Experimental Neurology 355 (2022) 114140

Contents lists available at ScienceDirect

Experimental Neurology

journal homepage: www.elsevier.com/locate/yexnr

Review article

A translational perspective on pathophysiological changes of oscillatory activity in dystonia and parkinsonism

Lisa Rauschenberger [a,1], Christopher Güttler [b,1], Jens Volkmann [a], Andrea A. Kühn [b,c,d,e,f], Chi Wang Ip [a], Roxanne Lofredi [b,g,*]

[a] Department of Neurology, University Hospital of Würzburg, Josef-Schneider-Straße 11, 97080 Würzburg, Germany
[b] Department of Neurology, Movement Disorders and Neuromodulation Unit, Campus Charité Mitte, Charité-Universitätsmedizin Berlin, Berlin, Germany
[c] Bernstein Center for Computational Neuroscience, Humboldt-Universität, Berlin, Germany
[d] NeuroCure, Exzellenzcluster, Charité-Universitätsmedizin Berlin, Berlin, Germany
[e] DZNE, German Center for Neurodegenerative Diseases, Berlin, Germany
[f] Berlin School of Mind and Brain, Humboldt-Universität zu Berlin, Berlin, Germany
[g] Berlin Institute of Health (BIH), Berlin, Germany

ARTICLE INFO

Key Words:
Deep brain stimulation
Local field potentials
Oscillatory activity
Beta oscillations
Theta activity
Basal ganglia
Parkinson's disease
Dystonia

ABSTRACT

Intracerebral recordings from movement disorders patients undergoing deep brain stimulation have allowed the identification of pathophysiological patterns in oscillatory activity that correlate with symptom severity. Changes in oscillatory synchrony occur within and across brain areas, matching the classification of movement disorders as network disorders. However, the underlying mechanisms of oscillatory changes are difficult to assess in patients, as experimental interventions are technically limited and ethically problematic. This is why animal models play an important role in neurophysiological research of movement disorders. In this review, we highlight the contributions of translational research to the mechanistic understanding of pathological changes in oscillatory activity, with a focus on parkinsonism and dystonia, while addressing the limitations of current findings and proposing possible future directions.

1. Introduction

1.1. A success story of translational research

In movement disorders, and specifically in Parkinson's disease (PD), understanding of the pathophysiological changes underlying motor symptoms were built on a continuous back and forth between animal and human studies, becoming a success story of translational research.

Particularly well known in this context are the results from the most phenotypically faithful animal model of parkinsonism to date: the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) -treated non-human primate (NHP), in which the neurotoxic MPTP causes a selective loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc) (Burns et al., 1983; Langston et al., 1984).

With the help of multisite recordings in NHP, the groundwork was laid for the best known basal ganglia model: the "rate model". Within the rate model, electrophysiological data suggested that the medium spiny neurons of the indirect pathway are overactive. The "direct" and an "indirect" striatal output pathway represent separate populations of striatal medium spiny neurons. In the 1980s to 1990s, it was shown that the direct pathway is an inhibitory projection between striatum and internal globus pallidus (GPi)/ substantia nigra pars reticularis (SNpr) with medium spiny neurons expressing dopamine D1-receptors (Albin et al., 1989; DeLong, 1990; Penney Jr. and Young, 1986). The indirect pathway was shown to be characterized by the presence of dopamine D2-receptors and inhibitory connections from the striatum to the external globus pallidus (GPe) and subsequently to GPi/SNpr, either directly or via the subthalamic nucleus (STN). Overactivity of the indirect pathway, as suggested by the "rate model", would thus lead to a reduction in neuronal activity in the GPe with a subsequent increase in STN and consecutively GPi activity, supposedly leading to a reduction in motor output, which is considered the neurophysiological correlate of

* Corresponding author at: Department of Neurology, Movement Disorders and Neuromodulation Unit, Campus Charité Mitte, Charité-Universitätsmedizin Berlin, Berlin, Germany.
E-mail address: roxanne.lofredi@charite.de (R. Lofredi).
[1] equal contribution.

https://doi.org/10.1016/j.expneurol.2022.114140
Received 28 January 2022; Received in revised form 14 May 2022; Accepted 3 June 2022
Available online 8 June 2022

parkinsonism (Bergman et al., 1994; Filion and Tremblay, 1991; Miller and Delong, 1987). Although these findings paved the path for targeted lesioning of the basal ganglia (Bergman et al., 1990) and the “renaissance” of functional stereotaxy in Parkinson’s disease, the "rate model" was soon criticized as leading to paradoxical predictions and being too simplistic (Marsden and Obeso, 1994).

In subsequent years, the observations on changes in firing rates were expanded with findings on altered patterns of neuronal activity, many of which were also discovered in animal models (Bergman et al., 1994; Leblois et al., 2007; Nini et al., 1995; Raz et al., 2000; Wichmann and Soares, 2006). Rapidly the focus shifted from observations of single neuron activity to population activity and information coding within and between basal ganglia nuclei. In particular, the interaction between oscillations and neuronal spiking activity gained interest.

Brain oscillations are thought to reflect the synchronized activity of large neuronal assemblies and are denominated “local field potentials” (LFP) if recorded intracranially. The biophysical origin of LFPs has been a matter of debate for years. By now, it is generally accepted, that LFPs predominantly result from temporal integration of slower excitatory and inhibitory postsynaptic potentials, whereas short-lasting axonal spikes exhibit less summation. Hence, LFPs reflect the neuronal input activity to the area surrounding the recording electrode rather than the output activity (Buzsáki et al., 2012). The amplitude of an oscillation increases along with the size of the neuronal population involved (Buzsáki et al., 2012). Interestingly, the synchronization of neuronal populations in specific oscillatory rhythms can be coupled across brain areas as well, which is considered a sign of functional connectivity (Fries, 2015).

In the motor circuit, a specific oscillatory pattern within and across areas of the motor system has been described: At rest, the motor network is coupled in the beta frequency range (13–35 Hz). As such, beta activity has been postulated to promote the status quo of motor control (Engel and Fries, 2010; Gilbertson et al., 2005; Little and Brown, 2014). Slightly before the initiation of a movement, beta amplitude in and across motor areas drops and during movement, neuronal assemblies synchronize in the gamma frequency range (40-90 Hz) (Cheyne, 2013). With the end of a movement sequence, a brief rebound of beta synchronization is observed (Cheyne, 2013). The movement-related oscillatory pattern seems robust across species, which indicates high inter-species transferability of findings in this field (Crone et al., 1998; Donoghue et al., 1998; Igarashi et al., 2013; Mirzaei et al., 2017; Murthy and Fetz, 1992).

Given the prominent characteristics of movement-related changes in oscillatory activity, their disturbance in patients presenting with movement disorders seems intuitive. However, findings from non-invasive recordings of patients with movement disorders have been inconsistent regarding disease-specific or symptom-related oscillatory characteristics (Boon et al., 2019). This might be related to a decrease of the signal-to-noise ratio, specifically for higher frequencies with lower amplitude, but also to the fact that most movement disorders are thought to originate in subcortical structures such as the basal ganglia or the cerebellum. These structures are difficult to investigate with non-invasive methods due to their localization deep in the brain.

With subcortical deep brain stimulation (DBS) being acknowledged as effective treatment for movement disorders, it became possible to perform electrophysiological recordings of DBS-target structures during the perioperative period, when DBS-electrodes are externalized. This allowed the characterization of pathological oscillatory patterns in subcortical structures of patients with movement disorders which are associated with symptom severity. Since these observations in humans are primarily correlative and not causal in nature, the study of oscillatory phenomena in animal models became increasingly important. In the following, we will focus on the significance, causality and transferability of pathophysiological oscillatory patterns in the motor system in patients with Parkinson’s disease and dystonia as well as in the corresponding animal models in NHP and rodents. The framework and main

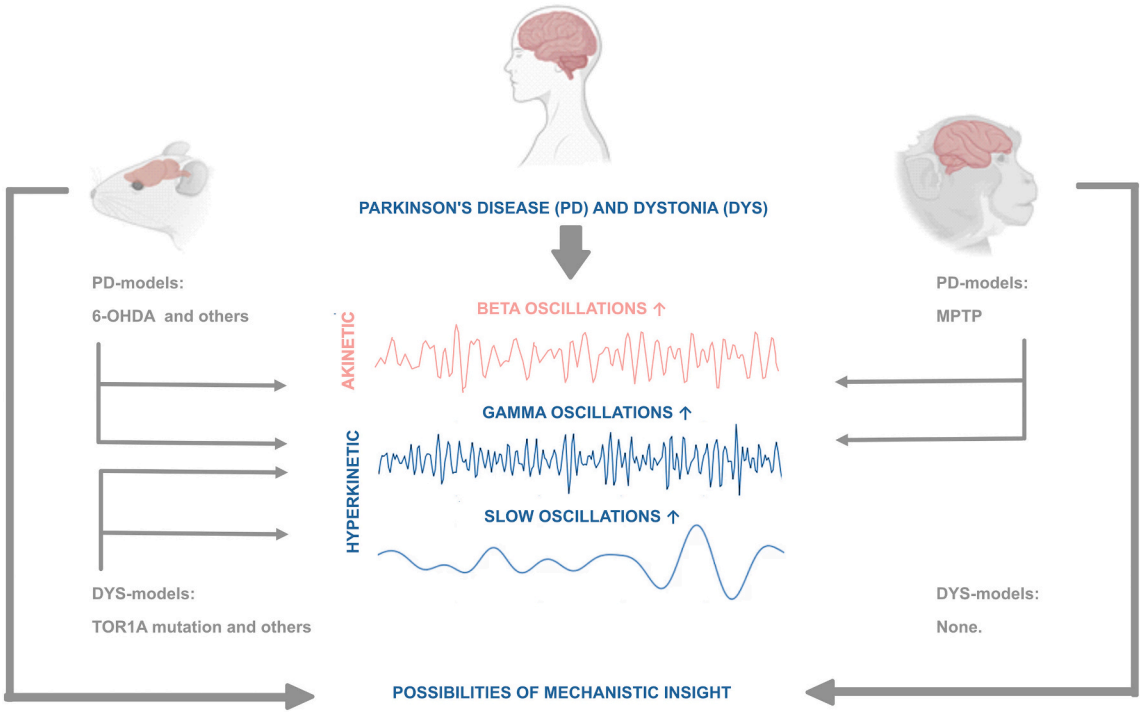

Fig. 1. Patterns of pathological oscillatory activity across species and disease models. Shown are illustrative traces of oscillatory activity in the beta, gamma and slow frequency range, as focused on in this review. Across species and disease models, exaggerated beta oscillations have been associated with akinetic states of PD, while specific patterns and localizations of increased gamma and slow oscillations (4–12 Hz) are seen both in hyperkinetic states of PD as well as in hyperkinetic movement disorders such as dystonia. Note that for PD, various disease models are available in rodents, while in NHP the primary disease model used and emphasized in this review is the MPTP-model. Both anatomy as well as physiology of NHP show higher similarity with the human brain than rodents, making results of NHP-research specifically valuable. Parts of the figure are generated with http://biorender.com.

focus of this review is visualized in Fig. 1.

2. Current limitations

Research from animal models for movement disorders allows for studies that are difficult to perform in humans – such as multiple recording sites, longitudinal studies i.e. with different states of alertness as well as additional morphological and neurochemical analyses of the brain after LFP recordings. Despite these advantages, the results should always be interpreted with some caution. In this regard, one should be aware that although the basal ganglia have the advantage of being phylogenetically old structures that are relatively consistent in their development across species, the basal ganglia of rats, monkeys and humans still show clear inter-species differences. In rodents, the GPi is located within the ventromedial internal capsule and often referred to as the entopeduncular nucleus, the striatum is not separated into caudate and putamen and the SNpc lacks neuromelanin which renders the human and NHP substantia nigra dark on macroscopic inspection. And while the brain of NHP shows a high degree of similarities to the human brain, animal research increasingly relies on the study of rodent models. The brain and the motor network of rodents, however, is much less complex. A study using resting state fMRI found that a large number of voxels in the striatum of humans and NHP could not be matched to the cortico-striatal circuit of rodents (Balsters et al., 2020). These unassigned voxels were related among others to executive function and concluded to form circuits unique to humans and NHP. Such inter-species differences clearly affect the study of LFPs. Moreover, most animal models, such as toxin- or vector based models, might emulate the phenotype, but still have the disadvantage of not representing the chronic and age-dependent nature of PD and dystonia. Then again in dystonia, animal models in general are rare and great hope lies in the development of new genetic models that may be suitable to mimic the vast range of motor symptoms that patients with dystonia may present with.

