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Molecular Psychiatry (2012) 17, 1077–1085

www.nature.com/mp

ORIGINAL ARTICLE

An aetiological *Foxp2* mutation causes aberrant striatal activity and alters plasticity during skill learning

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Mutations in the human *FOXP2* gene cause impaired speech development and linguistic deficits, which have been best characterised in a large pedigree called the KE family. The encoded protein is highly conserved in many vertebrates and is expressed in homologous brain regions required for sensorimotor integration and motor-skill learning, in particular corticostriatal circuits. Independent studies in multiple species suggest that the striatum is a key site of FOXP2 action. Here, we used *in vivo* recordings in awake-behaving mice to investigate the effects of the KE-family mutation on the function of striatal circuits during motor-skill learning. We uncovered abnormally high ongoing striatal activity in mice carrying an identical mutation to that of the KE family. Furthermore, there were dramatic alterations in striatal plasticity during the acquisition of a motor skill, with most neurons in mutants showing negative modulation of firing rate, starkly contrasting with the predominantly positive modulation seen in control animals. We also observed striking changes in the temporal coordination of striatal firing during motor-skill learning in mutants. Our results indicate that FOXP2 is critical for the function of striatal circuits *in vivo*, which are important not only for speech but also for other striatal-dependent skills.
Molecular Psychiatry (2012) **17,** 1077–1085; doi:10.1038/mp.2011.105; published online 30 August 2011

Keywords: Foxp2; *in vivo* recording; KE family; motor-skill learning; speech and language; striatum

Introduction

Speech is one of the most complex and refined motor skills that we perform. Developmental disorders of speech and language affect up to 7% of 5- to 7-year-olds[1] and are known to be highly heritable.[2] However, the inheritance patterns are usually complex, indicating that multiple genes are likely involved, a difficulty that has hindered investigations into the underlying molecular aetiology.[3] Identification of the genetic basis of a rare monogenic form of speech and language impairment has offered a unique opportunity to study these mechanisms.[4] In the large multigenerational KE family, around half the members carry a point mutation in one copy of the *FOXP2* gene, yielding an arginine-to-histidine substitution that disturbs the DNA-binding domain of the encoded transcription factor.[4,5] These people have difficulty mastering the sequences of orofacial motor movements necessary for fluent speech,[6] a feature that is proposed to be a core deficit of the disorder.[7] The speech motor deficits are accompanied by other expressive and receptive problems in both oral and written language.[6] Additional families have been identified with speech and language problems caused by *FOXP2* mutations,[8] but the KE family remains the most well-studied example to date.

In the developing human brain, FOXP2 is expressed in neuronal subpopulations of the cortex, basal ganglia, thalamus and cerebellum; regions that are known to be important for motor-related functions.[9] The striatum is the main recipient of cortical input to the basal ganglia, and neuroimaging studies of the KE family have implicated this structure in FOXP2-related speech and language deficits, uncovering changes in striatal grey-matter density,[10] as well as altered striatal activation during language-based tasks.[11,12] Importantly, striatal lesions in humans, resulting from brain trauma or stroke, can result in verbal aphasia and amusica (a pitch-processing deficit).[13,14] The FoxP2 protein sequence and neural expression pattern are highly conserved in a number of other vertebrates, including songbirds and rodents,[9,15–18] suggesting some common ancestral functions. (The standard nomenclature for FOX transcription factor proteins recommended by the

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Received 20 January 2011; revised 24 May 2011; accepted 3 June 2011; published online 30 August 2011

winged helix/forkhead nomenclature committee[19] is FOXP2 for humans, Foxp2 for mice and FoxP2 for all other species, with genes and RNA displayed in italics. To maintain brevity, we have used just FoxP2 when referring to several species.) For basic studies investigating the role of FoxP2 in skill learning and striatal function, these species are more amenable to experimentation.

We previously generated mutant mice (*Foxp2-R552H* line) that carry an identical mutation to that of the KE family.[20] Homozygous mutants show severe developmental delay and motor impairment, dying 3–4 weeks after birth. Heterozygous mutants have motor-skill deficits, and slice recordings show impaired long-term depression at glutamatergic inputs into the striatum.[20] Conversely, mice with a partially humanised version of Foxp2 have increased striatal long-term depression at corticostriatal synapses.[21] Furthermore, in the zebra finch, FoxP2 knockdown in area X, a striatal nucleus essential for song development, impairs vocal learning.[22]

