to be cortically related with the most significant effect on the receptive field sizes in the cortical area 3b. It was found that sensory rehabilitation after nerve regeneration can significantly improve sensory perception and changes in map organization after an injury, however, it does not completely produce normal maps of the hand representation. The effects of sensory enrichment on the functional organization of cortical area 3b is an important component that leads to more improved perceptual outcomes as a function of rehabilitation after a nerve injury.

Praag, H. V., Kempermann, G., Gage, F.H. (2000). Neural Consequences of Envrionmental Enrichment. *Macmillan Magazines LTD, 1* , 191-198.

This review paper examines the neuronal changes that occur in reaction to complex stimulation by an enriched environment. More specifically, the authors of this study focuses on the impact of certain elements of enrichment, including exercise and learning, on behavior and neurobiology. The paper reviews a variety of different studies (primarily of rats) that support the following: First, environmental enrichment has been shown to enhance spatial memory and exercise enhances spatial learning. Second, environmental enrichment enhances cell survival and exercise enhances cell proliferation. Third, research has shown that motor skill learning, through exercise, may lead to increased cortical thickness and synaptogenesis. Fourth, living in an enriched environment that integrates exercise may lead to higher levels of growth factors, which may impact learning and synaptic plasticity. Fifth, an enriched environment that integrates exercise has been shown to result in an increase in neurotransmitters, such as acetylcholine. Finally, enriched environments have been shown to facilitate a recovery in damaged or diseased brains, e.g. a brain that has suffered a stroke. However, additional research needs to be conducted in order to determine if these positive effects are long lasting.

van Praag, H., Kempermann, G. & Gage, F.H. (1999). Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus. *Nature Neuroscience 2*, 266 – 270.

Exposure to an enriched environment increases neurogenesis in the dentate gyrus of adult rodents. Environmental enrichment, however, typically consists of many components, such as expanded learning opportunities, increased social interaction, more physical activity and larger housing. We attempted to separate components by assigning adult mice to various conditions: water-maze learning (learner), swim-time-yoked control (swimmer), voluntary wheel running (runner), and enriched (enriched) and standard housing (control) groups. Neither maze training nor yoked swimming had any effect on bromodeoxyuridine (BrdU)-positive cell number. However, running doubled the number of surviving newborn cells, in amounts similar to enrichment conditions. Our findings demonstrate that voluntary exercise is sufficient for enhanced neurogenesis in the adult mouse dentate gyrus.