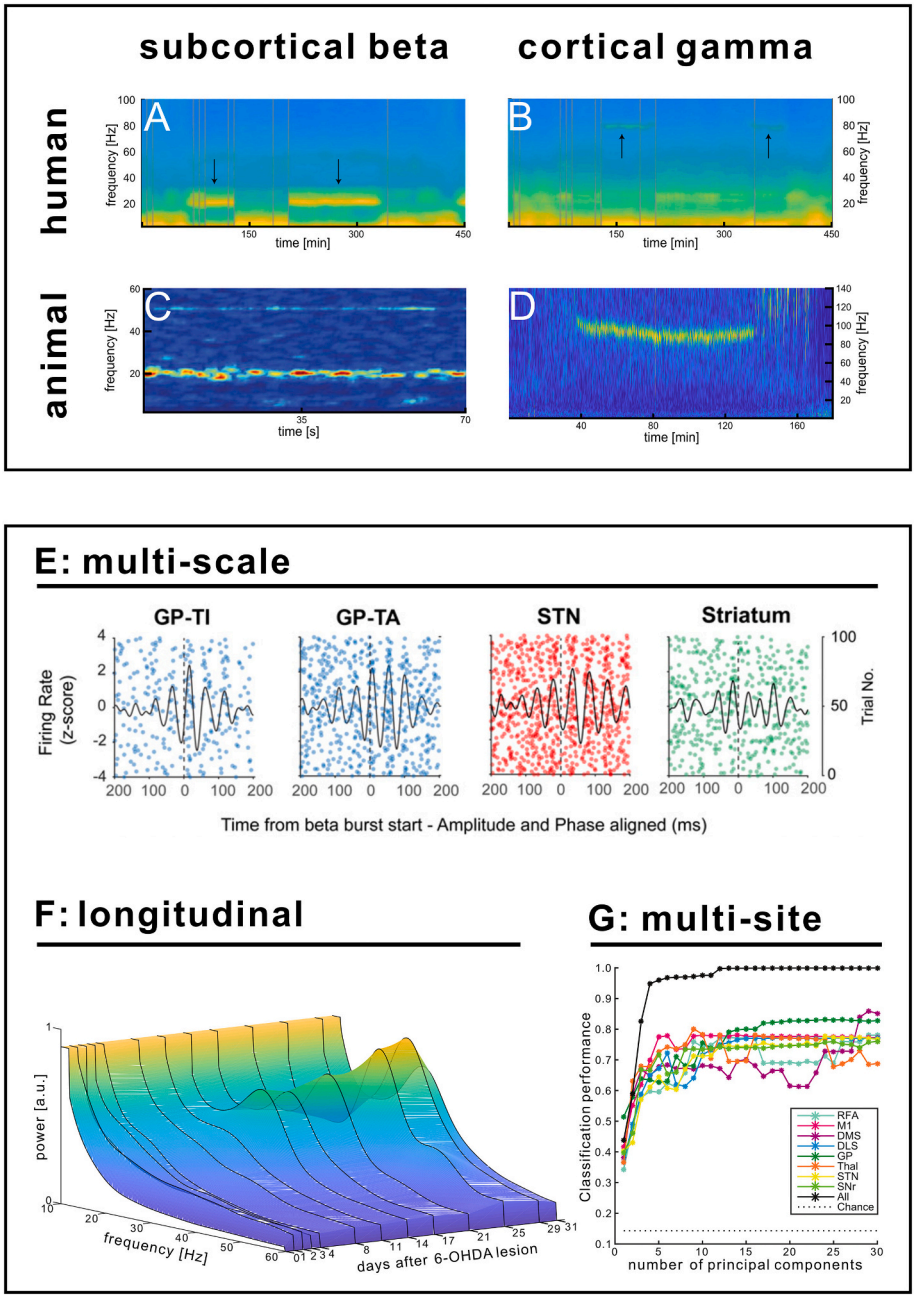

Fig. 2. Oscillatory activity in PD and additional insight through animal models. The upper panel shows exemplary spectograms of subcortical beta in the dopamine-depleted state and cortical gamma oscillations during dyskinesis in PD patients and animal models of the disease. The lower panel illustrates additional information gained from rodent models of PD. (A) Subthalamic and (B) cortical recordings of a PD Patient implanted with the Medtronic RC+S device reveal beta oscillations in the dopamine-depleted state whereas dyskinetic states are characterized by cortical gamma oscillations (adapted from Gilron et al., 2021). In 6-OHDA lesioned rats, a similar pattern can be observed with (C) subthalamic beta oscillations ipsilateral to the lesion (adapted from Mallet et al., 2008a) and (D) cortical gamma oscillations after repeated injections of levodopa inducing dyskinesia (adapted from Güttler et al., 2021). The advantages of animal models lie in the possibility of multi-scale (E), longitudinal (F) and multi-site recordings (G). For example, combining multi-structure single unit recordings with cortical LFP analysis revealed that oscillatory firing of single units in multiple subcortical structures is aligned with the onset of cortical beta bursts. (E, adapted from Cagnan et al., 2019; GP-TI refers to prototypic GPe neurons whereas GP-TA refers to arkypallidal GPe neurons). Animal models also allow for invasive recordings in healthy organisms which is important for characterizing the transition from healthy to disease states. Shown is a representative case of subthalamic activity before and up to 31 days after 6-OHDA lesion (unpublished, F). Combining the information from parallel recordings of multiple brain structures in a rodent model of PD is superior at identifying separate neurophysiological states of the disease and its pharmacological interventions (G, adapted from Tamtè et al., 2016).

3. Parkinson's disease

3.1. Exaggerated beta activity in Parkinson's disease patients and animal models

In the dopamine-depleted state of PD patients, the most prominent feature of pathophysiological changes in oscillatory activity of basal ganglia structures are exaggerated beta oscillations (Brown, 2003; Brown et al., 2001; Lofredi et al., 2018; Lofredi et al., 2022; Silberstein et al., 2003), see Fig. 2. Both at rest as well as during movement, beta activity has been shown to correlate with speed of single joint movements such as hand rotations or finger tapping (Feldmann et al., 2022; Kehnemouyi et al., 2021; Lofredi et al., 2019; Lofredi et al., 2019; Steiner et al., 2017). More broadly, beta oscillations correlate with motor symptoms (Neumann et al., 2016; Lofredi et al., 2022) and are reduced by levodopa or DBS (Eusebio et al., 2011; Kühn et al., 2009; Levy et al., 2002; Priori et al., 2004; Lofredi et al., 2022). The suppression of exaggerated beta activity is in turn correlated with an observed clinical improvement of bradykinesia and rigidity (Kühn et al., 2006; Kühn et al., 2008).

In line with the concept of beta activity being an anti-kinetic signal, parkinsonian tremor, which can be considered as hyperkinetic PD symptom, is not well captured by beta dynamics (Neumann and Kühn, 2017), but can still be detected from subcortical LFP-signals by using multi-feature machine learning approaches (He et al., 2020; Hirschmann et al., 2016; Yao et al., 2020).

While the association between bradykinetic-rigid symptoms and beta activity has been replicated in various studies (Kühn et al., 2006; Neumann et al., 2016), the prevalence of subcortical beta peaks seems to vary across studies, ranging between ~63% in smaller cohorts <10 patients (Tinkhauser et al., 2017b) and 91% in a large cohort of >100 PD-patients (Lofredi et al., 2022). The variance might be explained by the amount of patients with tremor-dominant subtype (Neumann and Kühn, 2017), the distance of the recording site to the dorso-lateral STN (Horn et al., 2017), the DBS-electrode type as well as the time of recording (intra- vs post-operative).

In contrast to subcortical beta activity, findings on the pattern of cortical beta activity have been less conclusive (Bosboom et al., 2006; Heinrichs-Graham et al., 2014; Pollok et al., 2012), specifically when recorded non-invasively. In invasive recordings from sensorimotor cortices of PD patients, it is the phase-amplitude coupling with gamma activity as well as the waveform shape of beta activity that seems to better reflect motor impairment in PD (Cole et al., 2017; de Hemptinne et al., 2015).

Across structures of the cortico-basal ganglia-thalamic loop, the beta band can be functionally subdivided into a low (~13–20 Hz) and a high beta band (~21–35 Hz), with low beta band activity classically being associated with the aforementioned parkinsonian motor symptoms and primarily responsive to levodopa in PD patients (Priori et al., 2004). High beta band activity has been proposed to reflect hyperdirect pathway activity as cortico-subcortical coupling occurs in this frequency band (Kato et al., 2015; Little et al., 2012; Little et al., 2013b; Litvak et al., 2011; López-Azcárate et al., 2010; Oswal et al., 2016; van Wijk et al., 2016).

3.2. The road to the 6-OHDA rodent model of Parkinson's disease

Early animal experimentation during the 19th century did not try to model the parkinsonian state but laid the foundation of basal ganglia research by studying the effect of cortical and subcortical lesioning in NHP, cats and other vertebrates (Sherrington, 1898; Wilson, 1914). Treating PD with surgical lesioning became more and more popular throughout the 20th century with a plethora of targets by then known to be involved in the control of movements. The recognition of parkinsonism as a hypodopaminergic syndrome and the advent of levodopa in the early 1970' marked a dramatic turn in the treatment of PD. It came along with the first pharmacological animal models of PD by dopaminergic receptor blockade (haloperidol) or vesicular monoamine depletion (reserpine) (Glow, 1959). In rodents, both substances induce catalepsy, a behavioral state of bradykinesia and rigidity, which can be reversed by levodopa treatment (Carlsson et al., 1958; Carlsson et al., 1957).

From the late 1960s on, the most widespread animal model of PD became the 6-hydroxydopamine (6-OHDA) model (Ungerstedt, 1968). 6-OHDA is an analogue of dopamine and as such exhibits a high affinity for dopamine (DAT) and norepinephrine transporters (NET) but induces neuronal cell death after its uptake. Injecting 6-OHDA to the medial forebrain bundle (MFB) or the SNpc causes a rapid and near complete lesion of the dopaminergic system, whereas injections into the striatum cause a more gradual decline, termed the partial PD model (Duty and Jenner, 2011). Of note, 6-OHDA is almost always injected unilaterally, as bilateral injections are associated with severe immobility and a high mortality rate (Marshall et al., 1974). To protect the noradrenergic neurons, desipramine is often administered prior to lesioning, although a combined noradrenergic and dopaminergic lesion might closely resemble the pathology of PD (Gesi et al., 2000; Wang et al., 2010). 6-OHDA is effective in rodents as well as NHP although MPTP is often preferred for the latter. Importantly, neither the 6-OHDA nor the MPTP model lead to Lewy body formation (Halliday et al., 2009).

Replicating results from PD patients, MPTP- treated NHP display increased low beta activity in the STN and internal pallidum, which is suppressed by STN-DBS and dopaminergic medication (Moran et al., 2012; Singh and Papa, 2020). Beyond typical DBS-target structures, increased beta activity can also be found across BG nuclei of MPTP-treated NHP such as the GPe, SNpr and striatum that are not commonly accessible in PD patients (Connolly et al., 2015; Deffains et al., 2016; Moran et al., 2012; Singh and Papa, 2020).

In rodents, the most popular PD-model is the 6-hydroxydopamine (6-OHDA) model (Ungerstedt, 1968), for more information see box "The road to the 6-OHDA rodent model of Parkinson's disease". While no animal model replicates all aspects of the disease in humans, different ways of testing for motor deficits that resemble the human phenotype have been established over the years. Regularly used tests in rodents are 1) the rotarod test, where the amount of time the animal manages to stay on an accelerating rotating rod is measured, 2) the rotation test, where contralateral rotations after an amphetamine injection are counted, 3) the adjusting steps test, where the number of adjusting steps made by the weight-bearing forepaw is counted while the animal is dragged over a flat surface and 4) the cylinder test, which assesses the limb use asymmetry during voluntary exploration of a glass cylinder. The choice of the behavioral test is not trivial and depends on the type of neurotoxin as well as the experimental design. For example, the rotarod test will, when performed more than 72 hours after the final dose of a MPTP treatment scheme in mice, show no difference between lesioned and control animals, unless the treatment is chronic and the mice have been extensively trained. For the 6-OHDA model, the cylinder test seems to be a sensitive measure of unilateral dopaminergic denervation whereas the rotations after amphetamine injection do not correlate linearly with the dopaminergic deficit. For an extensive overview see the article by Meredith and Kang (Meredith and Kang, 2006).

In 6-OHDA lesioned rats, exaggerated beta activity can be observed in GPe, STN, SNpr and motor cortex both under urethane anesthesia during episodes of cortical desynchronization as well as in awake animals at rest (Beck et al., 2016; Kühn et al., 2017; Mallet et al., 2008a; Mallet et al., 2008b), see Fig. 2. As in humans and NHP, beta activity is reduced by levodopa and apomorphine in 6-OHDA lesioned rats (Avila et al., 2010; Brazhnik et al., 2014; Delaville et al., 2015; Kühn et al., 2017).

Unlike 6-OHDA lesioned rats and MPTP-treated NHP, MPTP and 6-OHDA lesioned mice develop the clinical signs of PD but lack the emergence of subcortical beta oscillations (Chen et al., 2018; Lobb and Jaeger, 2015). In contrast, they display dopamine dependent delta

oscillations (Whalen et al., 2020). Interestingly, when using other parkinsonian models in mice, such as dopamine transporter knock out mice (Costa et al., 2006) or selective activation of striatal interneurons via optogenetics in healthy mice (Kondabolu et al., 2016), the parkinsonian phenotype is accompanied by increased beta oscillations in mice as well.

Thus, taken together, current animal models seem to reflect not only the phenotype of motor symptoms in PD but also mostly display similar oscillatory patterns in the dopamine-depleted state. This increases confidence that results from sites or scales that are not accessible in humans can be assumed to apply in humans as well. Regarding the interpretation of longitudinal findings of animal models, there is the major limitation that the time scale of the disease in all toxin-induced models contrasts with PD where the preclinical stage can last years. Similarly, novel approaches with cell type-specific targeting using optogenetic interventions to change neuronal population activity lead to acute development of parkinsonism as well. For example, acute parkinsonism could be observed when indirect medium spiny neurons were excited in transgenic mice with Cre-dependent viral expression of channel rhodopsin in D2-expressing striatal neurons (Kravitz et al., 2010). In contrast, activating D1-expressing striatal neurons (Kravitz et al., 2010) or cortical somatostatin-expressing interneurons (Valverde et al., 2020) alleviates motor symptoms in a parkinsonian mouse model. Possibly, novel genetic models of PD in which proteins that are known to be involved in inherited forms of PD like SNCA, Parkin, DJ-1, LRRK2 and PINK1 are targeted, may help overcome this current limitation. Indeed, such transgenic mice have slower disease dynamics and lead to a varying degree of neurodegeneration and clinical features of the disease in transgenic mice (Pingale and Gupta, 2020).

3.3. Association between spiking activity and beta oscillations

Whether the magnitude of beta oscillations modulates the neuronal output of subcortical nuclei is difficult to investigate in PD patients. Although it is possible to measure both oscillatory and unit activity intraoperatively, time constraints and the fact that in most cases solely the dopamine-depleted state can be examined are significant limitations.

More information can be drawn from animal models in which population as well as unit activity can be measured in parallel from several nodes of the cortico – basal ganglia – thalamo- cortical-loop (CBGTC-loop) in both dopaminergic states. In different rodent models it has been shown that the pathological state is not accompanied by a change in absolute firing rate, but rather a change to a more beta synchronized pattern across the entire network (Costa et al., 2006; Galvan and Wichmann, 2008; Mallet et al., 2008a).

This coupling of firing to beta oscillations is also observed in the dopamine-depleted state of PD patients and MPTP-treated NHP (Deffains et al., 2018; Soares et al., 2004). In PD patients, it is most robust in the pallidum and STN but has not been observed in the striatum (Kühn et al., 2005; Meng et al., 2020; Moshel et al., 2013; Valsky et al., 2020; Weinberger et al., 2006). This may be due to the fact that striatal coupling to beta activity seems to be cell-type specific: While striatal neurons with tonic activity show increased oscillatory activity in the beta range, no significant change in medium spiny neuron activity has been observed in MPTP-treated NHP (Deffains and Bergman, 2019; Sharott et al., 2017).