The evidence to date suggests that FoxP2 has a role in striatal function, with potential relevance for motor-skill learning. However, it is still unclear what impact the KE-family mutation has on striatal circuits during the learning of rapid motor sequences such as those required for speech. In this study, we show the consequences of the KE-family mutation on the ongoing activity of striatal circuits *in vivo*, and on the *in vivo* plasticity observed during skill learning, by performing multielectrode recordings in awake-behaving *Foxp2-R552H/+* mice during training on the accelerating rotarod. This task engages the circuits required for the striatal-dependent learning of rapid motor sequences,[23] which are likely to be functioning abnormally in this mouse line[20] and which have been proposed to be dysfunctional in affected members of the KE family.[7] We found that *Foxp2-R552H/+* mice displayed abnormally high ongoing striatal activity. Moreover, during acquisition of a motor skill, most striatal neurons in *Foxp2-R552H/+* mice showed negative modulation of firing rate unlike the positive modulation observed in controls. Changes in the temporal coordination of striatal firing were also evident during motor-skill learning in *Foxp2-R552H/+* mice. These results show that Foxp2 is critical for the normal functioning of striatal circuits during the acquisition of motor skills.

Materials and methods

Animals

The *Foxp2-R552H* and *Foxp2-S321X* lines were maintained on a C57BL/6J background, and heterozygotes and wild-type littermates, of between 2 and 6 months of age, were used for behavioural and recording experiments. The generation, marker-assisted backcrossing and genotyping of this strain are fully described in the references.[20,24,25] All procedures were approved by the National Institute on Alcohol Abuse and Alcoholism Animal Care and Use Committee.

Accelerating rotarod

A computer-interfaced rotarod (ENV-575M, Med-Associates, St Albans, VT, USA) was set to accelerate from 6 to 60 r.p.m. over a 300-s time period. Mice were trained for five consecutive days, with one daily session consisting of 10 trials separated by 300 s resting periods. Mice were placed on the rotarod and trials were deemed to have started when the rod began to turn. Trials ended when mice fell from the rod or after 300 s elapsed. Learning rate was calculated as follows (mean latency to fall $_{\text{trials 9 and 10}}$)−(mean latency to fall $_{\text{trials 1 and 2}}$)/9 (number of intertrial intervals).

In vivo extracellular recording

Implantation of multielectrode arrays and *in vivo* recording of neural activity in mice training on the accelerating rotarod were performed essentially as described in the reference.[23] Arrays had two rows of eight polyamide-coated tungsten wires, which were 35 μm in diameter with 90° blunt cut tips. Wires were separated by a 250-μm gap, both within a row and across rows. The centre of each array was surgically positioned 2.2–2.4 mm below the surface of the brain, 0.5 mm anterior to and 1.7 mm lateral to bregma. Final electrode positioning in the dorsomedial striatum was determined by stereotaxic coordinates and by neural activity, which was monitored as the electrodes were lowered into the brain. Mice were allowed to recover for at least 10 days post surgery after which single-unit and multi-unit activity was recorded using the Plexon data acquisition system (Plexon Inc., Dallas, TX, USA). The start and finish of each trial were signalled to the MAP recording system (Plexon) as events. The recording cables were held by a custom-made pulley system, allowing mice to run and fall relatively freely. Mice remained at the bottom of the apparatus during intertrial periods, usually in a fairly immobile state. Neural activity was initially sorted using an online sorting algorithm and then resorted, after recording, using an offline sorting algorithm based on waveform, amplitude and interspike interval histogram (Plexon). The total number of units recorded on days 1–5 was 56, 78, 80, 72 and 70, respectively, for wild-type mice and 55, 54, 64, 58 and 48, respectively, for *Foxp2-R552H/+* mice.

Neural data analyses

Data analyses were carried out using Neuroexplorer (Nex Technologies, Littleton, MA, USA) and custom-written programs in Matlab (The Mathworks Inc., Natick, MA, USA).

LFP power spectrum. The local field potential (LFP) power spectrum was estimated for 2 s sliding windows with 1-s steps by Welch's method; the parameters chosen allowed for a frequency resolution of 0.5 Hz. The percentage power for the following

frequency bands was calculated; delta 1.5–4 Hz, theta 4.5–9 Hz and gamma 30–55 Hz.

Spike-triggered average. Spike-triggered averages of the LFP were calculated for −3 s to 3 s intervals. A spike-triggered average was considered significant when 20 or more 1 ms bins within the interval −0.1 s to 0.1 s lay outside the maximum or minimum values of the intervals −3 to −1 s and 1 s to 3 s.

