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Environmental conditions strongly affect brain plasticity

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Abstract: During development, experience continuously interacts with genetic information to shape and optimize neuronal circuits and behaviour. Therefore, environmental conditions have a powerful impact on the brain. To date, accumulating evidence shows that raising animals in a so-called "enriched environment" elicits remarkable effects on the brain across molecular, anatomical, and functional levels when compared to animals raised in a "standard cage" environment. In our article, we provide a brief review of the field and illustrate the different results of "enriched" versus standard cage-raised rodents with examples from visual system plasticity. We also briefly discuss parallel studies of enrichment effects in humans. Collectively, these data highlight that results should always be considered in the context of the animals' environment.

Keywords: ageing; enrichment; ocular dominance; standard cage; visual cortex

Introduction and objectives

Canadian psychologist Donald Hebb is known for his influential theory on how neurons in the brain adapt during learning, presented in his classic work "The Organization of Behavior" (1949). Hebb's postulate is often summarized by the phrase: "Neurons wire together if they fire together" (Löwel and Singer, 1992). Though less well known, he is also an inadvertent founding father of research on so-called "enriched environment" effects on animal behaviour. In the 1940s, he took some laboratory rats home and let his kids play with them like pets. While in Hebb's house, the pet rats were taken out of their cages and provided the opportunity to play and socialize with the other pet rats. Anecdotally, Hebb observed that the pet rats were better at problem solving tasks compared to the laboratory rats (Hebb, 1947). In the 1960s, the psychologist Mark Rosenzweig reported that enriched adult rats had an 8% increase in thickness of the cerebral cortex (Rosenzweig et al., 1962). Despite this amazing finding, the idea that the brain could be plastic (grow and change) in adult rats – a property thought to be limited to juveniles – continued to escape attention of the scientific community. It was not until the landmark experiments by William T. Greenough in the late 1960s and 1970s, demonstrating greater dendritic growth in the visual cortex of rats that were raised in stimulating cages, with daily replacement of toys and repositioning of wooden climbing boards, that environmental influences on the brain came into focus. Indeed, this seminal work represented a paradigm shift: previously, the brain was believed to be fixed very early in life, largely under genetic control, while these findings revealed the profound influence of environment in shaping the brain (for a brief historical review see Markham and Greenough, 2004).

Since these first studies, there is a vast, and still accumulating, body of scientific studies examining enrichment effects on the brain. Enriched environment is classically defined as "a combination of complex inanimate and social stimulation" (Rosenzweig et al., 1962). While the specifics of enrichment vary between species, and between laboratories/studies, enrichment is generally characterized by enhanced opportunities to engage in voluntary physical, social, and cognitive stimulation. In the context of laboratory rodents, standard cages are relatively small, usually translucent, with a small number of animals (up to 5) housed together in an otherwise empty cage with woodchip bedding, and water and food *ad li-*

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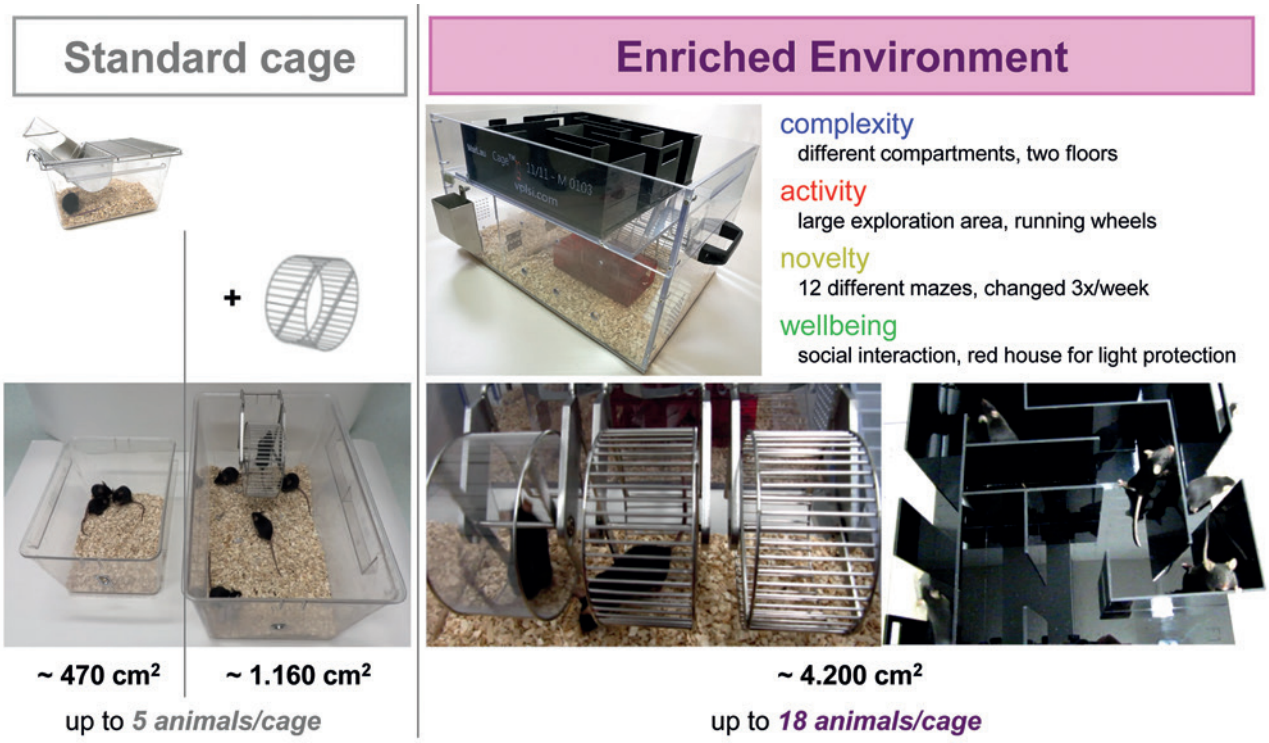

Fig. 1: Comparison of different mouse rearing conditions, as used in the Löwel-laboratory: standard cage, standard cage with running wheel, and "enriched" environment (EE) cage.

bitum. In contrast, enriched environment (EE) cages are bigger, house a larger number of animals, and provide a variety of stimulation, for example, running wheels, regularly changed labyrinths and toys (Figure 1; see also van Praag et al., 2000).

Animals raised in EE-cages, or transferred, even for a short period, show remarkable changes across molecular, anatomical, and functional levels, compared to standard cage-housed animals (for a review see Sale et al., 2014). For example, in rodents, enrichment alters expression of key signalling molecules involved in regulating brain excitability and plasticity (Cancedda et al., 2004), increases volume of many brain areas (Diamond et al., 1964; Beaulieu and Colonnier, 1987), and alters maternal behaviour (Sale et al., 2004).

Here, we review studies of enrichment effects on age-related declines in plasticity. Early in life, the brain is exceedingly 'plastic' and neural circuit organization and function is readily modified in response to experience. With age, the capability for plasticity declines. In this review, we use examples from enrichment studies in rodent visual cortex to discuss the influence of housing on plasticity capability at different ages, with standard cage-housed animals showing severely reduced neuronal plasticity and progressive decline in plasticity with age, which is prevented by enrichment housing.