3.4. Beta oscillations: Cause or epiphenomenon of parkinsonism?

In PD patients, LFP recordings are usually acquired from later stages of the disease, when patients undergo DBS-surgery because of motor complications. This makes it impossible to investigate how exaggerated beta oscillations arise in early stages of the disease. Only recently chronic recordings have become possible in PD patients through development of novel pulse generators with sensing capacity (such as Medtronic Activa PC+S, RC+S, Percept). Thus, it could be shown that subcortical beta oscillations are temporally stable biomarkers for bradykinetic-rigid symptoms in PD patients in those later disease stages (Kehnemouyi et al., 2021; Neumann et al., 2017b). Whether exaggerated beta oscillations are an epiphenomenon or causal to parkinsonian motor symptoms is difficult to assess in PD patients. One way of doing so, is by artificially inducing beta oscillations via low frequency STN-DBS or transcranial alternating-current stimulation, which has been shown to lead to a varying degree of akinetic symptoms in humans (Chen et al., 2011; Eusebio et al., 2008; Fogelson et al., 2005; Pogosyan et al., 2009). Up to now, these results could not be reproduced in animal models: Optogenetic stimulation of excitatory STN neurons with beta frequency pulses failed to elicit a behavioral response in behaving rats (Gradinaru et al., 2009) and electrical stimulation of the STN using beta-burst patterns neither caused discernable symptoms in intact animals nor in levodopa treated 6-OHDA lesioned rats, although downstream structures such as the SNpr showed a consecutive increase of beta oscillations (Swan et al., 2019). The dissociation of STN beta burst spiking activity and LFP beta oscillations was also observed by Pan et al. (2016), who blocked T-type calcium channels in the STN and recorded a suppression of local neuronal bursting alongside reduced bradykinesia in 6-OHDA lesioned rats while the oscillatory profiles remained unchanged.

In animal models of PD, unlike with human subjects, it is possible to acquire electrophysiological data from healthy animals as well as from all stages of the disease. For 6-OHDA treated rodents and MPTP-treated NHP, there is only weak evidence of a stable correlation between measures of symptom severity and beta power at rest in cortical and subcortical areas for the early course of disease. Most studies that examined pathological beta oscillations in rodents have been carried out with 6-OHDA lesions causing a >90% loss of dopaminergic innervation. The appearance of akinetic symptoms precedes a significant increase of beta power in cortex and STN in chronic rodent and NHP models of PD (Degos et al., 2009; Haumesser et al., 2021; Leblois et al., 2007; Quiroga-Varela et al., 2013) whereas acute models tend to show conflicting evidence (Beck et al., 2016; Costa et al., 2006; Dejean et al., 2011; Mallet et al., 2008b), see Fig. 2. In contrast to power, shift of peak frequency from higher to lower beta band seems to accompany the transition from healthy NHP to moderate parkinsonism after MPTP-treatment (Connolly et al., 2015; Iskhakova et al., 2021). Thus, in MPTP-treated NHP, shifts in beta peak frequency might be a more robust correlate of parkinsonian symptom severity than changes in beta power, which should be further investigated in PD-patients where longitudinal recordings just recently became available through sensing-enabled DBS-devices.

A recent study by Brazhnik et al. corroborates these findings by examining early changes in motor behavior and oscillatory power in motor cortex and SNpr using a variety of acute and chronic PD models in rats (Brazhnik et al., 2012). While significant motor symptoms by far preceded changes in beta-range LFP power in the motor cortex and basal ganglia, the authors report a concomitant early loss of cortical mid-gamma activity and an early, although delayed, increase in spike-LFP coherence between mortor cortex and SNpr. The authors could additionally show that chronic blockage of dopamine receptors can produce beta-oscillations, which persist even after the cessation of drug administration and subsequent motor recovery, strengthening the case for questioning a direct causative link between beta oscillations and motor impairment. Furthermore, subcortical beta oscillations and an increase of cortico-subcortical coherence have recently been observed in the striatum of parkin knock-out mice that lack nigral degeneration or any motor impairment (Baaske et al., 2020). The authors argue that changes in striatal microcircuitry could facilitate the initial emergence of beta oscillations but are not critical for their maintenance. This would be in line with the observation that direct infusion of cholinergic agonists into the striatum is sufficient to induce local strong oscillations in the beta frequency range (McCarthy et al., 2011). Although studies in NHP demonstrated that MSN spiking activity is not entrained to ongoing local beta oscillations, this has been shown for other structures of the CBGTC-loop including the STN (Deffains and Bergman, 2019; Deffains et al.,

2016).

3.5. The origin of pathological beta oscillations

Although the presence of pathological beta oscillations throughout the CBGTC-loop and their connection with parkinsonian symptoms has been convincingly shown, the origin of pathological beta oscillations is still a matter of debate. Various hypotheses have been posited and explored with the aid of computational modeling, placing the origin within the intrinsically oscillatory properties of the STN-GPe network (Holgado et al., 2010), the enhanced cholinergic drive of striatal medium spiny neurons (McCarthy et al., 2011) or the thalamo-cortical circuits via integration of excitatory bursts targeting proximal and distal dendrites of pyramidal neurons (Sherman et al., 2016). Oscillatory activity in the STN-GPe network can be suppressed by blocking glutamatergic inputs to the STN (Nambu and Tachibana, 2014), a possible explanation being that weak cortical oscillatory input to the STN may be amplified by feedback inhibition in the STN-GPe network through an enhancement of postsynaptic excitability (Baufreton et al., 2005). To date it is not clear whether these mechanisms generate or merely sustain ongoing pathological oscillations.

3.6. Beyond beta activity: Changes of gamma activity in Parkinson's disease

Across species, movement is preceded by an event-related desynchronization (ERD) of the beta band throughout the CBGTC-loop. Besides the decrease in beta power, movement is accompanied by a cortical and subcortical event-related synchronization (ERS) in the gamma band (40–90 Hz) which has therefore been considered a pro-kinetic activity. The movement-related gamma synchronization has been observed across the motor circuit in recordings of healthy humans (Muthukumaraswamy, 2010; Pfurtscheller et al., 2003) as well as in PD, dystonia and epilepsy (Alegre et al., 2005; Cassidy et al., 2002; Fogelson et al., 2005).

The subcortical gamma ERS has been shown to scale with movement kinematics, although there is an ongoing debate whether this scaling reflects motor output or motor effort (Brücke et al., 2012; Lofredi et al., 2018; Tan et al., 2013). In the dopamine-depleted state of PD-patients, the amount of movement-related gamma synchronization is reduced and loses its scaling capacity (Lofredi et al., 2018). In contrast to beta activity, movement-related gamma synchronization correlates both with dopamine-related motor improvement (Litvak et al., 2012) as well as absolute motor impairment in the dopamine-substituted state (Lofredi et al., 2018). Despite these findings, which point to the pathophysiological significance of movement-associated activity in the gamma band, there are only few studies investigating this pattern in animal models. Those existing only report high beta/low gamma band activity during walking of parkinsonian rodents without further investigation (Delaville et al., 2014; Sharott et al., 2005).

Besides movement-related gamma activity, a narrow oscillatory activity in the gamma band (60–90 Hz, finely-tuned gamma, FTG) can sometimes be observed across basal ganglia structures in the dopamine-substituted state of PD patients as well as other movement disorders (Jenkinson et al., 2013; Kühn et al., 2006). Interestingly, FTG can also be induced by STN-DBS in the absence of dopamine (Wiest et al., 2021). This stimulation-induced FTG has recently been shown to occur across nodes of the motor circuit, correlating with motor improvement through DBS (Muthuraman et al., 2020). Subcortical FTG is therefore considered a pro-kinetic, but physiological signal. On the cortical level however, FTG has primarily been observed during L-Dopa induced dyskinesia (LID) in PD patients (Swann et al., 2016), see Fig. 2, which is why it is rather categorized as pathological feature of a hyperkinetic motor state.

This matches findings of NHP and rodents, were FTG during medication-induced dyskinesia is most pronounced in cortical areas, although it can also be detected in the striatum and GPi (Cenci and Lundblad, 2007; Di Monte et al., 2000; Dupre et al., 2016; Halje et al., 2012; Kühn et al., 2017; Salvadè et al., 2016; Tamtè et al., 2016), see Fig. 2. The comparison of dopamine treated 6-OHDA lesioned rats with dopamine-intact control animals together with the observation that near complete dopaminergic lesions are a prerequisite for developing this characteristic and long-lasting FTG activity emphasizes the pathological nature of this phenomenon (Cenci and Lundblad, 2007). However, FTG is not detected when levodopa priming is performed with lower doses (Ye et al., 2021) or a GABA agonist is injected to the thalamus (Dupre et al., 2016), although dyskinesia still occur, which further challenges the assumption of a causal link between FTG and LID.

Nevertheless, using FTG across parallel multisite recordings in rodent models of PD allowed Tamtè and colleagues (Tamtè et al., 2016) a highly precise state-prediction of the animal. These findings, together with recent reports from chronic multisite recordings in humans (Gilron et al., 2021), show the importance of combining multisite targeting with spectral features beyond beta activity to yield improved motor state decoding in parkinsonism, see Fig. 2.

3.7. Temporal dynamics of oscillatory synchrony

Besides spectral features, oscillatory activity can also display varying characteristics in the time domain. In healthy subjects, PD patients, rodents and NHP, beta synchronization is not static but occurs in bursts (Feingold et al., 2015; Haumesser et al., 2021; Lofredi et al., 2018). Average increases of beta-power as seen in PD patients can be explained by a shift from short to long lasting bursts of activity (Deffains et al., 2018; Lofredi et al., 2019; Lofredi et al., 2022; Tinkhauser et al., 2017a; Tinkhauser et al., 2017b). Departing from the classic "signaling the status quo" hypothesis of beta (Engel and Fries, 2010), these brief beta events point towards more specific roles like content-specific disinhibition of neuronal ensembles (Sherman et al., 2016; Spitzer and Haegens, 2017). For example, a study that combined data from PD patients as well as from 6-OHDA lesioned rats demonstrated that phase-locking of spiking activity in STN as well as in GPe and striatum increases during cortical beta bursts (Cagnan et al., 2019), underscoring the biological relevance of this phenomenon, see Fig. 2.

The same methodology used to identify beta bursts has been applied to movement and dyskinesia-related gamma activity in humans and rodents. It could be shown that the rate of subthalamic gamma bursts in PD patients correlates with movement velocity and the availability of dopamine (Lofredi et al., 2018). In a rodent LID model, cortical gamma burst parameters outperformed the averaged FTG power when correlated with severity of dyskinesia (Güttler et al., 2021). Specifically in cortical structures, bursts of oscillatory activity are thought to arise from distinct excitatory synaptic inputs to deep and superficial cortical layers, which drive current flow in opposite directions (Bonaiuto et al., 2021; Sherman et al., 2016). In contrast, there is no conceptual framework or empirical evidence from animal studies how oscillatory bursts are generated in subcortical structures that lack the layered architecture of the neocortex.

4. Dystonia

4.1. Exaggerated low frequency activity as biomarker in dystonia patients

Contrary to the excessive beta band activity in PD, patients with dystonia show increased pallidal low frequency (LF) activity from 3–12 Hz (Chen et al., 2006; Liu et al., 2008; Lofredi et al., 2019; Silberstein et al., 2003; Zhu et al., 2018). This was shown to hold true for the GPi, primary target for DBS in dystonia patients, as well as – even though less consistently - for the GPe and the STN (Geng et al., 2017; Moll et al., 2014; Neumann et al., 2012). Additionally, cortical gamma activity at rest may be associated with dystonic movements, but has not been observed in basal ganglia structures of patients with dystonia (Miocinovic et al., 2018), see Fig. 3. On the network level, the functional

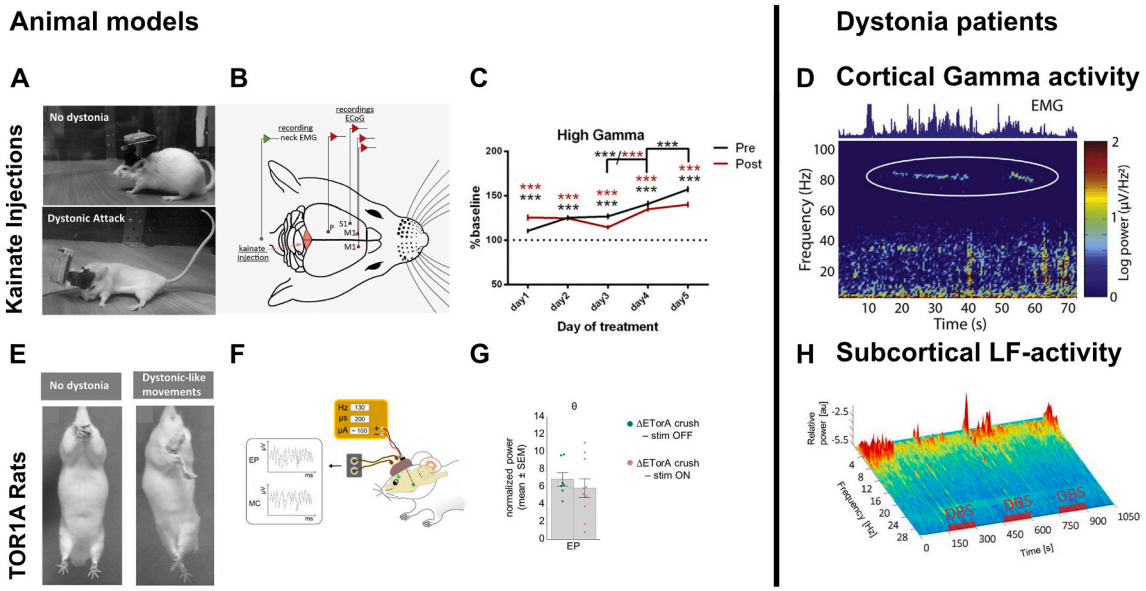

Fig. 3. Matching findings in recent animal models of dystonia and dystonia patients. Repetitive kainate injections in rat cerebellum induce dystonic attacks as shown in the lower image (A). Parallel sensorimotor and pallidal recordings were performed repetitively directly before and after kainate injections on consecutive days (B). There was both an immediate effect of kainate-injections on cortical gamma activity (see comparison of pre- and post-injection to baseline) as well as a stepwise increase over time (C). A similar pattern of increased cortical gamma activity was shown in a rare ECoG-recording from a single patient with dystonia along with dystonic posture, as visualized by increased EMG-activity (D). Dystonic-like movements could also be observed in a novel genetic rat model (TOR1A) after a peripheral nerve crush (E). When recording cortical and subcortical oscillations during DBS (F), a trend towards a decrease of subcortical low frequency activity was seen along with reduction of motor symptoms (G). A similar observation was made in a cohort of dystonia patients with predominantly phasic dystonic symptoms, where pallidal DBS led to a local suppression of LF-activity (H). Part (A), (B), (C) adapted from Georgescu et al., 2018; (D) adapted from Miocinovic et al., 2018; (E), (F). (G) adapted from Knorr et al., 2021; (H) adapted from Barow et al., 2014.

connectivity between internal pallidum and the cerebellum in the alpha band (9–12 Hz) is reduced in dystonia (Neumann et al., 2015). While pallidal LF activity shows a positive correlation with symptom severity in patients with cervical dystonia (Moll et al., 2014; Neumann et al., 2017a) even years after DBS-surgery (Scheller et al., 2019), pallido-cerebellar alpha connectivity is inversely correlated with dystonic symptoms.