Statistics
Statistical analyses were carried out using SPSS (SPSS Inc., Armonk, NY, USA) and Neuroexplorer. Task-related neurons were identified as having significant positive or negative modulation of firing rate during running. This was determined using a 99% confidence interval, which was calculated from the firing rate during the intertrial intervals. All results were averaged per subject, and subsequent analyses were performed on each subject's mean value. Data were analysed using repeated measures analysis of variance, and *post hoc* tests (Fisher's least significant difference) were applied when appropriate. Planned comparisons were used to analyse the LFP data.

Histology
Mice were perfused with 4% paraformaldehyde, and brains were removed and postfixed overnight in 4% paraformaldehyde. Electrode placement was verified by Nissl staining of 50 μm vibratome sections. For Foxp2 and interneuron immunohistochemistry, postfixed brains were transferred to 30% sucrose, and 40 μm coronal cryosections were cut on a sliding microtome. Immunohistochemistry was carried out using the Vectastain ABC or Vector MOM kit (both from Vector Laboratories, Peterborough, UK). Free-floating sections were incubated with Foxp2 (1:2000, goat N16, Santa Cruz Biotechnology Inc., Santa Cruz, CA, USA), ChAT (1:100, goat, Chemicon, Temecula, CA, USA) or PV (1:5000, mouse, Swant, Marly, Switzerland) antibodies. Proteins were visualised using the Vector VIP substrate purple kit (Vector Laboratories) or the DAB substrate kit (Fisher Scientific, Loughborough, UK). When looking at Foxp2 colocalisation with parvalbumin (PV) or cholineacetyltransferase (ChAT), nuclei were marked using methyl green counterstain (Vector Laboratories). To ascertain interneuron numbers, serial sections were taken throughout the striatum and stained alternatively with PV and ChAT antibodies. The top half of the striatum was considered to be dorsal, and this was subdivided into DM, DI and DL. The area of each region of interest and the number of positive cells within it were determined using ImageJ (http://rsbweb.nih.gov/ij/). Cell density (cells mm^{-2}) was calculated by dividing the cell count by the area.

Results

We first confirmed that mice carrying an aetiological *Foxp2* mutation display impaired motor-skill learning.[20] Mice were trained for five consecutive days on an accelerating rotarod, with one daily session consisting of 10 trials (running periods), separated by 300 s intervals. This intensive schedule uses a higher acceleration rate (6–60 r.p.m.) than previous experiments,[20,23,26] and robustly shows the motor-skill learning deficits of *Foxp2-R552H/+* animals. In line with previous findings,[20] latency to fall was reduced in *Foxp2-R552H/+* mice ($F_{1,19} = 9.87$, $P < 0.05$; Figure 1a). A significant difference in performance was evident early in training (*post hoc*, $P < 0.05$, comparison of third and fourth trials of session 1), and although *Foxp2-R552H/+* mice improved, they never reached the fall times of wild-type animals (*post hoc*, $P < 0.05$, comparison of final two trials of session 5). The early deficits observed in *Foxp2-R552H/+* mice do not seem to stem from alterations in basal motor coordination, as performance during the first two trials of session 1 was not impaired (*post hoc*, $P > 0.05$). Latency to fall from a fixed speed rat rotarod, a task that addresses motor coordination, was also not significantly different between *Foxp2-R552H/+* and wild-type animals (Supplementary Figure 1a). Rather, the deficits appear to be due to a slower rate of learning during the first session (*post hoc*, $P < 0.05$; Figure 1b). Notably, *Foxp2-R552H/+* mice do not have generalised striatal-dependent deficits in learning or motivation, because they learn to press a lever to earn a food reward in the same way as wild-type animals in an operant task, which

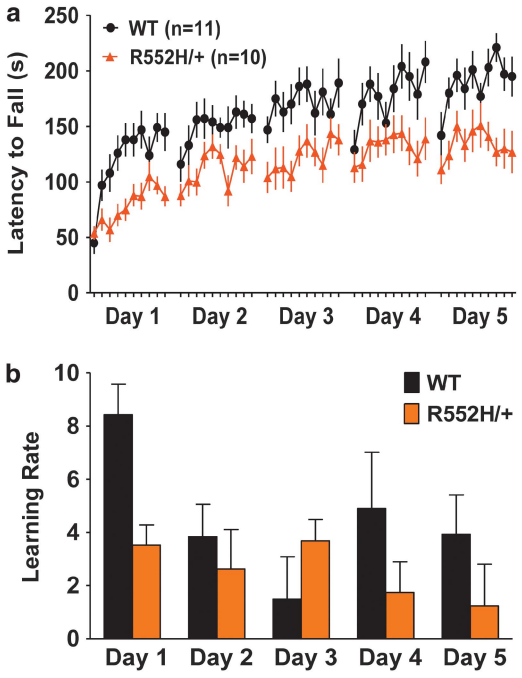

Figure 1 *Foxp2-R552H/+* mice show impaired motor-skill learning. (**a**) Latency to fall of wild-type and *Foxp2-R552H/+* mice during training on the accelerating rotarod. Mice received 10 trials a day for five consecutive days. (**b**) Rate of learning in wild-type and *Foxp2-R552H/+* mice during training on the accelerating rotarod. Error bars represent s.e.m.

