Three factors to characterize plastic potential transitions in the visual system

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ABSTRACT

A comprehensive understanding of brain-environment interactions is elusive even at the sensory level as neural plasticity waxes and wanes across the lifespan. Temporary and permanent visual deprivations remain pivotal approaches for studying the degree of experience-dependent plasticity of sensory functions. Natural models and experimental manipulations of visual experiences have contributed to uncovering some of the guiding principles that characterize transitions of plastic potentials in the human visual system. The existing literature regarding the neural plasticity associated with visual systems has been extensively discussed by two recent reviews articles (Röder et al., 2020; Castaldi et al., 2020) which provided an overview of different models of study and methods of investigations, gathering insights on both developing and adult brains. Here, we propose a framework of three main factors to characterize how the driving forces shaping visual circuits mutate, both quantitatively and qualitatively, between early development and adulthood.

Charles Nelson described plasticity "as the subtle but orchestrated dance that occurs between the brain and the environment; …, the ability of the brain to be shaped by experience and, in turn, for this newly remolded brain to facilitate the embrace of new experiences" (Nelson, 1999). Despite the elusive nature of this *orchestrated dance*, thanks to the intersection of models of study, neuroscience has progressively uncovered some of its guiding principles in the visual system (Fig. 1A). In non-human animals, experience-dependent plasticity has been investigated by experimentally manipulating the timing and quality of the available visual input. In humans, children and adults who have experienced permanent or temporary (months or years) visual deprivation provided opportunities to assess the impact of the lack of visual experience on sensory systems development (Ricciardi et al., 2020; Röder et al., 2020). Plasticity has also been uncovered in sighted adults by measuring the effects of binocular or monocular short-term (hours) deprivation (Castaldi et al., 2020).

Early development is potently characterized by time-windows of enhanced plasticity (Levelt and Hübener, 2012). During these phases, neural connectivity remodeling accounts for the emergence of essential neural representations; before and after these phases, system malleability is reduced. These critical -or sensitive- periods represent double-edged swords (Stevens and Neville, 2006). They provide the opportunity to acquire fundamentals or build dysfunctional

representations when environmental stimulation diverges from the expected one (Maurer, 2017). Studies on sight-recovery demonstrated that some visual computations could not reach full functional development when typical visual input was unavailable during specific developmental time-windows. Deficits persisted even many years after sight had been restored (for review, see Röder et al., 2020). Multiple sensitive periods in the visual system exist, and the age at which they occur and close varies considerably across functions (Maurer, 2017). Conversely, specific visual computations might rely more on genetic determinants. For instance, functions reaching a high level of maturity at birth (e.g., biological motion processing) proved to be less dependent on visual input availability in early developmental phases (for review, see Röder et al., 2020; Fig. 1B).

The closure of sensitive periods does not indicate complete loss of the plastic potential. For instance, reorganizations of retinotopic maps in V1 can occur in human adults after macular degeneration; altered short-term visual experience can modulate visual cortex excitability and affect visual functions previously considered immutable, such as ocular dominance. Homeostatic mechanisms, aimed at stabilizing neural circuits to cope with perturbations, are thought to be responsible for the documented residual plastic potentials in adulthood (for review, see Castaldi et al., 2020).

The driving forces shaping visual circuits mutate quantitatively

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between early development and adulthood. Remarkably, this shift in plastic potential can also be ascribed to qualitatively different aspects. Here, we identify three main interdependent factors.

(a) Biological markers of plasticity

Intrinsic biomarkers signal the transition from a developing brain to a mature one. As neural circuitries mature, system dominance shifts from excitation to inhibition (E-I). In primary sensory cortices, this transition is driven principally by the maturation of fast-spiking GABAergic parvalbumin-positive (PV) interneurons. With age, Perineuronal nets (PNN) encapsulate PV cells, contributing to constraining plasticity in adulthood (Hensch, 2005). Extensive, interconnected GABAergic networks represent distinctive features of cortical development. Inhibition promotes resilience to external inputs but limits the plastic potential in adult brains.