So far, only pallidal LF-activity has been shown to be directly associated with involuntary muscle contractions in dystonia patients as measured by EMG (Chen et al., 2006; Foncke et al., 2007; Sharott et al., 2008). Indeed, in a functional directionality analysis, Sharott et al. further consolidated this finding by showing that the pallidal LF-activity predicted EMG-assessed muscle activity significantly better than the other way around. From that, authors concluded that efferences to the muscle are more relevant regarding pathological muscle and intracerebral activity than the afferent muscle feedback signal (Sharott et al., 2008). This observation is rendering afferent feedback from the dystonic muscles to the GPi less likely a cause of increased LF activity. However, LF activity might be responsive to peripheral stimuli: Liu et al. found that sensory input, using a common physiotherapy massage vibrator, led to decrease of LF synchronization, providing a possible explanation for the alleviating effect of the "sensory trick" in dystonic patients (Liu et al., 2008). In the same line, others showed a LF desynchronization in patients with cervical dystonia after application of a sensory trick (Tang et al., 2007; Trenado et al., 2016).

Pallidal DBS has also been shown to lead to a LF desynchronization and is most efficient if applied close to the LF-peak location within the pallidum (Neumann et al., 2017a; Barow et al., 2014; Scheller et al., 2019). However, dystonic syndromes represent a heterogeneous group of hyperkinetic disorders, of which not all respond well to GPi or STN DBS. It is still unclear whether all forms of dystonia would show similar LFP activity and in how far the outcome of DBS can be related to this biomarker. One study aimed at differentiating the oscillatory patterns between phasic and tonic dystonia (Yokochi et al., 2018). Interestingly, the authors found a shift in pallidal peak frequency from the alpha band in patients with primarily phasic to the theta band in patients with primarily tonic dystonic symptoms. This somewhat contrasts with another study, that demonstrated suppression of theta band activity by high-frequency stimulation specifically in patients with predominantly phasic dystonia (Barow et al., 2014; Scheller et al., 2019), see Fig. 3. The authors related this to the clinical observation that mobile dystonia responds earlier and better to high-frequency stimulation than fixed dystonia (Krauss et al., 2004; Vidailhet et al., 2005; Volkmann and Benecke, 2002). However, an increase in LF power might not be disease- but rather symptom-specific. Indeed, excessive theta oscillations were recorded in PD patients with levodopa-induced dyskinesias, in patients with Tourette's syndrome as well as in a subset of myoclonus-dystonia and NBIA patients with predominantly dystonic symptoms (Alonso-Frech et al., 2006; Foncke et al., 2007; Huebl et al., 2019; Neumann et al., 2018).

4.2. *Symptomatic animal models of dystonia reveal similar oscillatory pattern and highlight cerebellar involvement*

Concerning animal studies for dystonia, research has been hindered by the fact that, contrary to PD, symptomatic animal models are very rare. Most forms of dystonia are slowly progressive and there are several genetic mutations that have been associated with dystonia. However, most genetic animal models are asymptomatic (Dang et al., 2005; Grundmann et al., 2007, 2012; Sharma et al., 2005; Shashidharan et al., 2005) and not in all symptomatic models electrophysiological recordings were performed. Symptomatic rodent models without electrophysiological recordings are for example a heterozygous *Gnal* mouse model, in which dystonia-like movements were observed following systemic administration of oxotremorine (an unselective cholinergic agonist) (Pelosi et al., 2017), mice with conditional deletion of torsinA in the central nervous system (Liang et al., 2014) or forebrain deletion of torsinA (Pappas et al., 2015), which presented abnormal movements as

well as *Tor1a* knockout mice, which showed dystonia-like movements after application of a peripheral nerve crush (Ip et al., 2016).

For many years, the genetically dystonic hamster (gene symbol: dt^{sz}) as well as the genetically dystonic rat, which is an autosomal recessive mutant with a suspected deficiency in the protein caytaxin, were the only animal models presenting with stress-induced dystonia-like attacks (Lorden et al., 1984; Löscher et al., 1989; Xiao and Ledoux, 2005). The genetically dystonic hamster has the caveat of a still unknown genetic mutation and the suspected mutation in the genetically dystonic rat has so far not been associated with dystonia in humans, which reduces their translational value for dystonia research. However, multi-unit recordings in dystonic rats revealed a more rhythmic bursting firing in the cerebellum when compared to healthy rats (LeDoux and Lorden, 2002). Interestingly, this pathological change of cerebellar firing pattern increased linearly with postnatal age, highlighting the possibility of disease-modifying therapies at an early age (LeDoux, 2011). In a more recently developed model for DYT1, the most common form of inherited dystonia, in which torsinA was acutely knocked down in the cerebellum resulting in dystonia-like movements, similar changes in cerebellar output activity were observed, but recordings from basal ganglia structures were not performed (Fremont et al., 2017).

However, extracellular recordings from the GPi-equivalent (entopeduncular nucleus, EP), which is downstream to cerebellum, have been performed in the dystonic hamster. Here, a change in firing pattern towards more desynchronized activity during EP-DBS was observed (Leblois et al., 2010). Although concomitant oscillatory activity was not recorded, the synchronized firing pattern of cerebellar neurons in the dystonic rat and desynchronized firing of EP-neurons during clinically effective EP-DBS potentially relate to the increased pallidal LF-synchronization (Neumann et al., 2017a), that is reduced by pallidal DBS in dystonia patients (Barow et al., 2014). Indeed, such increased LF-synchronization as well as its modulation by DBS has been observed in a novel rat model for DYT-TOR1A (ΔETorA rat model).

In this model, dystonia-like movements of the hindlimbs can be induced by a transient peripheral nerve crush (Knorr et al., 2021), see Fig. 3. Here, LFP-recordings from EP and the motor cortex revealed a significantly higher theta power in ΔETorA crush rats compared to wildtype crush rats. High-frequency stimulation of the EP led to a significant improvement of the dystonia-like movements in ΔETorA crush rats compared to non-stimulated ΔETorA crush controls. LFP-recordings post stimulation revealed a non-significant reduction of 15% in theta power of stimulated ΔETorA crush rats compared to non-stimulated crush ΔETorA animals, see Fig. 3.

Thus, results from animal models presenting with a chronic form of dystonia hint toward similar changes in neurophysiological patterns than those observed in dystonia patients and point toward a significant role of cerebellar output activity in these changes.

Further evidence for the importance of cerebellar involvement in the etiology of dystonia comes from animal models that mirror rapid-onset forms of dystonia. Here, dystonia-like movements are acutely induced by repeated cerebellar injections of either

i) kainate, as a potent neurotoxin (Georgescu et al., 2018; Pizoli et al., 2002),
ii) ouabain, which inhibits the sodium-potassium ion pump (Calderon et al., 2011; Fremont et al., 2014),
iii) small hairpin RNA via adeno-associated viruses to specifically knockdown α3-containing sodium pumps (Fremont et al., 2015).

Cerebellar ouabain-perfusions increased the amplitude of cerebellar EEG-activity. Reducing cerebellar activity by GABAergic agents as well as interrupting cerebellar projections to the basal ganglia by lesioning of the deep cerebellar nuclei, alleviated dystonic symptoms (Calderon et al., 2011). These findings are generally replicated when performing a selective knockdown of α3-containing sodium pumps in the cerebellum (Fremont et al., 2015).

Therefore, the authors suggested that pathological basal ganglia activity as recorded in dystonia patients might actually arise from a pathological cerebellar output that is conveyed to the basal ganglia via the thalamus. Indeed, another study provided further evidence for this hypothesis as striatal firing shifted to high frequency burst firing during cerebellar-induced dystonic postures and was normalized by lesioning or optogenetically silencing of intralaminar thalamic neurons bilaterally (Chen et al., 2014). Beyond altered cerebellar activity, cerebellar kainate-injections were associated with an increase of cortical gamma activity (Georgescu et al., 2018), which is similar to the pattern found in dystonia patients (Miocinovic et al., 2018), see Fig. 3.

Taken together, further studies with multi-site recordings are needed to foster our understanding of the network changes observed in dystonia. Furthermore, many studies highlighting a cerebellar involvement in dystonia might be biased, because neuronal recordings were performed in symptomatic animal models, which are based on experimental cerebellar interventions.

4.3. How is pathological low frequency activity in dystonia generated?

Due to the limited accessibility, little to nothing is known on how or where increased LF-oscillations in dystonia patients are generated. As oscillations are thought to reflect the input to a structure, pallidal LF oscillations likely rely on pathological input integration within or across upstream structures of the basal ganglia. As mentioned above, animal models of acute forms of dystonia suggest a cerebellar involvement in dystonia (Calderon et al., 2011; Georgescu et al., 2018), which matches findings from dystonia patients of decreased pallido-cerebellar connectivity (Neumann et al., 2015) and reduced integrity of cerebello-thalamo-cortical fiber tracts (Argyelan et al., 2009). Given that disynaptic short-latency projections from the cerebellum to the striatum via intralaminar thalamic nuclei have been shown to trigger striatal dopamine release thereby modulating striatal activity (Threlfell et al., 2012), increased cerebellar activity might lead to the supposed hyperactivity of the direct pathway in dystonia (Kaji et al., 2018). Besides cerebellar involvement, autopsy studies have observed striatal atrophy in some forms of dystonia (Goto et al., 2005), neuroimaging studies have reported a disorganization of somatosensory cortices (Bara-Jimenez et al., 1998) and non-invasive neuromodulation revealed a maladaptive cortical plasticity in motor excitability (Quartarone et al., 2008). The widely distributed pathological findings in dystonia spanning the entire motor circuit, qualify dystonia as a network disorder. The cerebellum, striatum as well as sensori-motor cortices can all be considered as upstream structures of the internal pallidum, which represents the major output structure of the basal ganglia. Given that oscillatory activity is thought to reflect pallidal input, pallidal LF activity possibly does not reflect a pallidal pathology but is rather driven by the striatum, where mismatching cortical and cerebellar inputs are thought to enter the basal ganglia loop. In order to further explore whether pallidal LF-activity reflects i) pathological pallidal processing or ii) the common end route of pathological signaling upstream to the internal pallidum, further investigations in animal models are needed that allow for multi-scale, multi-site and longitudinal recordings.

5. Outlook

As shown in this review, translational research on oscillatory patterns in movement disorders has been very valuable. Animal models have been validated in various species, specifically in PD, that mirror motor symptoms of human patients and display similar pathophysiological changes in oscillatory activity. This increases the confidence that findings on oscillatory patterns from disease-states, areas or circuitry levels that are not accessible in humans are nevertheless transferable between species. Current development of demand-adapted neuromodulation in movement disorders specifically aims at using oscillatory activity as a read-out of the motor state. The strong consensus that beta

oscillations can be considered an electrophysiological marker of the Parkinsonian "Off"-state, together with the observation that these oscillations are suppressed by clinically effective therapies (Eusebio et al., 2011; Kühn et al., 2008; Levy et al., 2002; Priori et al., 2004) led to the idea of adaptive or closed-loop stimulation of the STN with beta power as stimulation trigger. First experiments used GPi and M1 spikes as triggers for GPi stimulation in MPTP lesioned NHP (Rosin et al., 2011) and later studies in human PD patients showed promising results with reduced time on stimulation while preserving and in some cases improving the clinical effects of DBS (Little et al., 2016; Little et al., 2013a; Rosa et al., 2015).

Newly developed DBS-devices with integrated sensing capacity take these experimental results to the next level with a currently recruiting international, multi-center clinical trial (ADAPT-PD, NCT04547712). Similar ideas are up and coming for DBS in dystonia patients. In a first case report of a patient with medically refractory cervical dystonia and STN-DBS as well as chronically implanted electrodes in the sensorimotor cortex (Johnson et al., 2021), subthalamic DBS was triggered by cortical theta activity which showed an improvement of blinded clinical ratings compared to continuous DBS.

Further advances in aDBS will require a refinement of electrophysiological biomarkers apart from the power of the beta band itself. Johnson et al. could show in NHP that aDBS was inferior to classical DBS in improving peak velocity in a cued reaching task when assessing kinematic parameters (Johnson et al., 2016). The authors caution that choosing a single LFP frequency as a biomarker, which by itself is physiologically modulated during movement, is insufficient.

Following up this development, focus has shifted to multi-site recordings with multi-feature extraction from oscillatory activity that allows to explain the maximal amount of variance from all motor states and thus to yield optimized therapeutic results (Gilron et al., 2021; Neumann et al., 2018). For example, the close relationship between finely tuned gamma (FTG) and LID has led Swann et al. (2018) to conduct a proof-of-principle study using cortical FTG power as a biomarker for aDBS, allowing for energy savings while maintaining the therapeutic effects of stimulation of the STN. Further studies will be needed to examine whether this concept is able to reduce clinically relevant LID. Here, studies in animal models can help explore the feature-space and shape study designs for human patients or assess within-subject variance through longitudinal recordings.

Beyond DBS, the development of new genetic animal models as well as methodological advances such as those referenced in the review article of Peng et al. "*Current approaches to characterize micro- and macroscale circuit mechanisms of Parkinson's disease in rodent models*" of this special issue will allow the pathophysiological investigation of cell-type or population-specific changes which lead to varying oscillatory patterns. This might finally help to prevent the development of these pathological brain states, thereby guiding the exploration of disease-modifying treatment options.

Declaration of Competing Interest

The authors declare no competing interests.