Enrichment housing also induced beneficial effects in mouse models of many brain disorders, including Huntington's, multiple sclerosis, epilepsy, Parkinson's, Alzheimer's, schizophrenia, autism spectrum disorders, and depression (Hannan, 2014; Mo et al., 2015; Fischer, 2016). Though detailed discussion of translational and clinical studies is beyond the scope of this review, we give examples of complementary findings from enrichment studies in healthy humans.

As others have noted, 'enrichment' is obviously a relative term, and 'standard' cages in laboratory rodents represent an impoverished – rather than 'normal' – environment (Hannan, 2014). Although the influence of housing is routinely considered in preclinical and translational studies, particularly when assessing validity of mouse models (reviewed extensively elsewhere: Tkacs and Thompson, 2006; Burrows and Hannan, 2013; Burrows et al., 2015; Mo et al., 2015), in basic research, housing and other contextual factors have only recently gained attention. We argue that it is essential to consider the influence of housing on "baseline" or control measures when interpreting results from laboratory animals.

Environmental enrichment affects capability and rate of experience-dependent plasticity in rodent visual cortex

Ocular dominance (OD), or eye preference, refers to the relative strength of responses in primary visual cortex (V1) from inputs of one eye compared to the other eye. OD-plasticity in V1 of mammals is one of the best studied models of experience-dependent plasticity (Wiesel and Hubel, 1963, Espinosa and Stryker, 2012) and is a well-characterised paradigm in which to test effects of environmental enrichment on plasticity. As in humans, rodent V1 is divided into a monocular part, receiving inputs from only the contralateral eye, and a binocular part, receiving inputs from both eyes. The classic experiments of Hubel and Wiesel in the 1960s demonstrated in cats that disrupting normal binocular experience by closing one eye (monocular deprivation, an experimental model of cataract) during an early phase of postnatal development caused irreversible modifications of V1 circuits. Likewise, in rodents, V1 activity is normally dominated by inputs from the contralateral eye, however, with monocular deprivation, OD shifts to favour inputs from the open eye (Dräger, 1975, Dräger, 1978). In standard cage-raised mice, OD-plasticity peaks in juveniles (postnatal day (P) 28; Dräger, 1978; Gordon and Stryker, 1996; Sawtell et al., 2003) but declines with age (Gordon and Stryker, 1996; Cang et al., 2005). In adult mice, significant OD shifts are still possible up to age P110, but require a longer period of monocular deprivation (7 days vs. 4 days in juvenile mice) (Sato and Stryker, 2008). Beyond age P110, even 14 days of monocular deprivation failed to induce OD-plasticity in standard cage-housed mice (Lehmann and Löwel, 2008; Espinosa and Stryker, 2012; Levelt and Hübener, 2012).

Enrichment cages strongly influenced deprivation-induced changes in V1 activation (Greifzu et al., 2014) (Figure 2). In a first study, we compared standard cage and EE-raised mice up to age ~P200. In contrast to standard cage-housed mice, that lost OD-plasticity beyond P110, even the oldest EE-raised mice continued to display OD-plasticity after 7 days of monocular deprivation. Since 200 days represents a mature, but by no means 'elderly' age for laboratory mice, we tested even older mice and surprisingly observed that optically recorded OD-plasticity was preserved *lifelong* in mice raised in the EE-cages (Greifzu et al., 2016). Notably, transferring standard cage-raised mice to EE cages at an advanced age (beyond P 110), restored optically recorded OD-plasticity: even the oldest enriched mouse tested (P 922) still displayed OD-plasticity (Greifzu et al., 2014; Greifzu et al., 2016).

Another age-related feature of OD-plasticity is that a longer duration monocular deprivation is required for OD-plasticity in older compared to younger standard cage-housed animals. While young standard cage-housed mice require only 4 days monocular deprivation for OD-plasticity, older animals require at least 7 days monocular deprivation to induce the same magnitude of shift in OD, measured by optical imaging and electrophysiological methods (Gordon and Stryker, 1996; Lehmann and Löwel, 2008; Sato and Stryker, 2008). How about EE-housed mice? Recently, we showed that monocular deprivation-induced activation changes in V1 are already visible after only 2 days in EE-raised mice of all tested ages (up to P283), suggesting that EE enables this rapid plasticity at any age. In some cases of young EE-raised mice, OD-plasticity was present after just 1 day of monocular deprivation (Kalogeraki et al., 2017). These data clearly show that housing conditions affect not only capability but also rate of experience-dependent plasticity in visual cortex, and thus that standard cage housing may strongly slow down experience-dependent network changes.

While plasticity declines with aging, it is also compromised after brain injury. For example, adult standard cage-raised mice do not express OD-plasticity after small stroke lesions in cortical regions outside V1: primary somatosensory cortex (Greifzu et al., 2011, Greifzu et al., 2012), or motor cortex, despite being further from V1 (Pielecka-Fortuna et al., 2015). Interestingly, this was *not* the case in EE-raised mice: OD-plasticity persisted not only in much older mice, but also after an S1-stroke (Greifzu et al., 2014). We next tested whether juvenile (standard cage-raised) mice would also be less affected by the S1-stroke. This was also the case: Young standard cage-mice continued to display OD-plasticity in V1, resembling non-lesioned animals. Thus mice were protected from (at least some) stroke-induced impairments of cortical plasticity if they were either young or raised in EE-cages. In other words, adult mice had compromised OD-plasticity after a stroke *only* if they were raised in the impoverished standard cages.

What can we conclude from these observations? Since raising mice in less impoverished EE-cages preserves or rescues compromised OD-plasticity in aged and stroke-affected animals, in our opinion, the fairest conclusion is that standard cage housing conditions are detrimental to plasticity, resulting in a rapid decline in OD-plasticity with age.

