Rat navigation guided by remote control

Free animals can be 'virtually' trained by microstimulating key areas of their brains.

Procedures used to train laboratory animals often incorporate operant learning[1] paradigms in which the animals are taught to produce particular responses to external cues (such as aural tones) in order to obtain rewards (such as food). Here we show that by removing the physical contraints associated with the delivery of cues and rewards, learning paradigms based on brain microstimulation enable conditioning approaches to be used that help to transcend traditional boundaries in animal learning. We have used this paradigm to develop a behavioural model in which an experimenter can guide distant animals in a way similar to that used to control 'intelligent' robots.

Depending on the site of brain stimulation, an electrical stimulus can act as a cue or a reward[2–4]. Studies of these phenomena have generally been concerned with functional mechanisms of the nervous sytem[5], and little thought has been given to the potential of behavioural paradigms constructed wholly around such focal brain stimulations. We used stimulation of the somatosensory cortical (SI) and medial forebrain bundle (MFB)[3] as 'virtual' cues and rewards, respectively, delivered to freely roaming rats. We imposed behavioural contingencies so that an operator could accurately steer the animal, in real time, over any arbitrarily specified three-dimensional route and over a range of real-world terrains.

We implanted stimulating electrodes into the MFB of five rats; the same animals also received electrodes in the right and left SI whisker representations. We then mounted a backpack containing a microprocessor-based, remote-controlled microstimulator on each animal. This allowed the operator, using a laptop computer, to deliver brief trains of stimulus pulses (80 μA; typically 10 biphasic pulses, each 0.5 ms, 100 Hz, per train) to any of the implanted brain sites from distances of up to 500 m away.

We trained the rats for navigation in 10 sessions, during which they learned to interpret remote brain stimulation as instructions for directing their trajectory of locomotion. In a figure-of-eight-shaped maze, the animals first learned to obtain periodic MFB rewards (0.3–3.0 Hz) by running forwards and turning correctly whenever left- or right-turning cues were issued. These cues were presented as a virtual 'touch' to the left or right whiskers by stimulating their respective cortical representations[6]. We then placed the animals in open environments that lacked the boundaries and fixed choice points of the maze. All rats generalized their responses to their new
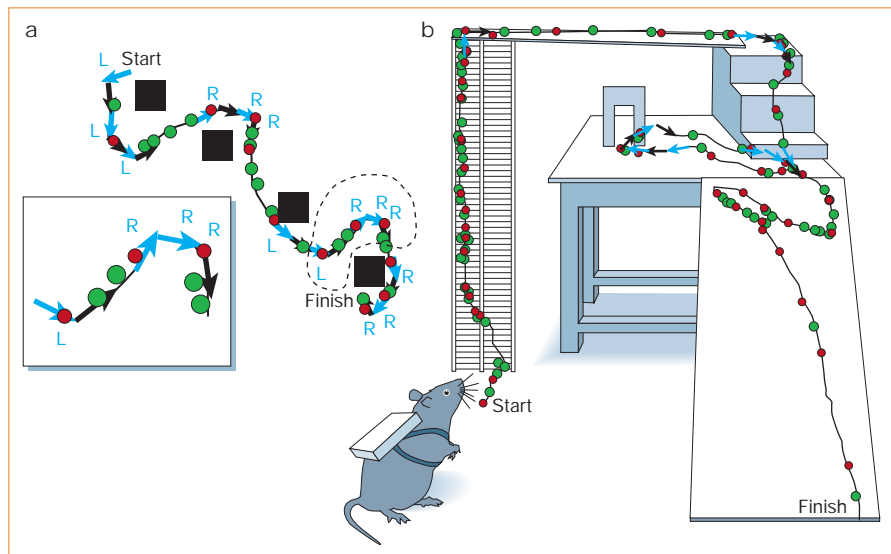
surroundings, running forwards and turning instantaneously on cue (Fig. 1a). They moved at speeds averaging 0.3 m s^{-1} and worked continuously for periods of up to a 1-hour test limit.

Navigation over three-dimensional structures was achieved by incorporating a unique behavioural attribute of MFB stimulation that reflected the known 'priming' qualities of MFB stimulation[7,8]. We found that MFB stimulation not only reinforced forward locomotion but also initiated and motivated further locomotion. Thus, an MFB reward itself served as an effective cue for rats to move forwards. Upon approaching objects such as a high step, 'forward' MFB stimulation would induce the rats to climb or descend from it. As a rule, the number of such stimulations required was proportional to the difficulty of negotiating the obstacle ahead (Fig. 1b). Superimposing 'forward' MFB stimulations onto the standard schedule was thus sufficient to steer the rats through a wide variety of complex, new and changing terrains.

Our rats were easily guided through pipes and across elevated runways and ledges, and could be instructed to climb, or jump from, any surface that offered sufficient purchase (such as trees). We were also able to guide rats in systematically exploring large, collapsed piles of concrete rubble,

and to direct them through environments that they would normally avoid, such as brightly lit, open arenas.

Our results show that 'virtual' learning, involving direct stimulation of the central substrates of cues and rewards, can effectively expand the scope of the operant method. Its chief benefit is its ability to dissociate explicit schedule variables such as cues and rewards from the physical variables that are normally associated with their delivery, freeing learning from the mechanical and parametric constraints that are imposed by particular physical settings. MFB reward stimulation is relatively non-satiating, and animals need not initiate consummatory behaviours to obtain such rewards. As virtual cues and rewards are perceived within a body-centred frame of reference, they may facilitate learning independently of the external environment. It may also be possible to increase the 'bandwidth' of conditionable information by stimulating multiple brain sites, thereby increasing the variety of reactions that can be elicited.