Acknowledgments

This work was funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) Project-ID 424778381-TRR 295. C. W.I. and L.R. received funding from the Interdisciplinary Center for Clinical Research (IZKF) at the University of Würzburg (A-421, N-362, Z2-CSP3).

References

Albin, R.L., Young, A.B., Penney, J.B., 1989. The functional anatomy of basal ganglia disorders. Trends Neurosci. 12, 366–375.

Alegre, M., Alonso-Frech, F., Rodríguez-Oroz, M.C., Guridi, J., Zamarbide, I., Valencia, M., Manrique, M., Obeso, J.A., Artieda, J., 2005. Movement-related changes in oscillatory activity in the human subthalamic nucleus: ipsilateral vs. contralateral movements. Eur. J. Neurosci. 22, 2315–2324.

Alonso-Frech, F., Zamarbide, I., Alegre, M., Rodríguez-Oroz, M.C., Guridi, J., Manrique, M., Valencia, M., Artieda, J., Obeso, J.A., 2006. Slow oscillatory activity and levodopa-induced dyskinesias in Parkinson's disease. Brain 129, 1748–1757.

Argyelan, M., Carbon, M., Niethammer, M., Ulug, A.M., Voss, H.U., Bressman, S.B., Dhawan, V., Eidelberg, D., 2009. Cerebellothalamocortical connectivity regulates penetrance in dystonia. J. Neurosci. 29, 9740–9747.

Avila, I., Parr-Brownlie, L.C., Brazhnik, E., Castañeda, E., Bergstrom, D.A., Walters, J.R., 2010. Beta frequency synchronization in basal ganglia output during rest and walk in a hemiparkinsonian rat. Exp. Neurol. 221, 307–319.

Baaske, M.K., Kramer, E.R., Meka, D.P., Engler, G., Engel, A.K., Moll, C.K.E., 2020. Parkin deficiency perturbs striatal circuit dynamics. Neurobiol. Dis. 137, 104737.

Balsters, J.H., Zerbi, V., Sallet, J., Wenderoth, N., Mars, R.B., 2020. Primate homologs of mouse cortico-striatal circuits. eLife 9, e53680. https://doi.org/10.7554/eLife.53680.

Bara-Jimenez, W., Catalan, M.J., Hallett, M., Gerloff, C., 1998. Abnormal somatosensory homunculus in dystonia of the hand. Ann. Neurol. 44, 828–831.

Barow, E., Neumann, W.J., Brücke, C., Huebl, J., Horn, A., Brown, P., Krauss, J.K., Schneider, G.H., Kühn, A.A., 2014. Deep brain stimulation suppresses pallidal low frequency activity in patients with phasic dystonic movements. Brain 137, 3012–3024.

Baufreton, J., Zhu, Z.T., Garret, M., Bioulac, B., Johnson, S.W., Taupignon, A.I., 2005. Dopamine receptors set the pattern of activity generated in subthalamic neurons. FASEB J. 19, 1771–1777.

Beck, M.H., Haumesser, J.K., Kühn, J., Altschüler, J., Kühn, A.A., van Riesen, C., 2016. Short- and long-term dopamine depletion causes enhanced beta oscillations in the cortico-basal ganglia loop of parkinsonian rats. Exp. Neurol. 286, 124–136.

Bergman, H., Wichmann, T., DeLong, M.R., 1990. Reversal of experimental parkinsonism by lesions of the subthalamic nucleus. Science 249, 1436–1438.

Bergman, H., Wichmann, T., Karmon, B., DeLong, M.R., 1994. The primate subthalamic nucleus. II. Neuronal activity in the MPTP model of parkinsonism. J. Neurophysiol. 72, 507–520.

Bonaiuto, J.J., Little, S., Neymotin, S.A., Jones, S.R., Barnes, G.R., Bestmann, S., 2021. Laminar dynamics of high amplitude beta bursts in human motor cortex. Neuroimage 242, 118479.

Boon, L.I., Geraedts, V.J., Hillebrand, A., Tannemaat, M.R., Contarino, M.F., Stam, C.J., Berendse, H.W., 2019. A systematic review of MEG-based studies in Parkinson's disease: the motor system and beyond. Hum. Brain Mapp. 40, 2827–2848.

Bosboom, J.L., Stoffers, D., Stam, C.J., van Dijk, B.W., Verbunt, J., Berendse, H.W., Wolters, E., 2006. Resting state oscillatory brain dynamics in Parkinson's disease: an MEG study. Clin. Neurophysiol. 117, 2521–2531.

Brazhnik, E., Cruz, A.V., Avila, I., Wahba, M.I., Novikov, N., Ilieva, N.M., McCoy, A.J., Gerber, C., Walters, J.R., 2012. State-dependent spike and local field synchronization between motor cortex and substantia nigra in hemiparkinsonian rats. J. Neurosci. 32, 7869–7880.

Brazhnik, E., Novikov, N., McCoy, A.J., Cruz, A.V., Walters, J.R., 2014. Functional correlates of exaggerated oscillatory activity in basal ganglia output in hemiparkinsonian rats. Exp. Neurol. 261, 563–577.

Brown, P., 2003. Oscillatory nature of human basal ganglia activity: relationship to the pathophysiology of Parkinson's disease. Mov. Disord. 18, 357–363.

Brown, P., Oliviero, A., Mazzone, P., Insola, A., Tonali, P., Di Lazzaro, V., 2001. Dopamine dependency of oscillations between subthalamic nucleus and pallidum in Parkinson's disease. J. Neurosci. 21, 1033–1038.

Brücke, C., Huebl, J., Schönecker, T., Neumann, W.J., Yarrow, K., Kupsch, A., Blahak, C., Lütjens, G., Brown, P., Krauss, J.K., Schneider, G.H., Kühn, A.A., 2012. Scaling of movement is related to pallidal γ oscillations in patients with dystonia. J. Neurosci. 32, 1008–1019.

Burns, R.S., Chiueh, C.C., Markey, S.P., Ebert, M.H., Jacobowitz, D.M., Kopin, I.J., 1983. A primate model of parkinsonism: selective destruction of dopaminergic neurons in the pars compacta of the substantia nigra by N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine. Proc. Natl. Acad. Sci. U. S. A. 80, 4546–4550.

Buzsáki, G., Anastassiou, C., Koch, C., 2012. The origin of extracellular fields and currents – EEG, ECoG, LFP and spikes. Nat. Rev. Neurosci. 13, 407–420.

Cagnan, H., Mallet, N., Moll, C.K.E., Gulberti, A., Holt, A.B., Westphal, M., Gerloff, C., Engel, A.K., Hamel, W., Magill, P.J., Brown, P., Sharott, A., 2019. Temporal evolution of beta bursts in the parkinsonian cortical and basal ganglia network. Proc. Natl. Acad. Sci. 116, 16095–16104.

Calderon, D.P., Fremont, R., Kraenzlin, F., Khodakhah, K., 2011. The neural substrates of rapid-onset Dystonia-Parkinsonism. Nat. Neurosci. 14, 357–365.

Carlsson, A., Lindqvist, M., Magnusson, T.O.R., 1957. 3,4-Dihydroxyphenylalanine and 5-hydroxytryptophan as reserpine antagonists. Nature 180, 1200.

Carlsson, A., Lindqvist, M., Magnusson, T., Waldeck, B., 1958. On the presence of 3-hydroxytyramine in brain. Science 127, 471.

Cassidy, M., Mazzone, P., Oliviero, A., Insola, A., Tonali, P., Di Lazzaro, V., Brown, P., 2002. Movement-related changes in synchronization in the human basal ganglia. Brain 125, 1235–1246.

Cenci, M.A., Lundblad, M., 2007. Ratings of L-DOPA-induced dyskinesia in the unilateral 6-OHDA lesion model of Parkinson's disease in rats and mice. Curr. Protoc. Neurosci. Chapter 9, Unit 9.25, 1–23.

Chen, C.C., Kühn, A.A., Hoffmann, K.T., Kupsch, A., Schneider, G.H., Trottenberg, T., Krauss, J.K., Wöhrle, J.C., Bardinet, E., Yelnik, J., Brown, P., 2006. Oscillatory pallidal local field potential activity correlates with involuntary EMG in dystonia. Neurology 66, 418–420.