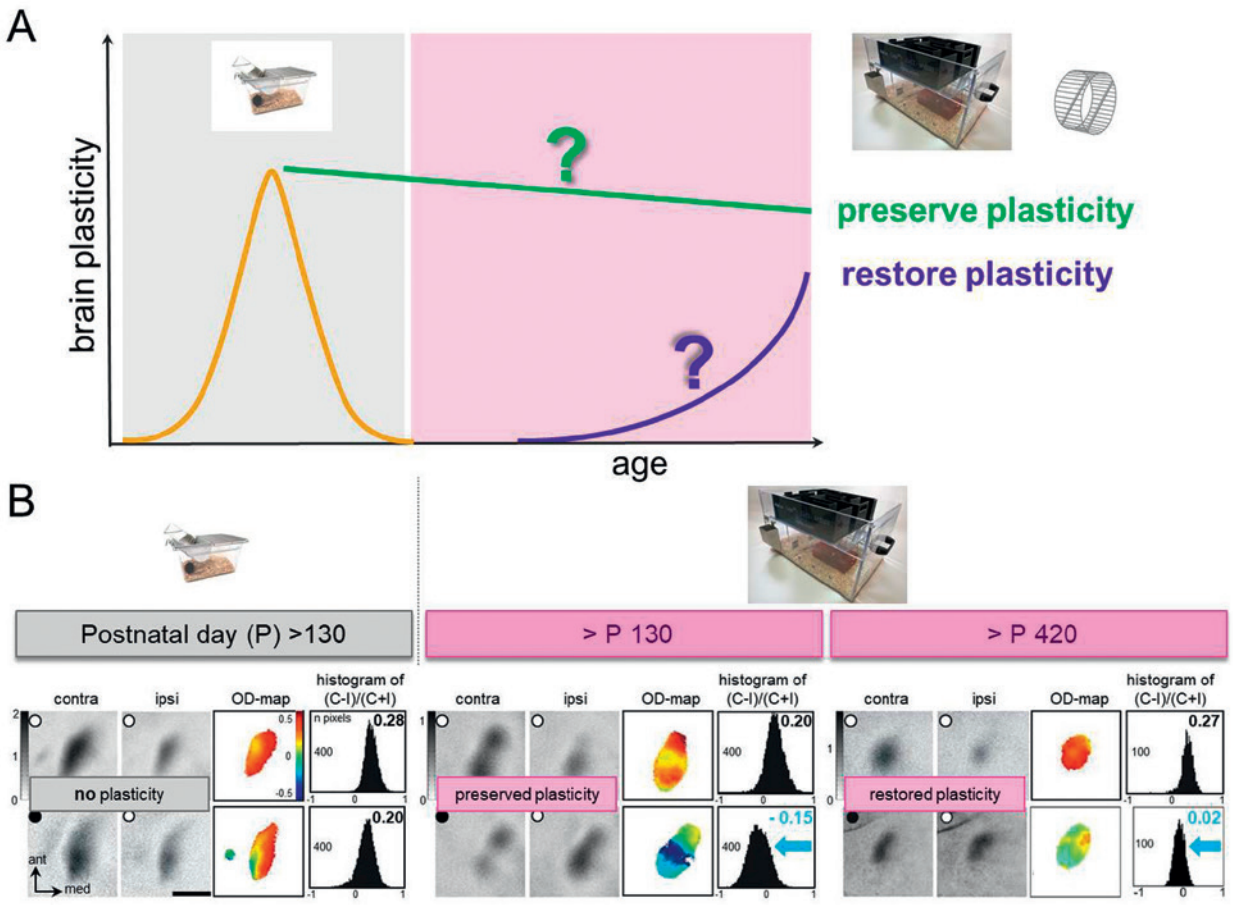

Fig. 2: Brain plasticity declines with age: a stimulating environment can both counteract age-dependent decline of plasticity and help with restoring plasticity in the brain. A: Scheme of the age-dependent decline of brain plasticity: there are windows of heightened plasticity in early postnatal brain development. B: Environmental enrichment (EE) preserved a lifelong ocular dominance (OD) plasticity in the primary visual cortex (V1), and restored plasticity, even if EE was started after postnatal day (P) 110. Activity-dependent changes in the activation of V1 were visualized using intrinsic signal optical imaging after stimulation of the contra- or ipsilateral eye before (upper row) and after monocular deprivation (lower row). Gray scale-coded activity maps from the binocular zone of V1 are illustrated: darker activity patches correspond to higher V1 activation. In addition, two-dimensional OD-maps, and the histogram of OD-scores, including the average OD-index are shown. Before monocular deprivation (black spot indicates deprived eye), the activity patch evoked by stimulation of the contralateral (contra) eye is darker than after stimulation of the ipsilateral (ipsi) eye in both standard cage-raised (left) and enriched mice (right), the two-dimensional OD-map shows warm colors (*red* represents positive, *blue* negative values) and the average OD-index is positive, indicating that V1-activity is dominated by the contralateral eye. After monocular deprivation of the contralateral eye, the OD shifts towards the open (ipsilateral) eye only in enriched, but not in adult standard cage mice: cold colors prevail in the OD-map and the OD-index is reduced (blue arrows). Note that the illustrated V1-activity maps after monocular deprivation (lower right) are from a P 922 mouse that still exhibited OD-plasticity. Modified from Greifzu et al., 2014; 2016.

How does environmental enrichment enhance plasticity?

One important question is whether OD-plasticity in EE-animals occurs via shared or distinct mechanisms as OD-plasticity in juvenile impoverished standard cage-animals. Inhibition-excitation balance is a key difference between juvenile and adult standard cage animals, and maturation of inhibition is suggested to play an important role in age-related changes in plasticity (Hensch, 2005). For instance, in juvenile standard cage-raised rodents, pharmacologically increasing inhibition results in precocious loss of visual cortical plasticity, while conversely, reducing inhibition promotes adult OD-plasticity (Maya-Vetencourt et al., 2008; Harauzov et al., 2010; Morishita et al., 2010). The implication is that a lower level of inhibition may be

permissive for plasticity, and that reducing inhibition is a prerequisite for plasticity expression in adults. In support of this hypothesis, intracortical inhibition in V1 of adult (>P130) EE-raised mice was as low as in juvenile standard cage-raised mice (Greifzu et al., 2014). Likewise, in rats, enrichment-induced plasticity after long term monocular deprivation was also accompanied by reduced extracellular GABA, indicating decreased inhibition (Sale et al., 2007; Baroncelli et al., 2010).

However, suggesting that the effects of enrichment are not a simple case of reactivating a juvenile-like brain state, there appear to be epigenetic, and even transgenerational, effects of enrichment on plasticity expression. For example, defective long-term potentiation normally associated with a particular knock-out (*ras-grf-/-*) was masked in both short-term enriched knock-out mice and their non-enriched offspring (Arai et al., 2009; Arai and Feig, 2011). Other changes accompanying enrichment have also been implicated in enhanced plasticity effects seen in adult rodents: enrichment altered expression of several key signalling factors known to regulate cortical activity and plasticity, including brain-derived neurotrophic factor (Falkenberg et al., 1992; Ickes et al., 2000; Cancedda et al., 2004; Sale et al., 2004), serotonin (Baroncelli et al., 2010), nerve growth factor (Mohammed et al., 1993; Pham et al., 1999), and insulin-like growth factor I (IGF; Carro et al., 2000; Ciucci et al., 2007).

EE combines motor, social, cognitive, and multisensory stimulation and exerts a global influence on the brain (van Praag et al., 2000). There is increasing evidence that primary sensory cortices receive and integrate multimodal input through cortico-cortical networks (Ghazanfar and Schroeder, 2006; Kayser and Logothetis, 2007; Driver and Noesselt, 2008; Henschke et al., 2017). Accordingly, environmental enrichment influences neuronal activity and plasticity in multiple cortical and subcortical brain areas concomitantly, and alters cortico-cortical network interactions beyond the local activity. For example, enrichment decreased coupling between local field potentials (LFPs) of visual and motor cortices of freely exploring mice in time scales pointing to a decorrelation in the direct monosynaptic connection between the two areas. This decorrelation might indicate a transition to a more active and stimulated brain state of enriched environment-housed animals during exploration (Di Garbo et al., 2011). Further suggesting a role for network activity interactions in plasticity, enrichment counteracted the LFP spectral shift and decorrelation between primary auditory cortex and V1 that occurs with ageing in standard cage-housed mice (Mainardi et al., 2014).