(b) Functional connectivity of neural networks

Together with structural changes, functional connectivity pathways

are also differently shaped across the lifespan. During sensitive phases, neural networks are predominantly sculpted by environmental statistics (e.g., frequency of occurrence, probability of co-occurrence; Fiser and Aslin, 2002). Learning is unsupervised, as no feedback or desired response is necessary. Conversely, adult plasticity is less driven by stimulus properties but mainly by the need to master relevant features to complete a task and often implies reinforcement and supervised learning (Watanabe and Sasaki, 2015). This functional transition from statistical learning to task-dependent learning parallels dominance shifts between connectivity forms (Singer, 1995; Röder et al., 2020). Feedforward connectivity, pivotal for input processing, allows the typical establishment of new pathways in early development. In adulthood, feedforward plasticity diminishes, and feedback and/or intracortical connectivity sustain learning (Castaldi et al., 2020).

(c) Hierarchical level of processing

Structural and functional changes in the visual system dictate shifts in plastic potential across the lifespan, but the temporal window of development is not the same for all functions; a third factor can be
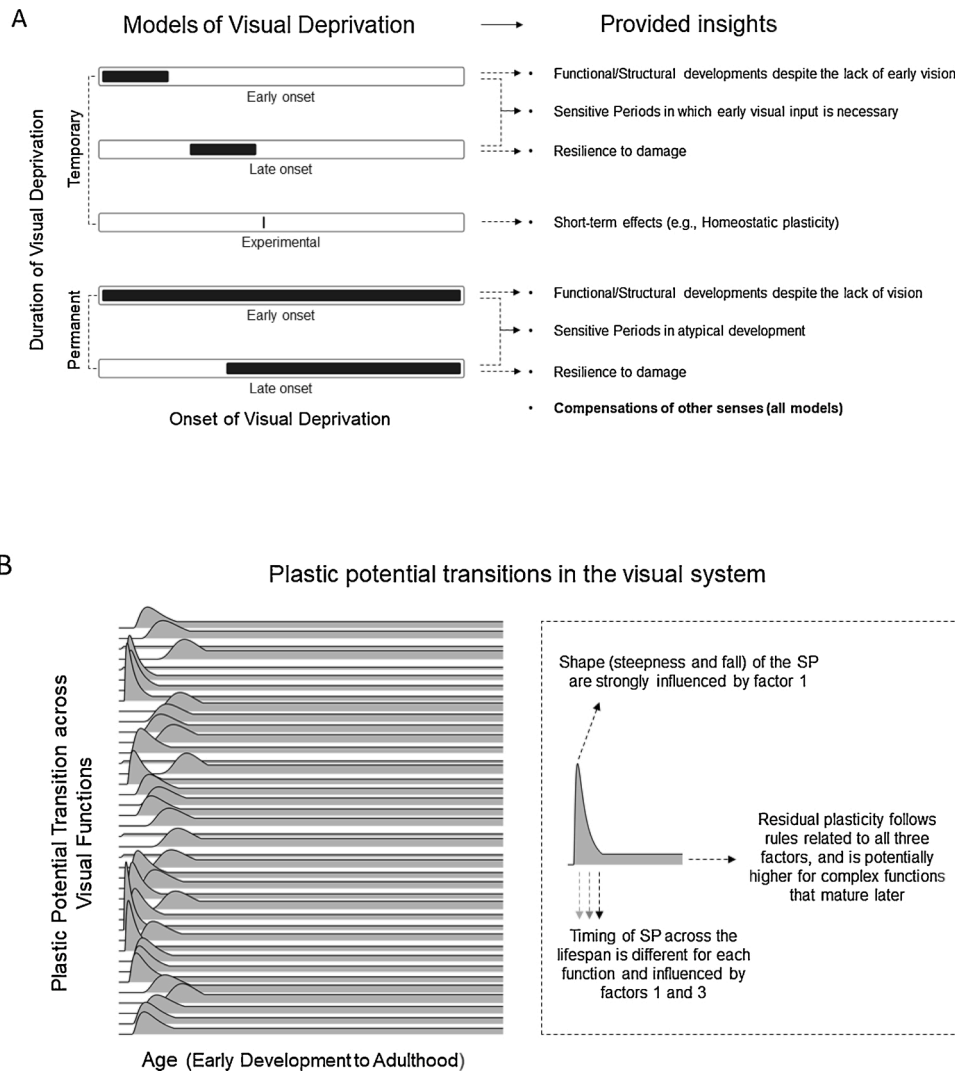