Chen, C.C., Lin, W.Y., Chan, H.L., Hsu, Y.T., Tu, P.H., Lee, S.T., Chiou, S.M., Tsai, C.H., Lu, C.S., Brown, P., 2011. Stimulation of the subthalamic region at 20 Hz slows the development of grip force in Parkinson's disease. Exp. Neurol. 231, 91–96.
Chen, C.H., Fremont, R., Arteaga-Bracho, E.E., Khodakhah, K., 2014. Short latency cerebellar modulation of the basal ganglia. Nat. Neurosci. 17, 1767–1775.
Chen, H., Lei, H., Xu, Q., 2018. Neuronal activity pattern defects in the striatum in awake mouse model of Parkinson's disease. Behav. Brain Res. 341, 135–145.
Cheyne, D.O., 2013. MEG studies of sensorimotor rhythms: a review. Exp. Neurol. 245, 27–39.
Cole, S.R., van der Meij, R., Peterson, E.J., de Hemptinne, C., Starr, P.A., Voytek, B., 2017. Nonsinusoidal beta oscillations reflect cortical pathophysiology in Parkinson's disease. J. Neurosci. 37, 4830–4840.
Connolly, A.T., Jensen, A.L., Bello, E.M., Netoff, T.I., Baker, K.B., Johnson, M.D., Vitek, J. L., 2015. Modulations in oscillatory frequency and coupling in globus pallidus with increasing parkinsonian severity. J. Neurosci. 35, 6231–6240.
Costa, R.M., Lin, S.C., Sotnikova, T.D., Cyr, M., Gainetdinov, R.R., Caron, M.G., Nicolelis, M.A., 2006. Rapid alterations in corticostriatal ensemble coordination during acute dopamine-dependent motor dysfunction. Neuron 52, 359–369.
Crone, N.E., Miglioretti, D.L., Gordon, B., Lesser, R.P., 1998. Functional mapping of human sensorimotor cortex with electrocorticographic spectral analysis. II. Event-related synchronization in the gamma band. Brain 121 (Pt 12), 2301–2315.
Dang, M.T., Yokoi, F., McNaught, K.S., Jengelley, T.A., Jackson, T., Li, J., Li, Y., 2005. Generation and characterization of Dyt1 DeltaGAG knock-in mouse as a model for early-onset dystonia. Exp. Neurol. 196, 452–463.
de Hemptinne, C., Swann, N.C., Ostrem, J.L., Ryapolova-Webb, E.S., San Luciano, M., Galifianakis, N.B., Starr, P.A., 2015. Therapeutic deep brain stimulation reduces cortical phase-amplitude coupling in Parkinson's disease. Nat. Neurosci. 18, 779–786.
Deffains, M., Bergman, H., 2019. Parkinsonism-related β oscillations in the primate basal ganglia networks - recent advances and clinical implications. Parkinsonism Relat. Disord. 59, 2–8.
Deffains, M., Iskhakova, L., Katabi, S., Haber, S.N., Israel, Z., Bergman, H., 2016. Subthalamic, not striatal, activity correlates with basal ganglia downstream activity in normal and parkinsonian monkeys. Elife 5.
Deffains, M., Iskhakova, L., Katabi, S., Israel, Z., Bergman, H., 2018. Longer β oscillatory episodes reliably identify pathological subthalamic activity in Parkinsonism. Mov. Disord. 33, 1609–1618.
Degos, B., Deniau, J.M., Chavez, M., Maurice, N., 2009. Chronic but not acute dopaminergic transmission interruption promotes a progressive increase in cortical beta frequency synchronization: relationships to vigilance state and akinesia. Cereb. Cortex 19, 1616–1630.
Dejean, C., Arbuthnott, G., Wickens, J.R., Le Moine, C., Boraud, T., Hyland, B.I., 2011. Power fluctuations in beta and gamma frequencies in rat globus pallidus: association with specific phases of slow oscillations and differential modulation by dopamine D1 and D2 receptors. J. Neurosci. 31, 6098–6107.
Delaville, C., Cruz, A.V., McCoy, A.J., Brazhnik, E., Avila, I., Novikov, N., Walters, J.R., 2014. Oscillatory activity in basal ganglia and motor cortex in an awake behaving rodent model of Parkinson's disease. Basal Ganglia 3, 221–227.
Delaville, C., McCoy, A.J., Gerber, C.M., Cruz, A.V., Walters, J.R., 2015. Subthalamic nucleus activity in the awake hemiparkinsonian rat: relationships with motor and cognitive networks. J. Neurosci. 35, 6918–6930.
DeLong, M.R., 1990. Primate models of movement disorders of basal ganglia origin. Trends Neurosci. 13, 281–285.
Di Monte, D.A., McCormack, A., Petzinger, G., Janson, A.M., Quik, M., Langston, W.J., 2000. Relationship among nigrostriatal denervation, parkinsonism, and dyskinesias in the MPTP primate model. Mov. Disord. 15, 459–466.
Donoghue, J.P., Sanes, J.N., Hatsopoulos, N.G., Gaál, G., 1998. Neural discharge and local field potential oscillations in primate motor cortex during voluntary movements. J. Neurophysiol. 79, 159–173.
Dupre, K.B., Cruz, A.V., McCoy, A.J., Delaville, C., Gerber, C.M., Eyring, K.W., Walters, J. R., 2016. Effects of L-dopa priming on cortical high beta and high gamma oscillatory activity in a rodent model of Parkinson's disease. Neurobiol. Dis. 86, 1–15.
Duty, S., Jenner, P., 2011. Animal models of Parkinson's disease: a source of novel treatments and clues to the cause of the disease. Br. J. Pharmacol. 164, 1357–1391.
Engel, A.K., Fries, P., 2010. Beta-band oscillations–signalling the status quo? Curr. Opin. Neurobiol. 20, 156–165.
Eusebio, A., Chen, C.C., Lu, C.S., Lee, S.T., Tsai, C.H., Limousin, P., Hariz, M., Brown, P., 2008. Effects of low-frequency stimulation of the subthalamic nucleus on movement in Parkinson's disease. Exp. Neurol. 209, 125–130.
Eusebio, A., Thevathasan, W., Doyle Gaynor, L., Pogosyan, A., Bye, E., Foltynie, T., Zrinzo, L., Ashkan, K., Aziz, T., Brown, P., 2011. Deep brain stimulation can suppress pathological synchronisation in parkinsonian patients. J. Neurol. Neurosurg. Psychiatry 82, 569–573.
Feingold, J., Gibson, D.J., DePasquale, B., Graybiel, A.M., 2015. Bursts of beta oscillation differentiate postperformance activity in the striatum and motor cortex of monkeys performing movement tasks. Proc. Natl. Acad. Sci. 112, 13687–13692.
Feldmann, L.K., Lofredi, R., Neumann, W.-J., Al-Fatly, B., Roediger, J., Bahners, B.H., Nikolov, P., Denison, T., Saryyeva, A., Krauss, J.K., Faust, K., Florin, E., Schnitzler, A., Schneider, G.-H., Kühn, A.A., 2022. Toward therapeutic electrophysiology: beta-band suppression as a biomarker in chronic local field potential recordings. npj Parkinson's Dis. 8, 44.
Filion, M., Tremblay, L., 1991. Abnormal spontaneous activity of globus pallidus neurons in monkeys with MPTP-induced parkinsonism. Brain Res. 547, 142–151.
Fogelson, N., Kühn, A.A., Silberstein, P., Limousin, P.D., Hariz, M., Trottenberg, T., Kupsch, A., Brown, P., 2005. Frequency dependent effects of subthalamic nucleus stimulation in Parkinson's disease. Neurosci. Lett. 382, 5–9.
Foncke, E.M., Bour, L.J., van der Meer, J.N., Koelman, J.H., Tijssen, M.A., 2007. Abnormal low frequency drive in myoclonus-dystonia patients correlates with presence of dystonia. Mov. Disord. 22, 1299–1307.
Fremont, R., Calderon, D.P., Maleki, S., Khodakhah, K., 2014. Abnormal high-frequency burst firing of cerebellar neurons in rapid-onset dystonia-parkinsonism. J. Neurosci. 34, 11723–11732.
Fremont, R., Tewari, A., Khodakhah, K., 2015. Aberrant Purkinje cell activity is the cause of dystonia in a shRNA-based mouse model of Rapid Onset Dystonia-Parkinsonism. Neurobiol. Dis. 82, 200–212.
Fremont, R., Tewari, A., Angueyra, C., Khodakhah, K., 2017. A role for cerebellum in the hereditary dystonia DYT1. Elife 6.
Fries, P., 2015. Rhythms for cognition: communication through coherence. Neuron 88 (1), 220–235. https://doi.org/10.1016/j.neuron.2015.09.034.
Galvan, A., Wichmann, T., 2008. Pathophysiology of parkinsonism. Clin. Neurophysiol. 119, 1459–1474.
Geng, X., Zhang, J., Jiang, Y., Ashkan, K., Foltynie, T., Limousin, P., Zrinzo, L., Green, A., Aziz, T., Brown, P., Wang, S., 2017. Comparison of oscillatory activity in subthalamic nucleus in Parkinson's disease and dystonia. Neurobiol. Dis. 98, 100–107.
Georgescu, E.L., Georgescu, I.A., Zahiu, C.D.M., Şteopoaie, A.R., Morozan, V.P., Pană, A.Ş., Zăgrean, A., Popa, D., 2018. Oscillatory cortical activity in an animal model of dystonia caused by cerebellar dysfunction. Front. Cell. Neurosci. 12.
Gesi, M., Soldani, P., Giorgi, F.S., Santinami, A., Bonaccorsi, I., Fornai, F., 2000. The role of the locus coeruleus in the development of Parkinson's disease. Neurosci. Biobehav. Rev. 24, 655–668.
Gilbertson, T., Lalo, E., Doyle, L., Di Lazzaro, V., Cioni, B., Brown, P., 2005. Existing motor state is favored at the expense of new movement during 13-35 Hz oscillatory synchrony in the human corticospinal system. J. Neurosci. 25, 7771–7779.
Gilron, R., Little, S., Perrone, R., Wilt, R., de Hemptinne, C., Yaroshinsky, M.S., Racine, C. A., Wang, S.S., Ostrem, J.L., Larson, P.S., Wang, D.D., Galifianakis, N.B., Bledsoe, I. O., San Luciano, M., Dawes, H.E., Worrell, G.A., Kremen, V., Borton, D.A., Denison, T., Starr, P.A., 2021. Long-term wireless streaming of neural recordings for circuit discovery and adaptive stimulation in individuals with Parkinson's disease. Nat. Biotechnol. 39, 1078–1085.
Glow, P.H., 1959. Some aspects of the effects of acute reserpine treatment on behaviour. J. Neurol. Neurosurg. Psychiatry 22, 11–32.
Goto, S., Lee, L.V., Munoz, E.L., Tooyama, I., Tamiya, G., Makino, S., Ando, S., Dantes, M. B., Yamada, K., Matsumoto, S., Shimazu, H., Kuratsu, J., Hirano, A., Kaji, R., 2005. Functional anatomy of the basal ganglia in X-linked recessive dystonia-parkinsonism. Ann. Neurol. 58, 7–17.
Gradinaru, V., Mogri, M., Thompson, K.R., Henderson, J.M., Deisseroth, K., 2009. Optical deconstruction of parkinsonian neural circuitry. Science 324, 354–359.
Grundmann, K., Glöckle, N., Martella, G., Sciamanna, G., Hauser, T.K., Yu, L., Castaneda, S., Pichler, B., Fehrenbacher, B., Schaller, M., Nuscher, B., Haass, C., Hettich, J., Yue, Z., Nguyen, H.P., Pisani, A., Riess, O., Ott, T., 2012. Generation of a novel rodent model for DYT1 dystonia. Neurobiol. Dis. 47, 61–74.
Grundmann, K., Reischmann, B., Vanhoutte, G., Hübener, J., Teismann, P., Hauser, T.K., Bonin, M., Wilbertz, J., Horn, S., Nguyen, H.P., Kuhn, M., Chanarat, S., Wolburg, H., Van der Linden, A., Riess, O., 2007. Overexpression of human wildtype torsinA and human DeltaGAG torsinA in a transgenic mouse model causes phenotypic abnormalities. Neurobiol. Dis. 27, 190–206.
Güttler, C., Altschüler, J., Tanev, K., Böckmann, S., Haumesser, J.K., Nikulin, V.V., Kühn, A.A., van Riesen, C., 2021. Levodopa-induced dyskinesia are mediated by cortical gamma oscillations in experimental parkinsonism. Mov. Disord. 36, 927–937.
Halje, P., Tamtè, M., Richter, U., Mohammed, M., Cenci, M.A., Petersson, P., 2012. Levodopa-induced dyskinesia is strongly associated with resonant cortical oscillations. J. Neurosci. 32, 16541–16551.
Halliday, G., Herrero, M.T., Murphy, K., McCann, H., Ros-Bernal, F., Barcia, C., Mori, H., Blesa, F.J., Obeso, J.A., 2009. No Lewy pathology in monkeys with over 10 years of severe MPTP Parkinsonism. Mov. Disord. 24, 1519–1523.
Haumesser, J.K., Beck, M.H., Pellegrini, F., Kühn, J., Neumann, W.J., Altschüler, J., Harnack, D., Kupsch, A., Nikulin, V.V., Kühn, A.A., van Riesen, C., 2021. Subthalamic beta oscillations correlate with dopaminergic degeneration in experimental parkinsonism. Exp. Neurol. 335, 113513.
He, S., Mostofi, A., Syed, E., Torrecillos, F., Tinkhauser, G., Fischer, P., Pogosyan, A., Hasegawa, H., Li, Y., Ashkan, K., Pereira, E., Brown, P., Tan, H., 2020. Subthalamic beta-targeted neurofeedback speeds up movement initiation but increases tremor in Parkinsonian patients. Elife 9.
Heinrichs-Graham, E., Kurz, M.J., Becker, K.M., Santamaria, P.M., Gendelman, H.E., Wilson, T.W., 2014. Hypersynchrony despite pathologically reduced beta oscillations in patients with Parkinson's disease: a pharmaco-magnetoencephalography study. J. Neurophysiol. 112, 1739–1747.
Hirschmann, J., Butz, M., Hartmann, C.J., Hoogenboom, N., Özkurt, T.E., Vesper, J., Wojtecki, L., Schnitzler, A., 2016. Parkinsonian rest tremor is associated with modulations of subthalamic high-frequency oscillations. Mov. Disord. 31, 1551–1559.
Holgado, A.J., Terry, J.R., Bogacz, R., 2010. Conditions for the generation of beta oscillations in the subthalamic nucleus-globus pallidus network. J. Neurosci. 30, 12340–12352.
Horn, A., Neumann, W.J., Degen, K., Schneider, G.H., Kühn, A.A., 2017. Toward an electrophysiological "sweet spot" for deep brain stimulation in the subthalamic nucleus. Hum. Brain Mapp. 38, 3377–3390.
Huebl, J., Poshtiban, A., Brücke, C., Siegert, S., Bock, A., Koziara, H., Kmiec, T., Rola, R., Mandat, T., Kühn, A.A., 2019. Subthalamic and pallidal oscillatory activity in