Enrichment-induced plasticity is not necessarily modality specific. Indeed, visual cortical plasticity does not require visual enrichment per se. Rats dark-reared in an enriched environment developed normal visual acuity, while rats dark-reared in standard cages showed impaired acuity (Bartoletti et al., 2004). Additionally, rat pups receiving body massage without any other form of enrichment showed accelerated visual acuity development which was accompanied by increased IGF expression across multiple brain regions, an effect also seen in multi-component enrichment paradigms (Guzzetta et al., 2009). This similarity could arise via direct connections between the brain areas stimulated by single-component sensory enrichment (e.g. massage), and/or via convergent effects of different enrichment components on shared molecular pathways (Maya-Vetencourt and Origlia, 2012; Vivar et al., 2013).

Effects of enriched environment have also been observed in other sensory modalities. In the auditory system, environmental enrichment paired with passive acoustic stimulation increased response strength and decreased response threshold of auditory cortex neurons (e.g. Dinse 2004; Engineer et al., 2004), and altered temporal processing and spatial representation of sound (Percaccio et al., 2005; Percaccio et al., 2007; Kilgard et al., 2007; Cai et al., 2009; Cai et al., 2010; Jakkamsetti et al., 2012). Environmental acoustic enrichment also promoted recovery from early noise-induced auditory dysfunction (Zhu et al., 2014; Jiang et al., 2015; Sturm et al., 2017), and long-term physical exercise was recently shown to delay the progression of age-related hearing loss (Han et al., 2016). Likewise, plasticity promoting effects of enrichment have been documented for the somatosensory cortex (e.g. Coq and Xerri, 1998; Florence et al., 2001; Godde et al., 2002; Bourgeon et al., 2004; Polley et al., 2004; Landers et al., 2011).

Are all components of the EE-cages necessary for the plasticity preserving effect?

As described above, EE paradigms feature the *combination* of physical activity, social and cognitive stimulation. The relative importance of each component to enrichment-induced changes appears to depend on the specific outcome and experimental model under study, suggesting multiple mechanisms of action, and likely combinatorial effects (Hannan, 2014). Although difficult to isolate, social aspects of enrichment may play a lesser role compared to visual enrichment and physical exercise for expression of

visual cortical plasticity in rodents. Indeed, although solitary housing was detrimental to plasticity in mice (Balog et al., 2014), increasing housing group size (predominantly a social enrichment) was not sufficient to alter plasticity outcomes in rats (Rosenzweig et al., 1978; Baroncelli et al., 2012). In contrast, engaging in a visual learning task (reflecting sensory, cognitive and motor enrichment, without social aspects) restored visual acuity in amblyopic rats (Baroncelli et al., 2012). Similarly, in amblyopic mice, the combination of locomotion and visual stimulation resulted in faster recovery of visual acuity (Kaneko and Stryker, 2014). However, visual enrichment alone could promote OD-plasticity in standard cage-housed mice (Matthies et al., 2013).

Furthermore, voluntary physical exercise also appears to contribute substantially to enrichment-induced changes in OD-plasticity: Adding a running wheel to standard (slightly larger) cages was sufficient to both preserve OD-plasticity into late adulthood, and to reactivate plasticity in old and stroke-lesioned mice (Kalogeraki et al., 2014; Kalogeraki et al., 2016). Notably, starting wheel running *after* the stroke lesion was sufficient to rescue OD-plasticity in mouse V1. Thus, voluntary physical exercise alone already strongly promoted V1-plasticity in adult mice, even if it was started late. Running is a particularly interesting parameter because running not only promotes brain plasticity and neurogenesis, but there is also evidence that running may alter attention to visual stimuli (Stryker, 2014; Fu et al., 2015; Pakan et al., 2016; Cooper et al., 2017).

Human brain plasticity resembles environmental enrichment effects seen in animal studies

The plasticity promoting effect of enrichment and voluntary physical exercise in animal studies is reminiscent of positive effects of physical exercise or a more "active lifestyle" in adult and ageing humans. Although it is more difficult to define exactly what kind of enrichment components are needed to promote human brain plasticity, there are numerous studies describing plasticity effects in humans which strikingly resemble the results from animal studies (reviewed in Hertzog et al., 2008; Hotting and Röder, 2013; Voss et al., 2013). For example, in healthy participants aged 65–84 years, dancing, which combines physical activity, social interaction, sensory and cognitive stimulation, improved performance in a range of cognitive, tactile and motor tasks (Figure 3, Kattenstroth et al., 2013; Dinse, 2016).

Similarly, in older adults, changes in physical fitness after stationary bicycle training correlated with higher stimulus-specificity in fMRI-measured activation, which is associated with cognitive ability and typically declines during ageing (Kleemeyer et al., 2017). Another study also identified regular physical exercise as a preventative factor against age-related worsening of odour detection threshold (Schubert et al., 2017) and Alzheimer's disease (Erickson et al., 2012; Santos-Lozano et al., 2016). Finally, moderate time spent video gaming is one form of environmental enrichment for humans because it incorporates intensive visual stimulation, sensory-motor integration together with cognitive stimulation and reward with completion of gaming tasks. Both action and non-action gaming improved not only visual capabilities such as contrast sensitivity, visual acuity and stereopsis, but also improved learning, attention and cognition performance in non-gaming tasks and is therefore a promising tool to increase plasticity in healthy older adults and to improve vision in amblyopic patients (Li et al., 2009; Li et al., 2011; Bavelier et al., 2012; Stryker and Löwel, 2017). Enrichment-based interventions have also demonstrated efficacy in treatment of many disorders, such as depression, schizophrenia and autism that are associated with self-deprivation (e.g. social withdrawal, sensitivity and avoidance of sensory stimuli, reduced novelty-seeking behaviour) (Mabunga et al., 2015). Also complementing findings in animal studies, in aged care settings, there is increased attention on mental and physical health benefits gained by providing activities including social interaction, exercise and cognitive/sensory stimulation, rather than merely meeting patients' basic needs.