involves the striatum[27] (Supplementary Figure 2). Furthermore, the severity of the deficits in rotarod skill learning appear to be related to the KE-family mutation, as the deficits observed in *Foxp2-S321X/+* mice, which carry a premature stop codon and have a half dosage of Foxp2 protein, were less severe than those observed in *Foxp2-R552H/+* mice (Supplementary Figure 3). *Foxp2-S321X/+* animals also have no impairment in basal motor coordination (Supplementary Figure 1b).

We therefore examined the impact of the KE-family mutation on striatal activity *in vivo* by performing multielectrode recordings in awake-behaving *Foxp2-R552H/+* mice ($n=5$) and control wild-type littermates ($n=6$). As skill learning deficits in *Foxp2-R552H/+* mice are apparent early in training, we targeted electrode arrays bilaterally to the dorsomedial striatum (Supplementary Figure 4), which is preferentially engaged during this initial phase of learning.[26] After recovery from electrode implantation surgery, neuronal activity (Figure 2a) and LFP oscillations were measured during training on the accelerating rotarod.

We first investigated changes in ongoing striatal activity in *Foxp2-R552H/+* mice by measuring the firing rate of striatal neurons during a 5-min period before the initial trial of each session, while mice were positioned at the bottom of the apparatus in a quiet but awake state (periods of no locomotion but occasional head movements). Intriguingly, we found that striatal neurons in *Foxp2-R552H/+* mice showed higher ongoing firing rates than those in wild-type controls across the 5 days of recording ($F_{1,9}=5.54$, $P<0.05$; Figure 2b). This is interesting because striatal medium spiny neurons (MSNs) usually display low *in vivo* firing rates,[28] a condition that is thought to be critical for normal action selection and movement.[29]

We next investigated the effects of the *Foxp2* mutation on the dynamic changes in striatal plasticity that are observed during motor-skill learning.[26] We determined whether the firing rate of striatal neurons increased or decreased during running compared with the intertrial intervals by calculating the modulation in firing rate ((run−interval)/(run + interval) × 100), at the beginning and end of each session (first two trials of session—'first'; last two trials of session—'last').[23] Consistent with previous experiments,[26] the average firing rate in wild-type dorsomedial striatum neurons increased during running compared with intertrial intervals in early training sessions, as revealed by positive modulation of firing rate (Figure 2c). However, striatal neurons in