patients with Neurodegeneration with Brain Iron Accumulation type I (NBIA-I). Clin. Neurophysiol. 130, 469–473.
Igarashi, J., Isomura, Y., Arai, K., Harukuni, R., Fukai, T., 2013. A θ-γ oscillation code for neuronal coordination during motor behavior. J. Neurosci. 33, 18515–18530.
Ip, C.W., Isaias, I.U., Kusche-Tekin, B.B., Klein, D., Groh, J., O'Leary, A., Knorr, S., Higuchi, T., Koprich, J.B., Brotchie, J.M., Toyka, K.V., Reif, A., Volkmann, J., 2016. Tor1a+/- mice develop dystonia-like movements via a striatal dopaminergic dysregulation triggered by peripheral nerve injury. Acta Neuropathol. Commun. 4, 108.
Iskhakova, L., Rappel, P., Deffains, M., Fonar, G., Marmor, O., Paz, R., Israel, Z., Eitan, R., Bergman, H., 2021. Modulation of dopamine tone induces frequency shifts in cortico-basal ganglia beta oscillations. Nat. Commun. 12, 7026.
Jenkinson, N., Kühn, A.A., Brown, P., 2013. γ oscillations in the human basal ganglia. Exp. Neurol. 245, 72–76.
Johnson, L.A., Nebeck, S.D., Muralidharan, A., Johnson, M.D., Baker, K.B., Vitek, J.L., 2016. Closed-loop deep brain stimulation effects on parkinsonian motor symptoms in a non-human primate - is beta enough? Brain Stimul. 9, 892–896.
Johnson, V., Wilt, R., Gilron, R., Anso, J., Perrone, R., Beudel, M., Piña-Fuentes, D., Saal, J., Ostrem, J.L., Bledsoe, I., Starr, P., Little, S., 2021. Embedded adaptive deep brain stimulation for cervical dystonia controlled by motor cortex theta oscillations. Exp. Neurol. 345, 113825.
Kaji, R., Bhatia, K., Graybiel, A.M., 2018. Pathogenesis of dystonia: is it of cerebellar or basal ganglia origin? J. Neurol. Neurosurg. Psychiatry 89, 488–492.
Kato, K., Yokochi, F., Taniguchi, M., Okiyama, R., Kawasaki, T., Kimura, K., Ushiba, J., 2015. Bilateral coherence between motor cortices and subthalamic nuclei in patients with Parkinson's disease. Clin. Neurophysiol. 126, 1941–1950.
Kehnemouyi, Y.M., Wilkins, K.B., Anidi, C.M., Anderson, R.W., Afzal, M.F., Bronte-Stewart, H.M., 2021. Modulation of beta bursts in subthalamic sensorimotor circuits predicts improvement in bradykinesia. Brain 144, 473–486.
Knorr, S., Rauschenberger, L., Ramirez Pasos, U., Friedrich, M.U., Peach, R.L., Grundmann-Hauser, K., Ott, T., O'Leary, A., Reif, A., Tovote, P., Volkmann, J., Ip, C. W., 2021. The evolution of dystonia-like movements in TOR1A rats after transient nerve injury is accompanied by dopaminergic dysregulation and abnormal oscillatory activity of a central motor network. Neurobiol. Dis. 154, 105337.
Kondabolu, K., Roberts, E.A., Bucklin, M., McCarthy, M.M., Kopell, N., Han, X., 2016. Striatal cholinergic interneurons generate beta and gamma oscillations in the corticostriatal circuit and produce motor deficits. Proc. Natl. Acad. Sci. U. S. A. 113, E3159–E3168.
Krauss, J.K., Yianni, J., Loher, T.J., Aziz, T.Z., 2004. Deep brain stimulation for dystonia. J. Clin. Neurophysiol. 21, 18–30.
Kravitz, A.V., Freeze, B.S., Parker, P.R., Kay, K., Thwin, M.T., Deisseroth, K., Kreitzer, A. C., 2010. Regulation of parkinsonian motor behaviours by optogenetic control of basal ganglia circuitry. Nature 466, 622–626.
Kühn, A.A., Trottenberg, T., Kivi, A., Kupsch, A., Schneider, G.H., Brown, P., 2005. The relationship between local field potential and neuronal discharge in the subthalamic nucleus of patients with Parkinson's disease. Exp. Neurol. 194, 212–220.
Kühn, A.A., Doyle, L., Pogosyan, A., Yarrow, K., Kupsch, A., Schneider, G.H., Hariz, M.I., Trottenberg, T., Brown, P., 2006. Modulation of beta oscillations in the subthalamic area during motor imagery in Parkinson's disease. Brain 129, 695–706.
Kühn, A.A., Kempf, F., Brücke, C., Gaynor Doyle, L., Martinez-Torres, I., Pogosyan, A., Trottenberg, T., Kupsch, A., Schneider, G.H., Hariz, M.I., Vandenberghe, W., Nuttin, B., Brown, P., 2008. High-frequency stimulation of the subthalamic nucleus suppresses oscillatory beta activity in patients with Parkinson's disease in parallel with improvement in motor performance. J. Neurosci. 28, 6165–6173.
Kühn, A.A., Tsui, A., Aziz, T., Ray, N., Brücke, C., Kupsch, A., Schneider, G.H., Brown, P., 2009. Pathological synchronisation in the subthalamic nucleus of patients with Parkinson's disease relates to both bradykinesia and rigidity. Exp. Neurol. 215, 380–387.
Kühn, J., Haumesser, J.K., Beck, M.H., Altschüler, J., Kühn, A.A., Nikulin, V.V., van Riesen, C., 2017. Differential effects of levodopa and apomorphine on neuronal population oscillations in the cortico-basal ganglia loop circuit in vivo in experimental parkinsonism. Exp. Neurol. 298, 122–133.
Langston, J.W., Forno, L.S., Rebert, C.S., Irwin, I., 1984. Selective nigral toxicity after systemic administration of 1-methyl-4-phenyl-1,2,5,6-tetrahydropyrine (MPTP) in the squirrel monkey. Brain Res. 292, 390–394.
Leblois, A., Meissner, W., Bioulac, B., Gross, C.E., Hansel, D., Boraud, T., 2007. Late emergence of synchronized oscillatory activity in the pallidum during progressive parkinsonism. Eur. J. Neurosci. 26, 1701–1713.
Leblois, A., Reese, R., Labarre, D., Hamann, M., Richter, A., Boraud, T., Meissner, W.G., 2010. Deep brain stimulation changes basal ganglia output nuclei firing pattern in the dystonic hamster. Neurobiol. Dis. 38, 288–298.
LeDoux, M.S., 2011. Animal models of dystonia: lessons from a mutant rat. Neurobiol. Dis. 42, 152–161.
LeDoux, M.S., Lorden, J.F., 2002. Abnormal spontaneous and harmaline-stimulated Purkinje cell activity in the awake genetically dystonic rat. Exp. Brain Res. 145, 457–467.
Levy, R., Ashby, P., Hutchison, W.D., Lang, A.E., Lozano, A.M., Dostrovsky, J.O., 2002. Dependence of subthalamic nucleus oscillations on movement and dopamine in Parkinson's disease. Brain 125, 1196–1209.
Liang, C.C., Tanabe, L.M., Jou, S., Chi, F., Dauer, W.T., 2014. TorsinA hypofunction causes abnormal twisting movements and sensorimotor circuit neurodegeneration. J. Clin. Invest. 124, 3080–3092.
Little, S., Brown, P., 2014. The functional role of beta oscillations in Parkinson's disease. Parkinsonism Relat. Disord. 20 (Suppl. 1), S44–S48.
Little, S., Pogosyan, A., Kuhn, A.A., Brown, P., 2012. β band stability over time correlates with Parkinsonian rigidity and bradykinesia. Exp. Neurol. 236, 383–388.
Little, S., Pogosyan, A., Neal, S., Zavala, B., Zrinzo, L., Hariz, M., Foltynie, T., Limousin, P., Ashkan, K., FitzGerald, J., Green, A.L., Aziz, T.Z., Brown, P., 2013a. Adaptive deep brain stimulation in advanced Parkinson disease. Ann. Neurol. 74, 449–457.
Little, S., Tan, H., Anzak, A., Pogosyan, A., Kühn, A., Brown, P., 2013b. Bilateral functional connectivity of the basal ganglia in patients with Parkinson's disease and its modulation by dopaminergic treatment. PLoS One 8, e82762.
Little, S., Beudel, M., Zrinzo, L., Foltynie, T., Limousin, P., Hariz, M., Neal, S., Cheeran, B., Cagnan, H., Gratwicke, J., Aziz, T.Z., Pogosyan, A., Brown, P., 2016. Bilateral adaptive deep brain stimulation is effective in Parkinson's disease. J. Neurol. Neurosurg. Psychiatry 87, 717–721.
Litvak, V., Jha, A., Eusebio, A., Oostenveld, R., Foltynie, T., Limousin, P., Zrinzo, L., Hariz, M.I., Friston, K., Brown, P., 2011. Resting oscillatory cortico-subthalamic connectivity in patients with Parkinson's disease. Brain 134, 359–374.
Litvak, V., Eusebio, A., Jha, A., Oostenveld, R., Barnes, G., Foltynie, T., Limousin, P., Zrinzo, L., Hariz, M.I., Friston, K., Brown, P., 2012. Movement-related changes in local and long-range synchronization in Parkinson's disease revealed by simultaneous magnetoencephalography and intracranial recordings. J. Neurosci. 32, 10541–10553.
Liu, X., Wang, S., Yianni, J., Nandi, D., Bain, P.G., Gregory, R., Stein, J.F., Aziz, T.Z., 2008. The sensory and motor representation of synchronized oscillations in the globus pallidus in patients with primary dystonia. Brain 131, 1562–1573.
Lobb, C.J., Jaeger, D., 2015. Bursting activity of substantia nigra pars reticulata neurons in mouse parkinsonism in awake and anesthetized states. Neurobiol. Dis. 75, 177–185.
Lofredi, R., Neumann, W.J., Bock, A., Horn, A., Huebl, J., Siegert, S., Schneider, G.H., Krauss, J.K., Kühn, A.A., 2018. Dopamine-dependent scaling of subthalamic gamma bursts with movement velocity in patients with Parkinson's disease. eLife 7, e31895.
Lofredi, R., Neumann, W.J., Brücke, C., Huebl, J., Krauss, J.K., Schneider, G.H., Kühn, A. A., 2019. Pallidal beta bursts in Parkinson's disease and dystonia. Mov. Disord. 34, 420–424.
Lofredi, R., Okudzhava, L., Irmen, F., Brücke, C., Huebl, J., Krauss, J.K., Schneider, G.-H., Faust, K., Neumann, W.-J., Kühn, A.A., 2022. Subthalamic beta bursts correlate with dopamine-dependent motor symptoms in 106 Parkinson's patients. BioRxiv. https://doi.org/10.1101/2022.05.06.490913, 2022.05.06.490913.
Lofredi, R., Tan, H., Neumann, W.J., Yeh, C.H., Schneider, G.H., Kühn, A.A., Brown, P., 2019 Jul. Beta bursts during continuous movements accompany the velocity decrement in Parkinson's disease patients. Neurobiol. Dis. 127, 462–471. https://doi.org/10.1016/j.nbd.2019.03.019.03.013.
López-Azcárate, J., Tainta, M., Rodríguez-Oroz, M.C., Valencia, M., González, R., Guridi, J., Iriarte, J., Obeso, J.A., Artieda, J., Alegre, M., 2010. Coupling between beta and high-frequency activity in the human subthalamic nucleus may be a pathophysiological mechanism in Parkinson's disease. J. Neurosci. 30, 6667–6677.
Lorden, J.F., McKeon, T.W., Baker, H.J., Cox, N., Walkley, S.U., 1984. Characterization of the rat mutant dystonic (dt): a new animal model of dystonia musculorum deformans. J. Neurosci. 4, 1925–1932.
Löscher, W., Fisher Jr., J.E., Schmidt, D., Fredow, G., Hönack, D., Iturrian, W.B., 1989. The sz mutant hamster: a genetic model of epilepsy or of paroxysmal dystonia? Mov. Disord. 4, 219–232.
Mallet, N., Pogosyan, A., Márton, L.F., Bolam, J.P., Brown, P., Magill, P.J., 2008a. Parkinsonian beta oscillations in the external globus pallidus and their relationship with subthalamic nucleus activity. J. Neurosci. 28, 14245–14258.
Mallet, N., Pogosyan, A., Sharott, A., Csicsvari, J., Bolam, J.P., Brown, P., Magill, P.J., 2008b. Disrupted dopamine transmission and the emergence of exaggerated beta oscillations in subthalamic nucleus and cerebral cortex. J. Neurosci. 28, 4795–4806.
Marsden, C.D., Obeso, J.A., 1994. The functions of the basal ganglia and the paradox of stereotaxic surgery in Parkinson's disease. Brain 117 (Pt 4), 877–897.
Marshall, J.F., Richardson, J.S., Teitelbaum, P., 1974. Nigrostriatal bundle damage and the lateral hypothalamic syndrome. J. Comp. Physiol. Psychol. 87, 808–830.
McCarthy, M.M., Moore-Kochlacs, C., Gu, X., Boyden, E.S., Han, X., Kopell, N., 2011. Striatal origin of the pathologic beta oscillations in Parkinson's disease. Proc. Natl. Acad. Sci. 108, 11620–11625.
Meng, D., Zhuang, P., Hallett, M., Zhang, Y., Li, J., Hu, Y., Li, Y., 2020. Characteristics of oscillatory pallidal neurons in patients with Parkinson's disease. J. Neurol. Sci. 410, 116661.
Meredith, G.E., Kang, U.J., 2006. Behavioral models of Parkinson's disease in rodents: a new look at an old problem. Mov. Disord. 21, 1595–1606.
Miller, W.C., Delong, M.R., 1987. In: Carpenter, M.B., Jayaraman, A. (Eds.), Altered Tonic Activity of Neurons in the Globus Pallidus and Subthalamic Nucleus in the Primate MPTP Model of Parkinsonism. Plenum, New York.
Miocinovic, S., Swann, N.C., de Hemptinne, C., Miller, A., Ostrem, J.L., Starr, P.A., 2018. Cortical gamma oscillations in isolated dystonia. Parkinsonism Relat. Disord. 49, 104–105.
Mirzaei, A., Kumar, A., Leventhal, D., Mallet, N., Aertsen, A., Berke, J., Schmidt, R., 2017. Sensorimotor processing in the basal ganglia leads to transient beta oscillations during behavior. J. Neurosci. 37, 11220–11232.
Moll, C.K., Galindo-Leon, E., Sharott, A., Gulberti, A., Buhmann, C., Koeppen, J.A., Biermann, M., Bäumer, T., Zittel, S., Westphal, M., Gerloff, C., Hamel, W., Münchau, A., Engel, A.K., 2014. Asymmetric pallidal neuronal activity in patients with cervical dystonia. Front. Syst. Neurosci. 8, 15.
Moran, A., Stein, E., Tischler, H., Bar-Gad, I., 2012. Decoupling neuronal oscillations during subthalamic nucleus stimulation in the parkinsonian primate. Neurobiol. Dis. 45, 583–590.
Moshel, S., Shamir, R.R., Raz, A., de Noriega, F.R., Eitan, R., Bergman, H., Israel, Z., 2013. Subthalamic nucleus long-range synchronization-an independent hallmark of human Parkinson's disease. Front. Syst. Neurosci. 7, 79.