In summary, findings both from animal models and humans demonstrate that living conditions influence brain plasticity in healthy, diseased, and aged brains. Therefore, to interpret and compare studies on brain plasticity in animals it is highly important to provide full details of housing conditions. Additionally, given that even short-term and temporary exposure to enrichment has marked effects on plasticity, procedures such as habituation and behavioural training and testing, should also be considered a form of enrichment and reported accordingly. It has become clear that to study 'normal' plasticity processes using animals as models of a healthy brain, enriched housing more closely resembles natural living conditions, and thus likely has superior construct validity. Finally, standard cage housing should more consciously be treated as the severely impoverished condition, with all

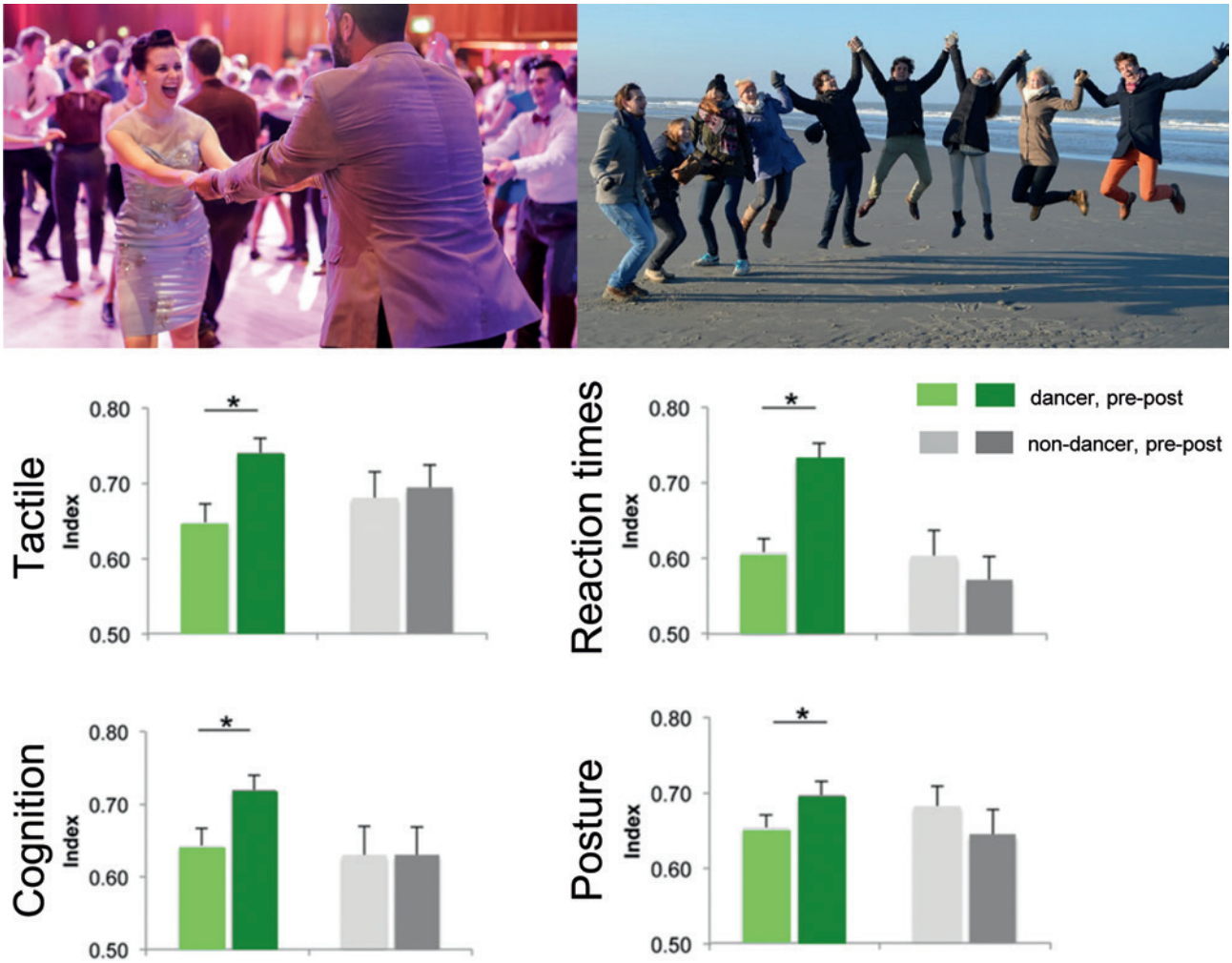

Fig. 3: Do sports, meet friends: an active lifestyle has been repeatedly shown to be effective in both counteracting age-dependent decline of cognitive, sensory and motor performance, as well as acting therapeutically by causing beneficial effects in a number of neurodegenerative diseases. Picture source (upper left): https://www.jazzmad.co.uk/learn-to-swing-dance/. Lower graphs: Six months of dance intervention (one hour/week) enhanced postural, sensorimotor, and cognitive performance in elderly participants (figure modified from Kattenstroth et al., 2013): Average indices characterizing individual performance for subjects in the dance (green) and control groups (grey) before (pre, brighter color) and after (post, darker color) a six-month period consisting of either dancing or no intervention. To compare performance across all tests and all subjects, the normalized performance indices for each subject, and each test were calculated as (wp-ip)/(wp-bp), where wp was the worst performance of all subjects, ip the individual performance, and bp the best performance of all subjects. The best ip is 1, while the worst ip is 0. Indices were subsequently averaged across tasks belonging to each particular domain as described above. Tactile ($p \leq 0.001$) comprises touch-threshold, two-point discrimination, and haptic object recognition. Reaction times ($p \leq 0.001$) comprise multiple-choice reaction times for the left and right hands and reaction time analysis. Cognition ($p \leq 0.001$) comprises the geriatric concentration test (AKT), Raven Standard Progressive Matrices (RSPM), Frankfurt Attention Inventory (FAIR), and Non-Verbal Learning Test (NVLT). Posture ($p = 0.001$) comprises posture and balance performance using seven static and dynamic tests on a force platform. The vertical bars show standard errors of the mean. Asterisks mark significant differences before and after the intervention or after six months of no intervention, respectively. Even moderate levels of dancing could counteract a wide range of age-related decline. For details see Kattenstroth et al. (2013).

the known consequences of deprivation on brain function and plasticity.

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References

Arai, J.A., Li, S., Hartley, D.M., and Feig, L.A. (2009). Transgenerational rescue of a genetic defect in long-term potentiation and memory formation by luvenile enrichment. J. Neurosci. 29, 1496–1502.

Arai, J.A., and Feig, L.A. (2011) Long-lasting and transgenerational effects of an environmental enrichment on memory formation. Brain Res. Bull. 85, 30–5.

Balog, J., Matthies, U., Naumann, L., Voget, M., Winter, C., and Lehmann, K. (2014). Social experience modulates ocular dominance plasticity differentially in adult male and female mice. Neuroimage. 103, 454–461.

Baroncelli, L., Bonaccorsi, J., Milanese, M., Bonifacino, T., Giribaldi, F., Manno, I., Cenni, M.C., Berardi, N., Bonanno, G., Maffei, L., and Sale, A. (2012). Enriched experience and recovery from amblyopia in adult rats: Impact of motor, social and sensory components. Neuropharmacol. 62, 2388–2397.

Baroncelli, L., Sale, A., Viegi, A., Maya-Vetencourt, J.F., De Pasquale, R., Baldini, S., and Maffei, L. (2010). Experience-dependent reactivation of ocular dominance plasticity in the adult visual cortex. Exp. Neurol. 226, 100–109.

Bartoletti, A., Medini, P., Berardi, N., and Maffei, L. (2004). Environmental enrichment prevents effects of dark-rearing in the rat visual cortex. Nat. Neurosci. 7, 215–216.

Bavelier, D., Green, C.S., Pouget, A., and Schrater, P. (2012). Brain plasticity through the life span: learning to learn and action video games. Annu. Rev. Neurosci. 35, 391–416.

