Signal propagation velocity in rat and human cortical pyramidal cells

Doctoral thesis

Gáspár Oláh

Supervisor:

Gábor Tamás, Ph.D., D.Sc.

University of Szeged

Department of Phisiology, Anatomy and Neuroscience

Doctoral School of Biology

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Introduction

The cerebral cortex is the latest central nervous system structure to evolve during phylogeny. The complexity of the cytoarchitecture of the neocortex has fascinated researchers since the late 19th century. The morphological diversity of cortical neurons was described in relative detail by Santiago Ramón y Cajal. Although a significant part of these early anatomical observations were made on human cortical specimens, experimental results on neurons and microcircuits to describe and understand their function have been predominantly derived from studies on rodent preparations.

The human cerebral cortex is significantly larger than that of rodents. However, besides the obvious differences in size, structural differences between the two species can also be observed. The human cerebral cortex is significantly thicker than that of rodents. The most striking difference appears to be in the extent of layer II/III, the cortical layer that has shown the greatest increase in size during evolution. However, it is not only in the thickness of the cortical layers that differences between rats and humans, but the size of the cells is also significantly larger in our species. There are also significant differences in the morphology of the dendrites of pyramidal cells in rat and human. The dendritic extent and morphological complexity of human pyramidal dendritic tree, i.e. the total length of the dendrites and the number of branches in the dendritic tree, are significantly greater. The rapid processing of signals from the outside world is important to avoid placing an organism at a selective disadvantage. Rodent and human electroencephalograms (EEGs) contain waves with similar frequency components, which also means that no significant differences in the time course of information processing can be expected. Consistent with this, our previous experiments suggest that the temporal resolution of human microcircuits is similar in the two species. Several independent studies have now shown that there are no significant differences in synaptic latencies between humans and rodents.

The question arises, what evolutionary innovation could be behind the fact that the human microcircuit has a similar temporal resolution as the rodent, despite the obvious differences in the size of the cells that make it up? What differences might there be in the functioning of the neurites involved in cell-to-cell communication?

Aims

The aims of my PhD work are:

1. to study the temporal dynamics of human and rodent neuron networks using paired whole-cell patch clamp recordings,

2. to determine the dendritic and axonal conduction velocities using simultaneous somatic and dendritic/axonic whole-cell recordings in both rat and human cortical pyramidal cells,

3. to investigate the mechanisms underlying differences in dendritic conduction velocity.

Materials and methods

Preparation of surviving brain slice preparations

Our experiments were performed on surviving neocortical brain slice preparations with the permission of the Ethics Committee of the University of Szeged (ref. no. XX/897/2018, ref. 75/2014) and in compliance with the Declaration of Helsinki. In our work we used young adult (P20-45) Wistar rats (regardless of gender) and surgically removed human cortical tissue pieces.

After anesthetizing the rats with halothane, the animals were decapitated and their brains were removed. The human brain tissue samples were placed in cold artificial cerebrospinal fluid (the composition of which was identical to that of the solution used to prepare the brain slices, see later) in the operating room and then kept cold until the end of the transportation. Human and rat brain tissues were then processed in the same way. Coronal slices 320 µm thick were prepared from the brain cortex. The brain slices were dissected in cold (4ºC) high sucrose artificial cerebrospinal fluid with the following composition in mM: 75 sucrose, 84 NaCl, 2.5 KCl, 1 NaH2PO4, 25 NaHCO3, 0.5 CaCl2, 4 MgSO4, 25 D-(+)-glucose. After sectioning, the brain slices were incubated at 36ºC for 30 min, after which the fluid was gradually replaced with low Ca2+ artificial cerebrospinal fluid with the following composition in mM: 130 NaCl, 3.5 KCl, 1 NaH2PO4, 24 NaHCO3, 1 CaCl2, 3 MgSO4, 10 D-(+)-glucose. After incubation, brain slices were kept at 17 ºC in artificial cerebrospinal fluid with low Ca2+ content until the start of the experiment. For the measurements, the brain slices were placed in a 36 ºC chamber through which

a recording solution flowed at a rate of 4-5 ml/min. The composition of the recording solution was identical to that of the artificial cerebrospinal fluid with low Ca2+ content, except for a higher concentration of 3 mM CaCl2 and a lower concentration of 1.5 mM MgSO4. Without exception, the solutions used to transport the human tissue, prepare the brain slices, and during the measurements were continuously saturated with a mixture of 95% oxygen and 5% carbon dioxide.