Fig. 1. (A) Models of visual deprivation as a function of duration (temporary or permanent) and onset (early, late, and experimentally induced) together with the main insights they provide. Horizontal black bars indicate the temporal window of visual deprivation. While all models provide knowledge concerning compensatory effects associated with the deprivation, only the combination of some allows assessing the presence of sensitive phases (SPs). (B) Plastic potential transitions (simulated data) during life (x-axis) and across visual functions (y-axis). Many visual functions display SPs of enhanced plasticity. Key properties are the shapes and timing of transitions in the plastic potential and the residual plasticity (note the non-uniform distribution of these properties across visual functions). A schematic representation of how these key properties relate to the three factors is provided in the right panel. The steepness and fall of plastic potential transition associated with SPs are strongly influenced by biological markers (factor 1) and sensory experience (e.g., visual deprivation can extend SP closure). The timing of SP is highly affected by the interaction between biological markers (factor 1), hierarchical level of processing (factor 3; e.g., basic visual computations heavily rely on early input availability), and sensory experience. The plastic potential is higher, and its transition shorter for sensitive periods (SP) occurring earlier during the development. Following the closure of SPs, the plastic potential is not over; residual plasticity exists and follows functional rules ascribed to all three factors, including functional connectivity of neural networks (factor 2), adapting to sensory experience. Residual plasticity increases with the processing hierarchy (here, SPs which occur later in development are associated with greater residual plasticity; this is graphically represented, as continuous horizontal area after SP closure is larger for functions developing later than for early ones). Finally, some visual functions do not display any sensitive period as they strongly rely on genetic determinants. The plastic potential transition was represented with lognormal dis-

tribution probability density functions to account for a steeper rise and shallower fall.

identified: the hierarchical level of processing. Sensitive periods for primitive visual functions close earlier than for more complex ones (Reh et al., 2020; Röder et al., 2020). For instance, the development of basic properties mapped in V1 (e.g., orientation selectivity, direction selectivity, and ocular dominance) heavily depends on visual inputs availability in the first few months after birth (Maurer, 2017); by contrast, complex response properties occurring at higher-order levels, such as face processing, continue developing until adolescence. Possibly because of this organization, adult perceptual learning seems to follow a reverse hierarchy. Higher-order visual computations are more susceptible to experience than basic ones (Ahissar and Hochstein, 2004), suggesting that, in the mature brain, the plastic potential increases with the processing hierarchy.

A full description of sensory and cognitive functions cannot be segregated from the definition of their dependences from these factors, which, to stick with Nelson's metaphor, by acting together in a well-coordinated dance will result in precise steps performed at the exact time, with compliance between the brain and the environment. In this framework, each function performs its own dance, as it pertains to its own determinants and experience-dependences as time unfolds (Fig. 1B). Intersections of these factors help to depict the dynamicity of transitions occurring because of experience and delineating the processes aimed at improving the signal-to-noise ratio and input selectivity, which characterize mature neural circuitries (e.g., *the perceptual narrowing*). Identifying factors that promote neural plasticity and qualifying the degree of interdependence of sensory functions development within and across sensory modalities yet represent a major challenge for the study of the nervous system and entails the potential to impact far beyond neuroscience.

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