Beaulieu, C., and Colonnier, M. (1987). Effect of the richness of the environment on the cat visual cortex. J. Comp. Neurol. 266, 478–494.

Bourgeon, S., Xerri, C., and Coq, J.O. (2004). Abilities in tactile discrimination of textures in adult rats exposed to enriched or impoverished environments. Behav. Brain Res. 153, 217–231.

Burrows, E.L., and Hannan, A.J. (2013). Characterizing social behavior in genetically targeted mouse models of brain disorders. Methods Mol. Bio. 1017, 95–104.

Burrows, E.L., McOmish, C.E., Buret, L.S., Van den Buuse, M., and Hannan, A.J. (2015). Environmental enrichment ameliorates behavioral impairments modeling schizophrenia in mice lacking metabotropic glutamate receptor 5. Neuropsychopharmacol. 40, 1947–1956.

Cai, R., Guo, F., Zhang, J., Xu, J., Cui, Y., and Sun, X. (2009). Environmental enrichment improves behavioral performance and auditory spatial representation of primary auditory cortical neurons in rat. Neurobiol. Learn. Mem. 91, 366–376.

Cai, R., Zhou, X., Guo, F., Xu, J., Zhang, J., and Sun, X. (2010). Maintenance of enriched environment induced changes of auditory spatial sensitivity and expression of GABAA, NMDA, and AMPA receptor subunits in rat auditory cortex. Neurobiol. Learn. Mem. 94, 452–460.

Cancedda, L., Putignano, E., Sale, A., Viegi, A., Berardi, N., and Maffei, L. (2004). Acceleration of visual system development by environmental enrichment. J. Neurosci. 24, 4840–4848.

Cang, J.H., Kalatsky, V.A., Löwel, S., and Stryker, M.P. (2005). Optical imaging of the intrinsic signal as a measure of cortical plasticity in the mouse. Vis. Neurosci. 22, 685–691.

Carro, E., Nuñez, A., Busiguina, S., and Torres-Aleman, I. (2000). Circulating insulin-like growth factor I mediates effects of exercise on the brain. J. Neurosci. 20, 2926–2933.

Ciucci, F., Putignano, E., Baroncelli, L., Landi, S., Berardi, N., and Maffei, L. (2007). Insulin-like growth factor 1 (IGF-1) mediates the effects of enriched environment (EE) on visual cortical development. PLoS One 2, e475.

Cooper, C., Moon, H.Y., and van Praag, H. (2017). On the run for hippocampal plasticity. Cold Spring Harb. Perspect. Med. 11. pii: a029736. doi: 10.1101/cshperspect.a029736. [Epub ahead of print].

Coq, J.O., and Xerri, C. (1998). Environmental enrichment alters organizational features of the forepaw representation in the primary somatosensory cortex of adult rats. Exp. Brain Res. 121, 191–204.

Di Garbo, A., Mainardi, M., Chillemi, S., Maffei, L., and Caleo, M. (2011). Environmental enrichment modulates cortico-cortical interactions in the mouse. PLoS One 6, e25285.

Diamond, M.C., Krech, D., and Rosenzweig, M.R. (1964). The effects of an enriched environment on the histology of the rat cerebral cortex. J. Comp. Neurol. 123, 111–119.

Dinse, H.R. (2004). Sound case for enrichment. J. Neurophysiol. 92, 36–37.

Dinse, H.R. (2016). Bereichernde umgebung – tanzen im alter aus sicht der neurowissenschaften. kulturräume+: Kubia 10, 13–17.

Dräger, U.C. (1975). Receptive fields of single cells and topography in mouse visual cortex. J. Comp. Neurol. 160, 269–289.

Dräger, U.C. (1978). Observations on monocular deprivation in mice. J. Neurophysiol. 41, 28–42.

Driver, J., and Noesselt, T. (2008) Multisensory interplay reveals crossmodal influences on 'sensory-specific' brain regions, neural responses, and judgments. Neuron. 57, 11–23.

Engineer, N.D., Percaccio, C.R., Pandya, P.K., Moucha, R., Rathbun, D.L., and Kilgard, M.P. (2004). Environmental enrichment improves response strength, threshold, selectivity, and latency of auditory cortex neurons. J. Neurophysiol. 92, 73–82.

Erickson, K.I., Weinstein, A.M., and Lopez, O.L. (2012). Physical activity, brain plasticity, and Alzheimer's disease. Arch. Med. Res. 43, 615–621.

Espinosa, J.S., and Stryker, M.P. (2012). Development and plasticity of the primary visual cortex. Neuron 75, 230–249.

Falkenberg, T., Mohammed, A.K., Henriksson, B., Persson, H., Winblad, B., and Lindefors, N. (1992). Increased expression of brain-derived neurotrophic factor mRNA in rat hippocampus is associated with improved spatial memory and enriched environment. Neurosci. Lett. 138, 153–156.

Fischer, A., Sananbenesi, F., Wang, X., Dobbin, M., and Tsai, L.-H. (2007). Recovery of learning and memory is associated with chromatin remodelling. Nature 447, 178–182.

Fischer, A. (2016) Environmental enrichment as a method to improve cognitive function. What can we learn from animal models? Neuroimage 131, 42–7.

Florence, S.L., Boydston, L.A., Hackett, T.A., Lachoff, H.T., Strata, F., and Niblock, M.M. (2001). Sensory enrichment after peripheral nerve injury restores cortical, not thalamic, receptive field organization. Europ. J. Neurosci. 13, 1755–1766.

Fu, Y., Kaneko, M., Tang, Y., Alvarez-Buylla, A., and Stryker, M.P. (2015). A cortical disinhibitory circuit for enhancing adult plasticity. eLife 4, e05558.

Ghazanfar, A. A., and Schroeder, C.E. (2006) Is neocortex essentially multisensory? Trends Cogn. Sci. 10, 278–285.

Godde, B., Berkefeld, T., David-Jürgens, M., and Dinse, H.R. (2002). Age-related changes in primary somatosensory cortex of rats: evidence for parallel degenerative and plastic-adaptive processes. Neurosci. Biobehav. Rev. 26, 743–752.

Gordon, J.A., and Stryker, M.P. (1996). Experience-dependent plasticity of binocular responses in the primary visual cortex of the mouse. J. Neurosci. 16, 3274–3286.

Greifzu, F., Kalogeraki, E., and Löwel, S. (2016). Environmental enrichment preserved lifelong ocular dominance plasticity, but did not improve visual abilities. Neurobiol. Aging 41, 130–137.

Greifzu, F., Pielecka-Fortuna, J., Kalogeraki, E., Krempler, K., Favaro, P.D., Schlüter, O.M., and Löwel, S. (2014). Environmental enrichment extends ocular dominance plasticity into adulthood and protects from stroke-induced impairments of plasticity. Proc Natl Acad Sci U.S.A. 111, 1150–1155.

Greifzu, F., Schmidt, S., Schmidt, K.F., Kreikemeier, K., Witte, O.W., and Löwel, S. (2011). Global impairment and therapeutic restoration of visual plasticity mechanisms after a localized cortical stroke. Proc Natl Acad Sci U.S.A. 108, 15450–15455.