Electrophysiological measurements

During our electrophysiological measurements, we performed simultaneous patch-clamp recordings. Cells were first visualized by differential interference contrast (DIC) video microscopy. Based on the shape and location of the cell bodies, we selected the layer II/III pyramidal cells for measurement. The pipettes used for somatic paired recordings (3-5 MΩ) were filled with intracellular solution containing 126 mM K-gluconate, 4 mM KCl, 4 mM ATP-Mg, 0.3 mM GTP-Na2, 10 mM HEPES, 10 mM keratin phosphate and 8 mM biocytin. After establishing the somatic whole-cell configuration, the passive electronic characteristics and firing pattern of the cells were assessed with an initial square-wave pulse of -100 pA for 800 ms at a command current of 0 pA, which was repeatedly increased by 20 pA until the firing frequency of the cell reached an average of 10 Hz over the sweep. The presence of synaptic connections between pyramidal cells was tested in current-clamp mode. If an EPSP was observed after a short delay (<2 ms) after the presynaptic action potential, the presence of a monosynaptic connection was assumed and the slice was fixed for further anatomical examination after the measurement was completed. The intracellular solution used for the somato-dendritic and somato-axonal simultaneous measurements contained an additional 10 µM Alexa 594 hydrazide fluorescent dye. We started our measurements with DIC video microscopy imaging as detailed above. After establishing the somatic whole-cell configuration, we recorded the cell firing pattern as previously described. Subsequently, the intracellular solution was allowed to diffuse into the dendrites for 5-10 min. 2 photon imaging was used to visualize the dendritic arbor of the measured cell, followed by targeted dendritic patch clamp recording using another electrode (12-25 MΩ). During the somato-dendritic measurements, somatic current injections above the cells rheobase were injected and the propagation of the resulting action potentials back into the dendrites was recorded. For the simulated EPSPs, a short descending "ramp" stimulation was applied, the amplitude of which was adjusted to a value between 1-3 mV of the signal amplitude measured at the somatic electrode. At

the end of the recordings, a Z-stack were taken in fluorescence mode of the dye-loaded cells, which subsequently allowed us to measure the length and thickness of the dendrite sections between the measuring points.

Nucleated patch recordings were used to determine the specific membrane capacity. For these measurements, a caesium-chloride-based intracellular solution was used according to a previously described protocol. Measurements were performed with sylgard-coated electrodes (3-5 MΩ) to minimize pipette capacitance. After the somatic whole-cell configuration was established, the nucleus was pulled out of the cell, taking care not to degrade the quality of the patch. If a leak current of more than 200 pA was measured at a holding potential of -70 mV, the measurement was not continued. While holding the nucleated patch at -70 mV, 300 short 10 ms voltage steps of -5mV were applied (Axon Multiclamp 700B). The electrode was then gently pressed against a sylgard ball to determine the residual capacitance. The current generated upon stimulation was digitized at 200 kHz (Molecular Devices, Axon Digidata 1440).

Anatomical analysis of measured cells

Following electrophysiological experiments, brain slices containing biocytin-labelled neurons were prepared for light microscopy. The brain slices were placed in a 0.1 M phosphate buffer solution (pH= 7.4) containing 4% paraformaldehyde, 15% picric acid and 1.25% glutaraldehyde and kept in this solution at 4ºC for at least 12 hours. The fixative solution was removed from the slices by repeated washing with 0,1 M phosphate buffer solution. The slices were then placed in a phosphate buffer solution containing 10% and then 20% sucrose. The brain slices were frozen in liquid nitrogen for a few seconds, then embedded in 10% gelatin and resected in cold phosphate buffer solution to 60 µm thick sections (Leica VT 1000S microtome). Sections were stored in avidin-biotin peroxidase complex (1:100; Vector Labs) dissolved in Tris buffer (pH= 7.4) at 4ºC overnight. For the enzyme reaction, 0,05 % 3'3-diaminobenzidine tetrahydrochloride (DAB) was used as chromogen and 0,01 % H_2O_2 as oxidant. Slices were post-fixed in 0.1 M phosphate buffer solution containing 1% OsO_4. After repeated washes with distilled water, they were treated with 1% uranyl acetate and dehydrated with a rising alcohol series. Finally, they were embedded in epoxy resin (Durcupan, SigmaAldrich, USA) and mounted on slides. Sections were examined under a light microscope and reconstructed (Neurolucida). Possible