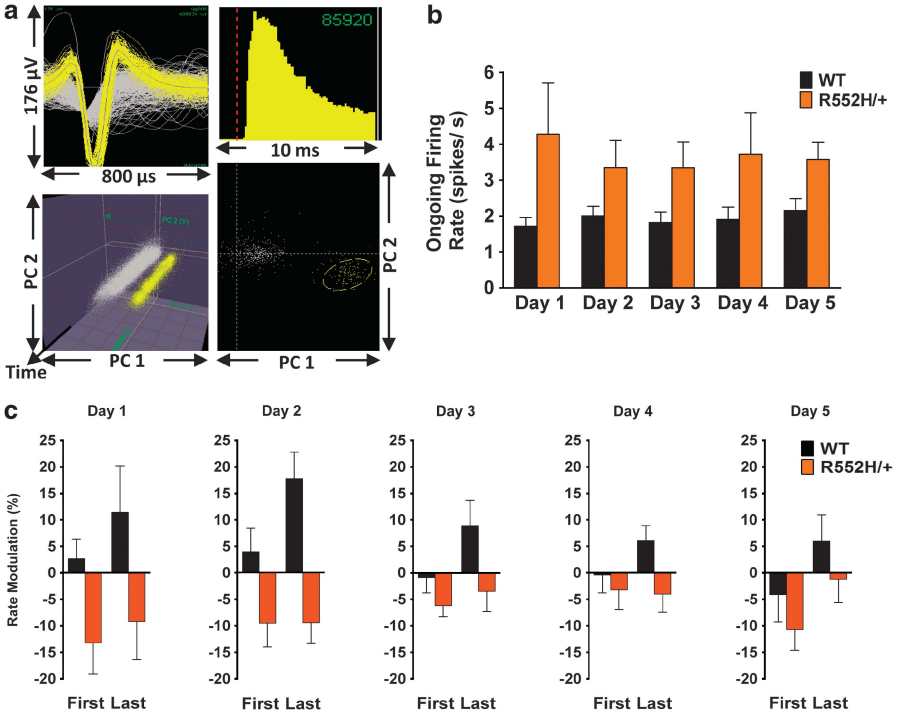

Figure 2 *Foxp2-R552H/+* mice have abnormally high ongoing striatal activity and show negative modulation of firing rate during skill learning. (**a**) Example of a single-unit waveform (top left). Units were distinguished from each other and from noise using interspike interval histograms (top right) and two-dimensional cluster separation based on principal component analysis, where the circled yellow cluster represents the unit and the grey cluster noise (bottom right). The stability of a unit recording over the course of a session was assessed using three-dimensional cluster displays with a time axis (bottom left). (**b**) Average ongoing firing rate in wild-type and *Foxp2-R552H/+* mice. (**c**) Average firing rate modulation during running compared with intertrial intervals, during the first and last trials of a session, in wild-type and *Foxp2-R552H/+* mice. Error bars represent s.e.m.

Foxp2-R552H/+ mice were substantially different ($F_{1,9} = 7.68$, $P < 0.05$), showing predominantly negative modulation during running. This negative modulation was most evident at early stages and progressively diminished, with the last trials of day 5 being significantly different from the first trials of day 1 (*post hoc*, $P < 0.05$), which is consistent with the dorsomedial striatum becoming less engaged with training.[26] Furthermore, in wild-type mice the firing rate was significantly more modulated during the last trials of a session than the first ($F_{1,5} = 27.88$, $P < 0.05$), revealing within-session plasticity. This plasticity was not observed in *Foxp2-R552H/+* animals, where no significant differences between the first and last trials of a session were found ($F_{1,4} = 3.96$, $P > 0.05$).

To examine how these differences in firing rate modulation emerge during skill learning, we determined the proportion of neurons whose firing rate changed significantly during running compared with the intertrial intervals (classified as task related, see Materials and methods and Figure 3a). The percentage of task-related neurons recorded was similar in wild-type and *Foxp2-R552H/+* animals and remained relatively constant throughout the training (Supplementary Figure 5). However, when task-related neurons were divided into those that increased or decreased firing rate during running, more neurons were found to increase firing rate in wild-type mice ($F_{1,10} = 22.25$, $P < 0.05$) and to decrease firing rate in *Foxp2-R552H/+* mice ($F_{1,8} = 7.12$, $P < 0.05$; Figure 3b). These results are consistent with the differences in firing rate modulation observed between *Foxp2-R552H/+* mutants and controls (Figure 2c).

We next investigated whether the negative modulation of firing rate observed in *Foxp2-R552H/+* during running on the rotarod was related to, or independent