Greifzu, F., Wolf, F., and Löwel, S. (2012). Network influences on cortical plasticity. e-Neuroforum 3, 41–48.

Guzzetta, A., Baldini, S., Bancale, A., Baroncelli, L., Ciucci, F., Ghirri, P., Putignano, E., Sale, A., Viegi, A., Berardi, N., Boldrini, A., Cioni, G., and Maffei, L. (2009). Massage accelerates brain development and the maturation of visual function. J. Neurosci. 29, 6042–6051.

Han, C., Ding, D., Lopez, M.C., Manohar, S., Zhang, Y., Kim, M.J., Park, H.J., White, K., Kim, Y.H., Linser, P., Tanokura, M., Leeuwenburgh, C., Baker, H.V., Salvi, R.J., and Someya, S. (2016). Effects of long-term exercise on age-related hearing loss in mice. J. Neurosci. 36, 11308–11319.

Hannan, A.J. (2014). Environmental enrichment and brain repair: harnessing the therapeutic effects of cognitive stimulation and physical activity to enhance experience-dependent plasticity. Neuropathol. Appl. Neurobiol. 40, 13–25.

Harauzov, A., Spolidoro, M., DiCristo, G., De Pasquale, R., Cancedda, L., Pizzorusso, T., Viegi, A., Berardi, N., and Maffei, L. (2010). Reducing intracortical inhibition in the adult visual cortex promotes ocular dominance plasticity. J. Neurosci. 30, 361–371.

Hebb, D.O. (1947). Spontaneous neurosis in chimpanzees; theoretical relations with clinical and experimental phenomena. Psychosom. Med. 9, 3–19.

Hebb, D.O. (1949). The organization of behavior. New York: Wiley & Sons.

Hensch, T.K. (2005). Critical period plasticity in local cortical circuits. Nat. Rev. Neurosci. 6, 877–88.

Henschke, J.U., Oelschlegel, A.M., Angenstein, F., Ohl, F.W., Goldschmidt, J., Kanold, P.O., and Budinger, E. (2017). Early sensory experience influences the development of multisensory thalamocortical and intracortical connections of primary sensory cortices. Brain Struct. Funct. Nov 1. doi: 10.1007/s00429-017-1549-1.

Hertzog, C., Kramer, A. F., Wilson, R.S., and Lindenberger, U. (2008). Enrichment effects on adult cognitive development: can the functional capacity of older adults be preserved and enhanced? Psychol. Sci. Pub. Interest. 9, 1–65.

Hotting, K., and Röder, B. (2013). Beneficial effects of physical exercise on neuroplasticity and cognition. Neurosci. Biobehav. Rev. 37, 2243–2257.

Ickes, B.R., Pham, T.M., Sanders, L.A., Albeck, D.S., Mohammed, A.H., and Granholm, A.C. (2000). Long-term environmental enrichment leads to regional increases in neurotrophin levels in rat brain. Exp. Neurol. 164, 45–52.

Jakkamsetti, V., Chang, K.Q., and Kilgard, M.P. (2012). Reorganization in processing of spectral and temporal input in the rat posterior auditory field induced by environmental enrichment. J. Neurophysiol. 107, 1457–1475.

Jiang, C., Xu, X., Yu, L., Xu, J., and Zhang. J. (2015). Environmental enrichment rescues the degraded auditory temporal resolution of cortical neurons induced by early noise exposure. Europ. J. Neurosci. 42, 2144–2154.

Kalogeraki, E., Greifzu, F., Haack, F., and Löwel, S. (2014). Voluntary physical exercise promotes ocular dominance plasticity in adult mouse primary visual cortex. J. Neurosci. 34, 15476–15481.

Kalogeraki, E., Pielecka-Fortuna, J., Hüppe, J.M., and Löwel, S. (2016). Physical exercise preserves adult visual plasticity in mice and restores it after a stroke in the somatosensory cortex. Front. Aging Neurosci. 8, 212.

Kalogeraki, E., Pielecka-Fortuna, J., and Löwel, S. (2017) Environmental enrichment accelerates ocular dominance plasticity in mouse visual cortex whereas transfer to standard cages resulted in a rapid loss of increased plasticity. PloS One. 12, e0186999.

Kaneko, M., and Stryker, M.P. (2014). Sensory experience during locomotion promotes recovery of function in adult visual cortex. eLife. 3, e02798.

Kattenstroth, J.C., Kalisch, T., Holt, S., Tegenthoff, M., and Dinse, H.R. (2013). Six months of dance intervention enhances postural, sensorimotor, and cognitive performance in elderly without affecting cardio-respiratory functions. Front. Aging Neurosci. 5, 5.

Kayser, C., and Logothetis, N.K. (2007) Do early sensory cortices integrate cross-modal information? Brain Struct. Funct. 212, 121–132.

Kilgard, M.P., Vazquez, J.L., Engineer, N.D., and Pandya, P.K. (2007). Experience dependent plasticity alters cortical synchronization. Hear Res. 229, 171–179.

Kleemeyer, M.M., Polk, T.A., Schaefer, S., Bodammer, N.C., Brechtel, L., and Lindenberger, U. (2017). Exercise-induced fitness changes correlate with changes in neural specificity in older adults. Front. Hum. Neurosci. 11, 123.

Landers, M.S., Knott, G.W., Lipp, H.P., Poletaeva, I., and Welker, E.(2011) Synapse formation in adult barrel cortex following naturalistic environmental enrichment. Neuroscience 199, 143–152.