synaptic sites were marked and their distance from the soma was measured based on the 3-dimensional reconstructions.

Measurement of dendrite length and thickness

On the Z-stacks prepared after dendritic and axonal recordings, the neurite sections between the measurement points were reconstructed and their lengths were determined (ImageJ, Simple Neurite Tracer plugin). The thickness of the reconstructed sections was determined using the SNT "fitting" algorithm. Dendrites were characterized by their average thickness value.

Analysis of electrophysiological signals

Our conductions were analysed with self-developed python scripts. Our measurements were exported to ASCII format (HEKA, Fitmaster). For paired leads, synaptic latency was defined as the time difference between the action potential elicited in the presynaptic cell and the onset of EPSP in the postsynaptic cell.

In the analysis of somato-dendritic discharges, the latency of back-propagating APs was also measured at different points in the waveforms measured at the two discharge points. A similar approach was followed for the somato-axonal and simulated EPSP recordings. The figures in the thesis show the latencies of the signals at the peak and the velocity values calculated from these latencies.

Nucleated patch recordings made for the determination of specific membrane capacitance were analyzed using Clampfit (Molecular Devices). Within individual measurements, the capacitive transients were averaged and then subtracted from the average of the transients recorded to determine the residual capacitance at the end of the measurement. An exponential curve was fitted to the ascending branch of the resulting capacitive transients, such that the fitting started 10 μs after the negative peak of the transient, and the endpoint of the fitting was determined 300 μs after the peak. The exponential fit was extrapolated to the starting point of the voltage step. The τ value of the resulting exponential curve was used to calculate the capacitance of the membrane surrounding the nucleus. The value of the nucleus capacitance was then expressed per unit area.

Membrane thickness measurement

Cell membrane thickness was measured on a data set already used for a previous publication of our group (Molnár et al., 2016). In transmission electron microscopy images, we searched for membrane structures that belonged to dendrites, as inferred from the presence of postsynaptic density in the given section. Thickness measurements were taken at least 20 nm from the postsynaptic densities. A line perpendicular to the membrane was drawn and along this line, the points at which the gradient magnitude exceeded the threshold of 50 were examined, and the distance between the two points along the line was measured.

Modelling

A computer model was designed to investigate the effect of dendritic thickness, active and passive membrane parameters on the shape and propagation velocity of APs. The model consisted of a somatic compartment, an axonal compartment, and a dendritic cable compartment, each 200 μm in length. The axonal and dendritic cable diameters were set to 1.6 and 1.2 mm, respectively. The somatic membrane capacitance of the model neuron was set to 40 pF, while the surface capacitance of the cable compartments was set to 20 fF/mm2. The somatic leakage conductance was 1.0 nS, and the reverse potential of the leakage current was -62 mV. The model included 7 voltage-dependent currents, namely transient and persistent Na currents, delayed rectifier K current, h current, slowly activated M-type K current, high voltage-activated Ca current, and Ca-dependent K current. The voltage-dependent transient Na, M and Kd currents were assigned to the axonal and somatic compartments, while the persistent Na, h, Ca and K(Ca) currents were assigned to the somatic and dendritic compartments. The model was tested with a current stepping protocol corresponding to the stimulation used in biological neurons (square pulses of 0.5 s duration starting at -100 pA and increasing by +20 pA). The delay of back-propagation of APs to the dendrite in response to the simulated somatic current injection was measured at the peak of the waveform.

Results

Synaptic latencies in human and rat microcircuits

Is there a difference in the temporal resolution of human and rat neocortical microcircuits? Paired recordings of pyramidal cell-pyramidal cell pairs were performed to investigate this question.