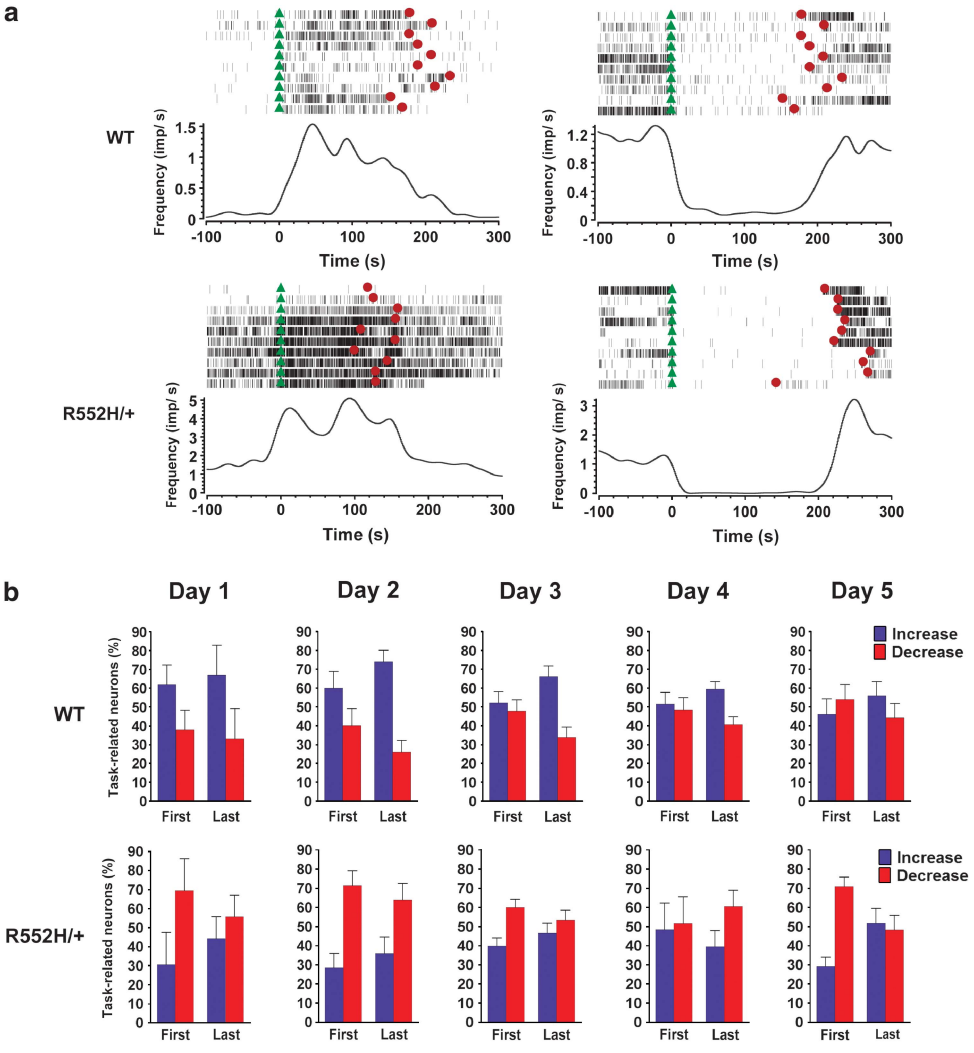

Figure 3 A higher proportion of task-related neurons decrease firing rate during skill learning in *Foxp2-R552H/+* mice. (**a**) Examples of neurons from wild-type (top) and *Foxp2-R552H/+* (bottom) mice that increased (left) or decreased (right) firing rate (impulses per second) during running compared with intertrial intervals. Green triangles represent the start of a trial and red circles the end. (**b**) Percentage of task-related neurons that increased or decreased firing rate during running compared with intertrial intervals, during the first and last trials of a session, in wild-type (top panel) and *Foxp2-R552H/+* (bottom panel) mice. Error bars represent s.e.m.

from, the higher ongoing activity of striatal neurons in these animals. It is plausible that neurons with high ongoing firing rates could be unable to increase firing further during running, and could even compensate by decreasing firing, hence resulting in the observed negative modulation of firing rate. However, we found that *Foxp2-R552H/+* neurons with high ongoing firing rates were not modulated differently during running compared with those with lower firing rates (Supplementary Figure 6). Furthermore, one would expect that if a significant proportion of *Foxp2-R552H/+* neurons were unable to modulate firing rate during running, then there would be a corresponding reduction in the number of task-related neurons, which is not observed (Supplementary Figure 5). Finally, if *Foxp2-R552H/+* neurons with high baseline firing rates were not able to positively modulate firing during running, then the most prominent differences in rate modulation between genotypes would occur when the greatest levels of positive modulation are observed in wild-type mice and vice versa. However, as previously discussed, firing rate is significantly more modulated in the last trials of a session compared with the first in wild-type mice, but this within-session plasticity is clearly not evident in *Foxp2-R552H/+* mice (Figure 2c). Taken together, these data indicate that the changes in striatal activity observed during skill learning in *Foxp2-R552H/+* mice are not simply a direct consequence of the increased ongoing firing.

In addition to changes in firing frequency, temporal coordination of striatal activity has also been shown to be important for striatal functions, such as action selection and movement.[29,30] We therefore measured LFP oscillations, which mostly reflect the coordinated input into an area, in *Foxp2-R552H/+* and control mice. We observed no significant differences in power at any of the frequencies examined, despite a tendency for higher power gamma oscillations in *Foxp2-R552H/+* mice on day 1 (Supplementary Figure 7). We then investigated the temporal relationship between the oscillatory phase of the LFP (reflecting mostly input) and the firing of individual striatal neurons (reflecting output). We determined whether a neuron fired preferentially during a particular phase of the LFP (was 'entrained' to the LFP) during running and intertrial intervals (Supplementary Figure 8), using spike-triggered averages of the LFP oscillations (see Materials and methods and refs 29,30; Figure 4a). We calculated how many neurons became entrained or lost entrainment to the LFP oscillations during running compared with the intertrial intervals. In wild-type mice, more neurons lost entrainment to the LFP oscillations during running in the first trials of a session compared with the last ($F_{1,5}=9.00$, $P<0.05$), but in *Foxp2-R552H/+* animals this within-session plasticity was not evident ($F_{1,4}=0.80$, $P>0.05$) (Figure 4b). In addition, more neurons became entrained to the LFP during running in *Foxp2-R552H/+* than in wild-type mice ($F_{1,8}=6.21$, $P<0.05$), an effect that was particularly apparent during the late phase of training. These results show that the temporal coordination of striatal input and output differs between *Foxp2-R552H/+* and wild-type mice.