The specific behavioural model presented here — a guided animal — may have implications for new neurophysiological studies into directed animal navigation. MFB-based exploratory behaviours have already been shown to be useful in studying

Figure 1 Examples of guided rat navigation using brain microstimulation. Sketches are constructed from digitized video recordings. Red dots indicate rat head positions at 1-s intervals; green dots indicate positions at which reward stimulations were administered to the medial forebrain bundle (MFB); blue arrows indicate positions at which right (R) and left (L) directional cues were issued; black arrows indicate positions 0.5 s after directional commands. **a**, Route followed by a rat guided through a slalom course. Inset, detail of the events that took place inside the dashed enclosure. **b**, Route taken by a rat guided over a three-dimensional obstacle course. The animal was instructed to climb a vertical ladder, cross a narrow ledge, descend a flight of steps, pass through a hoop and descend a steep (70°) ramp. Two rounds of high-density MFB stimulation were required to guide the rat successfully down the ramp, demonstrating the motivational qualities of MFB stimulation.

hippocampal place cells[9]. Our model may also represent an extension of operant conditioning into useful real-world applications, such as search and rescue in areas of urban destruction and landmine detection. Combined with electronic sensing and navigation technology, a guided rat can be developed into an effective 'robot' that will possess several natural advantages over current mobile robots. Moreover, the ability to receive brain sensory activity remotely[10] and interpret it accurately could allow a guided rat to function as both a mobile robot and a biological sensor.

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Development

Linguistic ability and early language exposure

For more than 100 years, the scientific and educational communities have thought that age is critical to the outcome of language learning[1,2], but whether the onset and type of language experienced during early life affects the ability to learn language is unknown. Here we show that deaf and hearing individuals exposed to language in infancy perform comparably well in learning a new language later in life, whereas deaf individuals with little language experience in early life perform poorly, regardless of whether the early language was signed or spoken and whether the later language was spoken or signed. These findings show that language-learning ability is determined by the onset of language experience during early brain development, independent of the specific form of the experience.

The ability to learn language, whether spoken or signed, declines with age[3–6]. How the onset and type of the initial language experience contributes to this critical-period phenomenon is unclear. This question cannot be investigated by studying hearing individuals only, because the factors of age and experience are inseparable in these individuals — all hearing babies experience language from birth. But the question can be investigated by studying individuals who were born deaf, because they often do not experience any language until they are enrolled in special programmes[7,8]. We therefore compared the language-learning capacities of deaf and hearing individuals as a function of early language experience.

We first investigated whether early experience of a spoken language could facilitate subsequent learning of a signed language. We tested two groups of adults who had
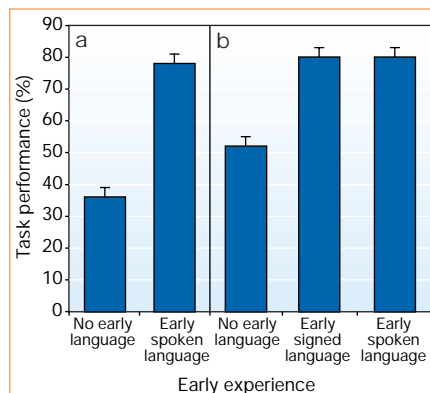

Figure 1 Effects of early experience on later language learning. **a**, American Sign Language (ASL) performance of deaf adults who had experienced no language in early life, and of deaf adults who had experienced spoken language in early life. Subjects were tested using a task requiring recall of complex ASL sentences. **b**, English performance of deaf adults who had had no experience of language in early life, of deaf adults who had experienced ASL in infancy, and of hearing adults who had experienced a spoken language other than English in infancy. Subjects were tested using a task requiring judgements of whether complex English sentences given in print were grammatically correct; chance performance is 50%. Further details are available from the authors.

learned American Sign Language (ASL) at school between the matched ages of 9 and 15 years and who had used it for over two decades. One group ($n=9$) was born hearing, had experienced spoken English in early life, and had later learned ASL after becoming profoundly deaf (≥ 90 decibels) as a result of viral infection; the second group ($n=9$) was born profoundly deaf and had had little experience of language before being exposed to ASL in school (auditory speech-perception abilities were at chance levels even with hearing aids). Deaf adults who had little experience of language in early life showed low levels of ASL performance; in contrast, late-deafened adults showed high levels of ASL performance (Fig. 1; paired $t=4.17$; d.f., 8; $P<0.001$).

We next investigated whether early experience of a signed language facilitates subsequent learning of a spoken language. We tested three groups of adults who had learned English in school at comparable ages between 4 and 13 years and who had used it for over 12 years. One group ($n=14$) was born profoundly deaf and had had little language experience before being exposed to ASL in school; the second group ($n=13$) was born profoundly deaf and had experienced ASL in infancy; the third group ($n=13$) was born hearing and had experienced various spoken languages in infancy (Urdu, French, German, Italian or Greek). Deaf and hearing adults who had experienced either a signed or a spoken language in early life showed similarly high levels of performance on the later learned language, English, whereas deaf adults who had little experience of language in early life showed low levels of performance (Fig. 1; $F_{2,37}=11.32$, $P<0.0001$).

Our results show that the ability to learn language arises from a synergy between early brain development and language experience, and is seriously compromised when language is not experienced during early life. This is consistent with current knowledge about how experience affects visual development in animals[9] and humans[10], and about learning and brain development in animals[11,12]. The timing of the initial language experience during human development strongly influences the capacity to learn language throughout life, regardless of the sensorimotor form of the early experience.

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