During paired recordings, we examined the latency of postsynaptic responses following AP in the presynaptic cell. We found no significant difference in synaptic latencies measured from rats (n=24) and human samples (n=30) (rat: 1.132 ± 0.239 ms, human: 1.122 ± 0.381 ms, Mann-Whitney test: P=0. 657). Following the electrophysiological measurements, a subset of cell pairs with both presynaptic axons and postsynaptic dendrites fully labelled (n=5 rat, n=8 human) were subjected to light microscopic analysis. The distance of potential synaptic contact sites from the cell body was measured on both postsynaptic and presynaptic cells. The length of axons from presynaptic cells to synaptic sites and the length of dendrites from synaptic sites to the cell body of the postsynaptic cell were measured and the intersomatic length was determined as the sum of these two numbers. We observed significantly longer intersomatic distance for cell pairs from human samples compared to rat samples (rat: 262.22 ± 53.639 µm, human: 385.7 ± 74.277 µm, two-sample t-test: P = 0.008).

These results suggest that information propagation is faster in human neocortical networks compared to rodents. But what could account for the difference between the two species? To answer this question, direct measurement of the conduction velocity of nerve processes may provide an answer.

Axonal propagation velocity measurement

To determine the axonal signal propagation velocity, simultaneous whole-cell clamp recordings were performed from the soma and axon blebs of layer II/III pyramidal cells. From the latency (of APs induced on cells by somatic current injection) at two electrodes and the axon length, the axonal conduction velocity can be approximately calculated. Assuming that the site of APs initiation in the two species is at the same distance from the cell body, no significant difference in the latency of appearance of the peak of somatically induced APs measured at the two recording

sites was found between the two species. Our measurements suggest that APs travel through the axons of rat and human layer II/III pyramidal cells at similar speeds (rat: n=8, 0.848 ± 0.291 m/s, human: n=9, 0.851 ± 0.387 m/s, two-sample t-test: p=0.282).

Since the results of our axonal recordings do not explain the difference in information flow velocity between the two species observed in the paired mesurements, we started a systematic investigation of the dendrites.

Investigation of the propagation speed of simulated EPSPs

Simultaneous recordings were performed on the cell body and apical dendrites of pyramidal cells, during which the propagation of membrane potential changes in response to both dendritic and somatic current injection was investigated on the cells. First, we performed a current injection simulating postsynaptic current through the dendritic pipette. The propagation velocity of these simulated EPSPs (sEPSPs) was significantly faster in humans than in rat dendrites (rat: 0.074 ± 0.018 m/s vs. human: 0.093 ± 0.025 m/s, two-sample t test: P = 0.004). Subsequently, we also examined the propagation velocity of bAPs in these dendrites and found a significant correlation between the orthogonal and retrograde conduction velocities of the dendrites.

As the quality of measurements oftenly were significantly degraded (large leakage currents were measured after current injection) after current injection trough the dendritic pipette and we found a significant correlation between the different directions of conduction of the dendrites, we performed further pharmacological experiments on the backpropagation of APs into the dendrite after somatic current injection. To do this, we first examined in more detail whether there was any difference in the propagation velocity of bAPs in the two species.

Propagation speed of propagating action potentials

The propagation velocity of bAPs in the rat was 0.233 ± 0.095 m/s, whereas in humans a significantly higher velocity of 0.344 ± 0.139 m/s was measured (Mann-Whitney test: P = 6.369 × 10-6). Our measurements therefore indicate that in human dendrites, electrical signals propagate significantly faster both from the dendrite to the soma and from the cell body to the dendrite. The orthodromic conduction was ~1.26 times faster while the propagation velocity of bAPs was ~1.47 times faster in human dendrites compared to rats.