Discussion

Previous neuroimaging studies of the KE family as well as experiments in mice and songbirds have highlighted possible roles for FoxP2 in the striatum, with potential relevance for motor-skill learning. However, the impact of the KE-family mutation on striatal function during the learning of rapid motor sequences was unclear. In this study, we demonstrate *in vivo* that this mutation dramatically alters the functioning of striatal circuits during motor-skill learning. We found that in contrast to control animals, which showed positive modulation of firing rate during skill acquisition, *Foxp2-R552H/+* mice exhibited negative modulation of firing rate. We also found alterations in the temporal coordination of striatal activity in *Foxp2-R552H/+* mice compared with controls.

We found *Foxp2-R552H/+* mice to have abnormally high ongoing striatal activity. Striatal MSNs, which represent the vast majority of striatal neurons, usually display low *in vivo* firing rates.[28] This property, together with appropriate levels of concurrent activity between MSNs, is thought to be critical for normal action selection.[29] The high ongoing striatal firing rate in *Foxp2-R552H/+* mice could therefore result in increased collateral inhibition, which may interfere with action selection and plasticity processes in this brain region. Our previous *ex vivo* data, which shows strong impairment of long-term depression at glutamatergic synapses onto MSNs in *Foxp2-R552H/+* mice,[20] is consistent with increased ongoing striatal activity. Nevertheless, it is important to note that besides glutamatergic input MSNs receive dopaminergic input from the mid-brain, and GABAergic input from interneurons and from other MSNs.[28] Hence, elevated MSN activity could also result from changes in the strength of any of these other inputs (for example, increased dopaminergic input or decreased GABAergic input), as well as increased neuronal excitability. However, we found only modest colocalisation of Foxp2 with PV or ChAT, markers for the main subtypes of striatal interneurons, and there were equivalent numbers of PV- or ChAT-positive cells in the striata of wild-type and *Foxp2-R552H/+* mice (Supplementary Figure 9), suggesting that striatal interneurons are unlikely to have a direct influence. We also showed that the increased ongoing striatal activity and the negative firing rate modulation during skill acquisition observed in *Foxp2-R552H/+* mice are not correlated. This suggests that the underlying mechanisms of the two phenomena are dissociable and raises the possibility that they are mechanistically distinct. Although any of the mechanisms outlined above could contribute to the firing rate modulation