Murthy, V.N., Fetz, E.E., 1992. Coherent 25- to 35-Hz oscillations in the sensorimotor cortex of awake behaving monkeys. Proc. Natl. Acad. Sci. U. S. A. 89, 5670–5674.
Muthukumaraswamy, S.D., 2010. Functional properties of human primary motor cortex gamma oscillations. J. Neurophysiol. 104, 2873–2885.
Muthuraman, M., Bange, M., Koirala, N., Ciolac, D., Pintea, B., Glaser, M., Tinkhauser, G., Brown, P., Deuschl, G., Groppa, S., 2020. Cross-frequency coupling between gamma oscillations and deep brain stimulation frequency in Parkinson's disease. Brain 143, 3393–3407.
Nambu, A., Tachibana, Y., 2014. Mechanism of parkinsonian neuronal oscillations in the primate basal ganglia: some considerations based on our recent work. Front. Syst. Neurosci. 8, 74.
Neumann, W.J., Jha, A., Bock, A., Huebl, J., Horn, A., Schneider, G.H., Sander, T.H., Litvak, V., Kühn, A.A., 2015. Cortico-pallidal oscillatory connectivity in patients with dystonia. Brain 138, 1894–1906.
Neumann, W.-J., Kühn, A.A., 2017. Subthalamic beta power—Unified Parkinson's disease rating scale III correlations require akinetic symptoms. Mov. Disord. 32, 175–176.
Neumann, W.J., Huebl, J., Brücke, C., Ruiz, M.H., Kupsch, A., Schneider, G.H., Kühn, A. A., 2012. Enhanced low-frequency oscillatory activity of the subthalamic nucleus in a patient with dystonia. Mov. Disord. 27, 1063–1066.
Neumann, W.J., Degen, K., Schneider, G.H., Brücke, C., Huebl, J., Brown, P., Kühn, A.A., 2016. Subthalamic synchronized oscillatory activity correlates with motor impairment in patients with Parkinson's disease. Mov. Disord. 31, 1748–1751.
Neumann, W.J., Horn, A., Ewert, S., Huebl, J., Brücke, C., Slentz, C., Schneider, G.H., Kühn, A.A., 2017a. A localized pallidal physiomarker in cervical dystonia. Ann. Neurol. 82, 912–924.
Neumann, W.J., Staub-Bartelt, F., Horn, A., Schanda, J., Schneider, G.H., Brown, P., Kühn, A.A., 2017b. Long term correlation of subthalamic beta band activity with motor impairment in patients with Parkinson's disease. Clin. Neurophysiol. 128, 2286–2291.
Neumann, W.J., Huebl, J., Brücke, C., Lofredi, R., Horn, A., Saryyeva, A., Müller-Vahl, K., Krauss, J.K., Kühn, A.A., 2018. Pallidal and thalamic neural oscillatory patterns in tourette's syndrome. Ann. Neurol. 84, 505–514.
Nini, A., Feingold, A., Slovin, H., Bergman, H., 1995. Neurons in the globus pallidus do not show correlated activity in the normal monkey, but phase-locked oscillations appear in the MPTP model of parkinsonism. J. Neurophysiol. 74, 1800–1805.
Oswal, A., Beudel, M., Zrinzo, L., Limousin, P., Hariz, M., Foltynie, T., Litvak, V., Brown, P., 2016. Deep brain stimulation modulates synchrony within spatially and spectrally distinct resting state networks in Parkinson's disease. Brain 139, 1482–1496.
Pan, M.K., Kuo, S.H., Tai, C.H., Liou, J.Y., Pei, J.C., Chang, C.Y., Wang, Y.M., Liu, W.C., Wang, T.R., Lai, W.S., Kuo, C.C., 2016. Neuronal firing patterns outweigh circuitry oscillations in parkinsonian motor control. J. Clin. Invest. 126, 4516–4526.
Pappas, S.S., Darr, K., Holley, S.M., Cepeda, C., Mabrouk, O.S., Wong, J.M., LeWitt, T.M., Paudel, R., Houlden, H., Kennedy, R.T., Levine, M.S., Dauer, W.T., 2015. Forebrain deletion of the dystonia protein torsinA causes dystonic-like movements and loss of striatal cholinergic neurons. Elife 4, e08352.
Pelosi, A., Menardy, F., Popa, D., Girault, J.A., Hervé, D., 2017. Heterozygous gnal mice are a novel animal model with which to study dystonia pathophysiology. J. Neurosci. 37, 6253–6267.
Penney Jr., J.B., Young, A.B., 1986. Striatal inhomogeneities and basal ganglia function. Mov. Disord. 1, 3–15.
Pfurtscheller, G., Graimann, B., Huggins, J.E., Levine, S.P., Schuh, L.A., 2003. Spatiotemporal patterns of beta desynchronization and gamma synchronization in corticographic data during self-paced movement. Clin. Neurophysiol. 114, 1226–1236.
Pingale, T., Gupta, G.L., 2020. Classic and evolving animal models in Parkinson's disease. Pharmacol. Biochem. Behav. 199, 173060.
Pizoli, C.E., Jinnah, H.A., Billingsley, M.L., Hess, E.J., 2002. Abnormal cerebellar signaling induces dystonia in mice. J. Neurosci. 22, 7825–7833.
Pogosyan, A., Gaynor, L.D., Eusebio, A., Brown, P., 2009. Boosting cortical activity at Beta-band frequencies slows movement in humans. Curr. Biol. 19, 1637–1641.
Pollok, B., Krause, V., Martsch, W., Wach, C., Schnitzler, A., Südmeyer, M., 2012. Motor-cortical oscillations in early stages of Parkinson's disease. J. Physiol. 590, 3203–3212.
Priori, A., Foffani, G., Pesenti, A., Tamma, F., Bianchi, A.M., Pellegrini, M., Locatelli, M., Moxon, K.A., Villani, R.M., 2004. Rhythm-specific pharmacological modulation of subthalamic activity in Parkinson's disease. Exp. Neurol. 189, 369–379.
Quartarone, A., Morgante, F., Sant'angelo, A., Rizzo, V., Bagnato, S., Terranova, C., Siebner, H.R., Berardelli, A., Girlanda, P., 2008. Abnormal plasticity of sensorimotor circuits extends beyond the affected body part in focal dystonia. J. Neurol. Neurosurg. Psychiatry 79, 985–990.
Quiroga-Varela, A., Walters, J.R., Brazhnik, E., Marin, C., Obeso, J.A., 2013. What basal ganglia changes underlie the parkinsonian state? The significance of neuronal oscillatory activity. Neurobiol. Dis. 58, 242–248.
Raz, A., Vaadia, E., Bergman, H., 2000. Firing patterns and correlations of spontaneous discharge of pallidal neurons in the normal and the tremulous 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine vervet model of parkinsonism. J. Neurosci. 20, 8559–8571.
Rosa, M., Arlotti, M., Ardolino, G., Cogiamanian, F., Marceglia, S., Di Fonzo, A., Cortese, F., Rampini, P.M., Priori, A., 2015. Adaptive deep brain stimulation in a freely moving Parkinsonian patient. Mov. Disord. 30, 1003–1005.
Rosin, B., Slovik, M., Mitelman, R., Rivlin-Etzion, M., Haber, S.N., Israel, Z., Vaadia, E., Bergman, H., 2011. Closed-loop deep brain stimulation is superior in ameliorating parkinsonism. Neuron 72, 370–384.
Salvadè, A., D'Angelo, V., Di Giovanni, G., Tinkhauser, G., Sancesario, G., Städler, C., Möller, J.C., Stefani, A., Kaelin-Lang, A., Galati, S., 2016. Distinct roles of cortical and pallidal β and γ frequencies in hemiparkinsonian and dyskinetic rats. Exp. Neurol. 275 (Pt 1), 199–208.
Scheller, U., Lofredi, R., van Wijk, B.C.M., Saryyeva, A., Krauss, J.K., Schneider, G.H., Kroneberg, D., Krause, P., Neumann, W.J., Kühn, A.A., 2019. Pallidal low-frequency activity in dystonia after cessation of long-term deep brain stimulation. Mov. Disord. 34, 1734–1739.
Sharott, A., Magill, P.J., Harnack, D., Kupsch, A., Meissner, W., Brown, P., 2005. Dopamine depletion increases the power and coherence of beta-oscillations in the cerebral cortex and subthalamic nucleus of the awake rat. Eur. J. Neurosci. 21, 1413–1422.
Sharma, N., Baxter, M.G., Petravicz, J., Bragg, D.C., Schienda, A., Standaert, D.G., Breakefield, X.O., 2005. Impaired motor learning in mice expressing torsinA with the DYT1 dystonia mutation. J Neurosci. 25, 5351–5355.
Sharott, A., Grosse, P., Kühn, A.A., Salih, F., Engel, A.K., Kupsch, A., Schneider, G.H., Krauss, J.K., Brown, P., 2008. Is the synchronization between pallidal and muscle activity in primary dystonia due to peripheral afferance or a motor drive? Brain 131, 473–484.
Sharott, A., Vinciati, F., Nakamura, K.C., Magill, P.J., 2017. A population of indirect pathway striatal projection neurons is selectively entrained to parkinsonian beta oscillations. J. Neurosci. 37, 9977–9998.
Shashidharan, P., Sandu, D., Potla, U., Armata, I.A., Walker, R.H., McNaught, K.S., Weisz, D., Sreenath, T., Brin, M.F., Olanow, C.W., 2005. Transgenic mouse model of early-onset DYT1 dystonia. Hum Mol Genet. 14, 125–133.
Sherman, M.A., Lee, S., Law, R., Haegens, S., Thorn, C.A., Hämäläinen, M.S., Moore, C.I., Jones, S.R., 2016. Neural mechanisms of transient neocortical beta rhythms: converging evidence from humans, computational modeling, monkeys, and mice. Proc. Natl. Acad. Sci. U. S. A. 113, E4885–E4894.
Sherrington, C.S., 1898. Decerebrate rigidity, and reflex coordination of movements. J. Physiol. 22, 319–332.
Silberstein, P., Kühn, A.A., Kupsch, A., Trottenberg, T., Krauss, J.K., Wöhrle, J.C., Mazzone, P., Insola, A., Di Lazzaro, V., Oliviero, A., Aziz, T., Brown, P., 2003. Patterning of globus pallidus local field potentials differs between Parkinson's disease and dystonia. Brain 126, 2597–2608.
Singh, A., Papa, S.M., 2020. Striatal oscillations in parkinsonian non-human primates. Neuroscience 449, 116–122.
Soares, J., Kliem, M.A., Betarbet, R., Greenamyre, J.T., Yamamoto, B., Wichmann, T., 2004. Role of external pallidal segment in primate parkinsonism: comparison of the effects of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced parkinsonism and lesions of the external pallidal segment. J. Neurosci. 24, 6417–6426.
Spitzer, B., Haegens, S., 2017. Beyond the status quo: a role for beta oscillations in endogenous content (re)activation. eNeuro 4.
Steiner, L.A., Neumann, W.J., Staub-Bartelt, F., Herz, D.M., Tan, H., Pogosyan, A., Kuhn, A.A., Brown, P., 2017. Subthalamic beta dynamics mirror Parkinsonian bradykinesia months after neurostimulator implantation. Mov. Disord. 32, 1183–1190.
Swan, C.B., Schulte, D.J., Brocker, D.T., Grill, W.M., 2019. Beta frequency oscillations in the subthalamic nucleus are not sufficient for the development of symptoms of parkinsonian bradykinesia/akinesia in rats. eNeuro 6.
Swann, N.C., de Hemptinne, C., Miocinovic, S., Qasim, S., Wang, S.S., Ziman, N., Ostrem, J.L., San Luciano, M., Galifianakis, N.B., Starr, P.A., 2016. Gamma oscillations in the hyperkinetic state detected with chronic human brain recordings in Parkinson's disease. J. Neurosci. 36, 6445–6458.
Swann, N.C., de Hemptinne, C., Thompson, M.C., Miocinovic, S., Miller, A.M., Gilron, R., Ostrem, J.L., Chizeck, H.J., Starr, P.A., 2018. Adaptive deep brain stimulation for Parkinson's disease using motor cortex sensing. J. Neural Eng. 15, 046006.
Tamtè, M., Brys, I., Richter, U., Ivica, N., Halje, P., Petersson, P., 2016. Systems-level neurophysiological state characteristics for drug evaluation in an animal model of levodopa-induced dyskinesia. J. Neurophysiol. 115, 1713–1729.
Tan, H., Pogosyan, A., Anzak, A., Ashkan, K., Bogdanovic, M., Green, A.L., Aziz, T., Foltynie, T., Limousin, P., Zrinzo, L., Brown, P., 2013. Complementary roles of different oscillatory activities in the subthalamic nucleus in coding motor effort in Parkinsonism. Exp. Neurol. 248, 187–195.
Tang, J.K.H., Mahant, N., Cunic, D., Chen, R., Moro, E., Lang, A.E., Lozano, A.M., Hutchison, W.D., Dostrovsky, J.O., 2007. Changes in cortical and pallidal oscillatory activity during the execution of a sensory trick in patients with cervical dystonia. Exp. Neurol. 204, 845–848.
Threlfell, S., Lalic, T., Platt, N.J., Jennings, K.A., Deisseroth, K., Cragg, S.J., 2012. Striatal dopamine release is triggered by synchronized activity in cholinergic interneurons. Neuron 75, 58–64.
Tinkhauser, G., Pogosyan, A., Little, S., Beudel, M., Herz, D.M., Tan, H., Brown, P., 2017a. The modulatory effect of adaptive deep brain stimulation on beta bursts in Parkinson's disease. Brain 140, 1053–1067.
Tinkhauser, G., Pogosyan, A., Tan, H., Herz, D.M., Kühn, A.A., Brown, P., 2017b. Beta burst dynamics in Parkinson's disease OFF and ON dopaminergic medication. Brain 140, 2968–2981.
Trenado, C., Hartmann, C.J., Elben, S., Pauls, K.A.M., Friggemann, L., Groiss, S.J., Timmermann, L., Vesper, J., Schnitzler, A., Wojtecki, L., 2016. Local field potential oscillations of the globus pallidus in cervical and tardive dystonia. J. Neurol. Sci. 366, 68–73.
Ungerstedt, U., 1968. 6-Hydroxy-dopamine induced degeneration of central monoamine neurons. Eur. J. Pharmacol. 5, 107–110.
Valsky, D., Heiman Grosberg, S., Israel, Z., Boraud, T., Bergman, H., Deffains, M., 2020. What is the true discharge rate and pattern of the striatal projection neurons in Parkinson's disease and Dystonia? Elife 9.

Valverde, S., Vandecasteele, M., Piette, C., Derousseaux, W., Gangarossa, G., Aristieta Arbelaiz, A., Touboul, J., Degos, B., Venance, L., 2020. Deep brain stimulation-guided optogenetic rescue of parkinsonian symptoms. Nat. Commun. 11, 2388.

van Wijk, B.C., Beudel, M., Jha, A., Oswal, A., Foltynie, T., Hariz, M.I., Limousin, P., Zrinzo, L., Aziz, T.Z., Green, A.L., Brown, P., Litvak, V., 2016. Subthalamic nucleus phase-amplitude coupling correlates with motor impairment in Parkinson's disease. Clin. Neurophysiol. 127, 2010–2019.

Vidailhet, M., Vercueil, L., Houeto, J.L., Krystkowiak, P., Benabid, A.L., Cornu, P., Lagrange, C., Tézenas du Montcel, S., Dormont, D., Grand, S., Blond, S., Detante, O., Pillon, B., Ardouin, C., Agid, Y., Destée, A., Pollak, P., 2005. Bilateral deep-brain stimulation of the globus pallidus in primary generalized dystonia. N. Engl. J. Med. 352, 459–467.

Volkmann, J., Benecke, R., 2002. Deep brain stimulation for dystonia: patient selection and evaluation. Mov. Disord. 17, S112–S115.

Wang, Y., Zhang, Q.J., Liu, J., Ali, U., Gui, Z.H., Hui, Y.P., Chen, L., Wu, Z.H., Li, Q., 2010. Noradrenergic lesion of the locus coeruleus increases apomorphine-induced circling behavior and the firing activity of substantia nigra pars reticulata neurons in a rat model of Parkinson's disease. Brain Res. 1310, 189–199.

Weinberger, M., Mahant, N., Hutchison, W.D., Lozano, A.M., Moro, E., Hodaie, M., Lang, A.E., Dostrovsky, J.O., 2006. Beta oscillatory activity in the subthalamic nucleus and its relation to dopaminergic response in Parkinson's disease. J. Neurophysiol. 96, 3248–3256.

Whalen, T.C., Willard, A.M., Rubin, J.E., Gittis, A.H., 2020. Delta oscillations are a robust biomarker of dopamine depletion severity and motor dysfunction in awake mice. J. Neurophysiol. 124, 312–329.

Wichmann, T., Soares, J., 2006. Neuronal firing before and after burst discharges in the monkey basal ganglia is predictably patterned in the normal state and altered in parkinsonism. J. Neurophysiol. 95, 2120–2133.

Wiest, C., Tinkhauser, G., Pogosyan, A., He, S., Baig, F., Morgante, F., Mostofi, A., Pereira, E.A., Tan, H., Brown, P., Torrecillos, F., 2021. Subthalamic deep brain stimulation induces finely-tuned gamma oscillations in the absence of levodopa. Neurobiol. Dis. 152, 105287.

Wilson, S.A.K., 1914. An experimental research into the anatomy and physiology of the corpus striatum. Brain 36, 427–492.

Xiao, J., Ledoux, M.S., 2005. Caytaxin deficiency causes generalized dystonia in rats. Brain Res. Mol. Brain Res. 141, 181–192.

Yao, L., Brown, P., Shoaran, M., 2020. Improved detection of Parkinsonian resting tremor with feature engineering and Kalman filtering. Clin. Neurophysiol. 131, 274–284.

Ye, T., Bartlett, M.J., Sherman, S.J., Falk, T., Cowen, S.L., 2021. Spectral signatures of L-DOPA-induced dyskinesia depend on L-DOPA dose and are suppressed by ketamine. Exp. Neurol. 340, 113670 https://doi.org/10.1016/j.expneurol.2021.113670.

Yokochi, F., Kato, K., Iwamuro, H., Kamiyama, T., Kimura, K., Yugeta, A., Okiyama, R., Taniguchi, M., Kumada, S., Ushiba, J., 2018. Resting-state pallidal-cortical oscillatory couplings in patients with predominant phasic and tonic dystonia. Front. Neurol. 9, 375.

Zhu, G., Geng, X., Tan, Z., Chen, Y., Zhang, R., Wang, X., Aziz, T., Wang, S., Zhang, J., 2018. Characteristics of globus pallidus internus local field potentials in hyperkinetic disease. Front. Neurol. 9, 934.