Different voltage-dependent ion channels play an important role in the propagation of electrical signals. Previous work has already shown that there are significant differences in the density of HCN channels between rodents and humans. Kalmbach and colleagues predicted from their modelling experiments that eliminating the conductance of HCN channels increases the delay in the propagation of synaptic signals into the cell body. But do their differences between the two species explain the differences in dendritic conduction velocity we observed? To answer this question, we performed experiments using specific blockade of HCN channels. After 10 min of recording a control, 20 µM ZD7288 was washed onto the cell and the propagation velocity of bAPs was measured for a further 20-30 min. Based on our experiments, blocking HCN channels led to a slight decrease in dendritic conduction velocity in both species (rat: control: 0.163 ± 0.054 m/s, ZD7288: 0.149 ± 0.057 m/s, n = 9, paired sample t test: P = 0.062) and this change was found to be statistically significant in human pyramidal cells (control: 0.322 ± 0.073 m/s, ZD7288: 0.268 ± 0.066 m/s, n = 8, paired sample t test: P = 0.022). The more significant change in human cells in response to the deactivation of the conductance of HCN channels is in agreement with the results of Kalmbach et al. In human neocortical layer II/III pyramidal cells, more HCN channels are found than in rodent cells, so their inhibition should have a more prominent effect on electrophysiological properties. In our case, we found a significantly greater reduction in propagation speed in human apical dendrites after blocking HCN channels compared to the rat (rat: -0.014 ± 0.019 m/s, human: -0.054 ± 0.052 m/s, two-sample t test: P = 0.048). Nevertheless, it can be stated that the differences in HCN channel properties observed between the two species are not sufficient in themselves to produce the higher conduction velocity characteristic of human cells, since human cells were still characterized by faster conduction velocities after channel blockage.

It is possible that differences similar to HCN channels may also exist between the two species for other voltage-dependent channels. Voltage-dependent Na+ channels play an important role in the propagation of bAPs. The question arises, could differences in voltage-dependent channels involved in the generation of dendritic regenerative events be responsible for the higher conduction velocity in human cells? To answer this question, further pharmacological experiments were performed. In our simultaneous somato-dendritic recordings, after recording a 10 min control, we perfused the slices with aCSF containing 1 µM TTX, 200 µM CdCl2, and 20 µM AP5 to block voltage-dependent Na, Ca, and NMDA channels. This resulted in a near passive state of the dendrites, so that the propagation of bAPs was determined by the cable properties of the

dendrites. Blocking voltage-dependent channels in both rat and human pyramidal cells significantly reduced dendritic conduction velocity (rat control: 0.199 ± 0.053 m/s, rat TTX/CdCl2/AP5: 0.076 ± 0.03 m/s, paired sample t test: P = 2.099 × 10-5, human control: 0.395 ± 0.14 m/s, human TTX/CdCl2/AP5: 0.184 ± 0.061 m/s, Wilcoxon test: P = 0.016).

On dendrites brought to a "passive" state by this pharmacological method, it was still observed that the signals travel significantly faster along the human cell dendrites compared to the rat ones (rat: 0.076 ± 0.03 m/s, n = 8, human: 0.184 ± 0.061 m/s, n = 8, Mann-Whitney test: P = 0.001).

By these results, we conclude that the difference between the two species can be better understood by further investigation of passive parameters.

Specific membrane capacity of human and rat pyramidal cells

Based on our paired recordings and simultaneous somato-dendritic measurements, we can therefore conclude that excitation can travel faster in human pyramidal cells and that the difference between the two species is not due to species-specific characteristics of voltage-dependent ion channels. If we think of dendrites as passive cables, there are two basic parameters that can affect the speed at which electrical signals propagate. The capacitance of the cell membrane and the axial resistance of the process.

Since there are conflicting results in the literature regarding the specific membrane capacitance of human and rodent cells, we felt it necessary to perform our own measurements. Nucleated patches were pulled from layer II/III pyramidal cells, and using the surface area and capacitance values of these membranes, we calculated the specific membrane capacitance (Cm).