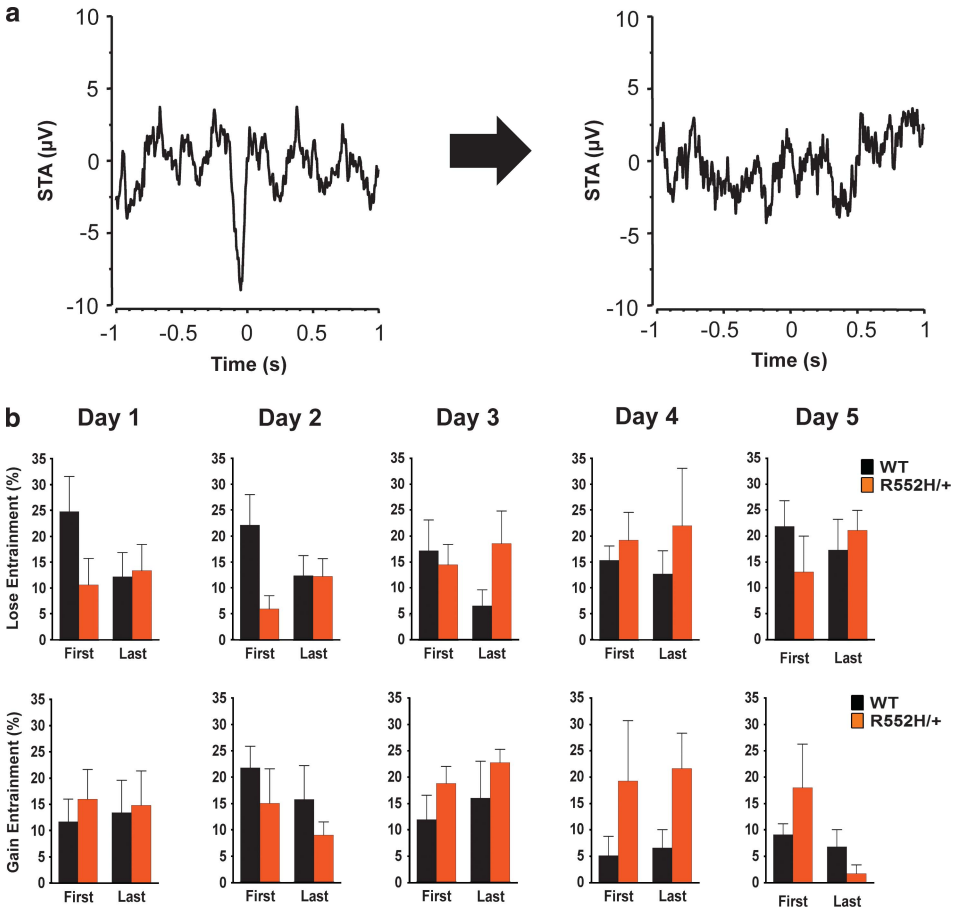

Figure 4 The temporal coordination of striatal activity is altered during skill learning in *Foxp2-R552H/+* mice. (**a**) Spike-triggered average histograms showing a neuron that is entrained to the local field potential (LFP) during intertrial intervals (left) but loses entrainment during running periods (right). (**b**) Percentage of neurons that lost entrainment from (top panel) or gained entrained to (bottom panel) the LFP between intertrial interval and running during the first and last trials of a session. Error bars represent s.e.m.

differences that we observed, it seems unlikely that impaired long-term depression could directly give rise to an increase in negative modulation of firing rate. Selective deletion of Foxp2 will be a useful tool to investigate how specific cells types and brain regions contribute to changes in striatal activity as well as other phenotypes.[31]

Foxp2-S321X/+ and *Foxp2-R552H/+* mice express a half dosage of normal wild-type Foxp2 protein, and thus both could potentially display haploinsufficiency. However, *Foxp2-R552H/+* mice also simultaneously express a full-length mutant product with abnormal functional properties. *In vitro* studies indicate that the R552H mutation disrupts the DNA-binding and transactivation functions of Foxp2,[5] suggesting that the mutant protein could act in a dominant-negative manner. Foxp2 has been shown to function as a homodimer, and also as a heterodimer with Foxp1 or Foxp4;[32] hence dominant-negative effects could be exerted through protein–protein interactions or direct disturbance of transcription. In support of this proposal, we observed a less severe motor-skill learning phenotype in *Foxp2-S321X/+* mice than in *Foxp2-R552H/+* mice (Figure 1 and Supplementary Figure 3); further work will be necessary to determine whether this is indeed the case. Studies using chromatin immunoprecipitation, followed by microarray analysis, have been used to identify direct neural targets of FOXP2 and have indicated roles in neurodevelopment, neurite outgrowth, axon guidance, neurotransmission and synaptic plasticity.[33,34] The *Foxp2-R552H* mutation is likely to cause inappropriate or inefficient regulation of downstream targets mediating these processes,[35] resulting in the dramatic changes in striatal neural activity that we observe.

In conclusion, the use of multielectrode recordings in awake-behaving mice with an aetiological Foxp2 mutation has allowed for a detailed assessment of its impact on the neuronal dynamics of striatal circuits during the learning of rapid motor sequences, beyond the resolution of human neuroimaging. The resulting data give novel insight into the mechanistic consequences of this mutation, which is important not only for speech but also for other striatal-dependent skills. It will be interesting to see whether the increased

ongoing striatal activity and generalised motor-skill learning deficits observed in mice extend to people with disorders attributed to FOXP2 dysfunction. Although it is difficult to perform invasive electrophysiology studies on such people, our data suggest that resting state functional imaging and relatively demanding tests of motor-skill learning ability could be highly informative.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

We thank Sonali Darbar, Rathi Puliyadi, Terrell D Holloway and Amber Luo for excellent technical assistance; John Burkhardt and Shih-Chieh Lin for help with Matlab; Emma Doran for running the operant learning task; and the staffs of the British Heart Foundation Functional Genetics Facility and the NIAAA vivarium for mouse husbandry. This work was supported by a Human Frontier Science Program short-term fellowship (to CAF); a Royal Society Research Fellowship (to SEF); the Wellcome Trust (075491/Z/04; 080971); the Division of Intramural Clinical and Basic Research of the National Institute on Alcohol Abuse and Alcoholism, US National Institutes of Health; the Champalimaud Neuroscience Programme; the European Research Council (STG 243393); and the Max Planck Society.

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