Lehmann, K., and Löwel, S. (2008). Age-dependent ocular dominance plasticity in adult mice. PLoS One 3, e3120.
Levelt, C.N., and Hübener, M. (2012). Critical-period plasticity in the visual cortex. Ann. Rev. Neurosci. 35, 309–330.
Li, R., Polat, U., Makous, W., and Bavelier, D. (2009). Enhancing the contrast sensitivity function through action video game training. Nat. Neurosci. 12, 549–551.
Li, R.W., Ngo, C., Nguyen, J., and Levi, D.M. (2011). Video-game play induces plasticity in the visual system of adults with amblyopia. PLoS Biol. 9, 30.
Löwel, S., and Singer, W. (1992). Selection of intrinsic horizontal connections in the visual cortex by correlated neuronal activity. Science 255, 209–212.
Mabunga, D.F., Gonzales, E.L., Kim, J.W., Kim, K.C., and Shin, C.Y. (2015). Exploring the validity of valproic acid animal model of autism. Exp. Neurobiol. 24, 285–300.
Mainardi, M., Di Garbo, A., Caleo, M., Berardi, N., Sale, A., and Maffei, L. (2014). Environmental enrichment strengthens corticocortical interactions and reduces amyloid-β oligomers in aged mice. Front. Aging Neurosci. 6, 1.
Markham, J.A., and Greenough, W.T. (2004). Experience-driven brain plasticity: beyond the synapse. Neuron Glia Biol. 1, 351–363.
Matthies, U., Balog, J., and Lehmann, K. (2013). Temporally coherent visual stimuli boost ocular dominance plasticity. J. Neurosci. 33, 11774–11778.
Maya-Vetencourt, J.F., and Origlia, N. (2012). Visual cortex plasticity: A complex interplay of genetic and environmental influences. Neural Plast. 2012, 631965. doi: 10.1155/2012/631965.
Maya-Vetencourt, J.F., Sale, A., Viegi, A., Baroncelli, L., De Pasquale, R., O'Leary, O.F., Castren, E., and Maffei, L. (2008). The antidepressant fluoxetine restores plasticity in the adult visual cortex. Science 320, 385–388.
Mo, C., Hannan, A.J., and Renoir, T. (2015). Environmental factors as modulators of neurodegeneration: insights from gene-environment interactions in Huntington's disease. Neurosci. Biobehav. Rev. 52, 178–192.
Mohammed, A.H., Henriksson, B.G., Soderstrom, S., Ebendal, T., Olsson, T., and Seckl, J.R. (1993). Environmental influences on the central nervous system and their implications for the aging rat. Behav. Brain Res. 57, 183–191.
Morishita, H., Miwa, J.M., Heintz, N., and Hensch, T.K. (2010). Lynx1, a cholinergic brake limits plasticity in adult visual cortex: (a cure for amblyopia through nicotinic receptor signaling). Science 330, 1238–1240.
Pakan, J.M., Lowe, S.C., Dylda, E., Keemink, S.W., Currie, S.P., Coutts, C.A., and Rochefort, N.L. (2016). Behavioral-state modulation of inhibition is context-dependent and cell type specific in mouse visual cortex. Elife 5, e14985.
Percaccio, C.R., Engineer, N.D., Pruette, A.L., Pandya, P.K., Moucha, R., Rathbun, D.L., and Kilgard, M.P. (2005). Environmental enrichment increases paired-pulse depression in rat auditory cortex. J. Neurophysiol. 94, 3590–3600.
Percaccio, C.R., Pruette, A.L., Mistry, S.T., Chen, Y.H., and Kilgard, M.P. (2007). Sensory experience determines enrichment-induced plasticity in rat auditory cortex. Brain Res. 1174, 76–91.
Pham, T.M., Ickes, B., Albeck, D., Söderström, S., Granholm, A.C., and Mohammed, A.H. (1999). Changes in brain nerve growth factor levels and nerve growth factor receptors in rats exposed to environmental enrichment for one year. Neurosci. 94, 279–286.
Pielecka-Fortuna, J., Kalogeraki, E., Greifzu, F., and Löwel, S. (2015). A small motor cortex lesion abolished ocular dominance plasticity in the adult mouse primary visual cortex and impaired experience-dependent visual improvements. PLoS One 10, e0137961.
Polley, D.B., Kvasnak, E., and Frostig, R.D. (2004). Naturalistic experience transforms sensory maps in the adult cortex of caged animals. Nature 429, 67–71.
Rosenzweig, M.R., Bennett, E.L., Hebert, M., and Morimoto, H. (1978). Social grouping cannot account for cerebral effects of enriched environments. Brain Res. 153, 563–576.
Rosenzweig, M.R., Krech, D., Bennett, E.L., and Diamond, M.C. (1962). Effects of environmental complexity and training on brain chemistry and anatomy: a replication and extension. J. Comp. Physiol. Psychol. 55, 429–437.
Sale, A., Berardi, N., and Maffei, L. (2014). Environment and brain plasticity: towards an endogenous pharmacotherapy. Physiol. Rev. 94, 189–234.
Sale, A., Maya-Vetencourt, J.F., Medinin, P., Cenni, M.C., Baroncelli, L., De Pasquale, R., and Maffei, L. (2007). Environmental enrichment in adulthood promotes amblyopia recovery through a reduction of intracortical inhibition. Nat. Neurosci. 10, 679–681.
Sale, A., Putignano, E., Cancedda, L., Landi, S., Cirulli, F., Berardi, N., and Maffei, L. (2004). Enriched environment and acceleration of visual system development. Neuropharmacol. 47, 649–660.
Santos-Lozano, A., Pareja-Galeano, H., Sanchis-Gomar, F., Quindos-Rubial, M., Fiuza-Luces, C., Cristi-Montero, C., Emanuele, E., Garatachea, N., and Lucia, A. (2016). Physical Activity and Alzheimer Disease: A Protective Association. Mayo Clin. Proc. 91, 999–1020.
Sato, M., and Stryker, M.P. (2008). Distinctive features of adult ocular dominance plasticity. J. Neurosci. 28, 10278–10286.
Sawtell, N.B., Frenkel, M.Y., Philpot, B.D., Nakazawa, K., Tonegawa, S., and Bear, M.F. (2003). NMDA receptor-dependent ocular dominance plasticity in adult visual cortex. Neuron 38, 977–985.
Schubert, C.R., Fischer, M. E., Pinto, A. A., Klein, B.E.K., Klein, R., and Cruickshanks, K.J. (2017). Odor detection thresholds in a population of older adults. Laryngoscope 127, 1257–1262.
Stryker, M.P. (2014) A neural circuit that controls cortical state, plasticity, and the gain of sensory responses in mouse. Cold Spring Harb. Symp. Quant. Biol. 79, 1–9.
Stryker, M.P. and Löwel, S. (2017). Amblyopia: New molecular/pharmacological and environmental approaches. Chapter 7. In: Lasker-Foundation Report on Amblyopia 2017, http://www.laskerfoundation.org/new-noteworthy/articles/amblyopia-challenges.
Sturm, J.J., Zhang-Hooks, Y.-X., Roos, H., Nguyen, T., and Kandler, K. (2017). Noise trauma-induced behavioral gap detection deficits correlate with reorganization of excitatory and inhibitory local circuits in the inferior colliculus and are prevented by acoustic enrichment. J. Neurosci. 37, 6314–6330.
Tkacs, N.C., and Thompson, H.J. (2006). From bedside to bench and back again: research issues in animal models of human disease. Biol. Res. Nurs. 8, 78–88.

van Praag, H., Kempermann, G., and Gage, F.H. (2000). Neural consequences of environmental enrichment. Nat. Rev. Neurosci. 1, 191–198.
Vivar, C., Potter, M.C., and van Praag, H. (2013). All about running: synaptic plasticity, growth factors and adult hippocampal neurogenesis. Curr. Top. Behav. Neurosci. 15, 189–210.
Voss, M.W., Vivar, C., Kramer, A. F., and van Praag, H. (2013). Bridging animal and human models of exercise-induced brain plasticity. Trends Cogn. Sci. 17, 525–544.
Wiesel, T.N., and Hubel, D.H. (1963). Effects of visual deprivation on morphology and physiology of cells in the cat's lateral geniculate body. J. Neurophysiol. 26, 978–993.
Zhu, X., Wang, F., Hu, H., Sun, X., Kilgard, M.P., Merzenich, M.M., and Zhou, X. (2014). Environmental acoustic enrichment promotes recovery from developmentally degraded auditory cortical processing. J. Neurosci. 34, 5406–5415.

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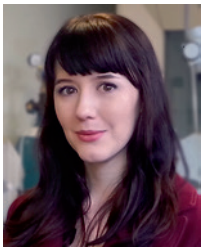

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