No difference in Cm was found between the two species (rat: n = 20, 1.092 ± 0.14 µF/cm2, human: n = 19, 0.987 ± 0.196 µF/cm2, two-sample t test: P = 0.0615). The specific membrane capacitance is determined by the dielectric constant of the membrane and the thickness of the insulator separating the two charged compartments, and consequently the thickness of the membrane. The thickness of the cell membrane can be measured experimentally. To confirm our electrophysiological measurements, we investigated whether there is a difference in cell membrane thickness between the two species using transmission electron microscopy. If the cell membrane is thicker, this causes a decrease in its capacitance, as the electromagnetic interaction created by

ions on the opposite side of the membrane is significantly reduced. In our electron micrographs, we measured the membrane thickness of structures that could be clearly attached to a dendrite. No difference in cell membrane thickness was found between the two species (rat: n = 3, ROI n = 151, 4.122 ± 0.779 nm, human: n = 3, ROI n = 213, 4.271 ± 0.873 nm, Mann-Whitney test: P = 0.212). Our electrophysiological results were therefore supported by an independent method.

This suggests that the difference in the conduction velocity of cells from different species is not due to specific membrane capacitance.

Thickness of the dendrites

The conduction velocity of a dendrite may depend on its axial resistance. Axial resistance can be influenced by two parameters: the composition of the cytoplasm and the thickness of the structure. Since we dialyzed the cells through the somatic electrode, thus introducing the fluorescent tracer into the intracellular space, any differences in cytoplasmic composition were significantly reduced. As a consequence, we hypothesized that the axial resistance of the dendrite sections was predominantly determined by the thickness of the branch between the measurement points. We took Z-directional serial images of the measured dendrite sections using a 2-photon microscope. The resulting images were used to reconstruct the measured dendrites, whose thickness was measured. The average dendritic thickness between the cell body and the dendritic recording site was determined for each measured cell. The dendritic thickness (average diameter of the structure) was significantly greater in human samples than in the rat samples (human: n = 62, 2.272 ± 0.584 µm; rat: n = 46, 2.032 ± 0.413 µm, two-sample t test: P = 0.019). We observed a positive correlation between the dendritic thickness and conduction velocity in both rat and human cells.

All this suggests that the ability of human cortical pyramidal cells to conduct stimuli faster through dendrites may be due to the simple biophysical property of thicker neuronal processes with lower axial resistance, and to the higher expression of HCN channels in the dendrite. Exploring the causal relationship between dendrite thickness and conduction velocity is difficult to investigate experimentally, as it would require an intervention in the measurements that changes the dendritic diameter but has no effect on the basic physiological parameters of the cell. Since this is technically almost impossible, we have tried to explore the hypothesized causal relationship by exploiting the possibilities offered by modelling.

Effect of dendrite thickness on signal propagation speed in a model

To investigate the effect of dendrite thickness on conduction velocity, a relatively simple model was constructed in which the cell body was an isoelectric sphere and the dendrite and axon by a cylinder of constant diameter in each longitudinal direction. We placed different voltage-dependent channels in the axon and dendrite, and the distribution of these channels in the model reproduced many of the physiological features of a cortical neuron.

In the model, we examined how dendrites function in the passive state and when they have active conductances. During the simulation, the various parameters were kept fixed, only the thickness of the dendrites was varied, the delay measured at the peak of the back-propagating APs.

This relatively simple model proved suitable for exploring the causal relationship between dendritic thickness and signal propagaion velocity. Our results show that the conduction velocity in both passive and active dendrites increased proportionally with variation in dendritic diameter.

Discussion

It has long been known in neurobiology that the brains of different animals are made up of cells of different sizes. Even early EEG measurements showed that both sensory evoked responses and spontaneous oscillations in the cerebral cortex exhibit similar conserved temporal dynamics. The question has therefore long been raised: is the propagation of excitation faster in species with larger cells?

For our experiments, we chose the widely used rodent model (rat) and surgically removed human brain tissue to answer the question: is information flow really faster in microcircuits created by layer II/III pyramidal cells in the human cortex?

Using pairpaired patch clamp recordings, we show that monosynaptic communication between human cortical pyramidal cells is characterized by similar synaptic delays as between rat cells, but in humans the intersomatic distance the signal had to travel was on average 1.47 times longer. This implies that the stimulus has to travel faster through the cells of the human cortex. We then performed axonal and dendritic recordings to investigate which type of neuronal process might play a role in this phenomenon. To the best of our knowledge, we were the first to measure electrical signals from human axons, and thus the first to determine the conduction velocity of single axons within the range of the distance of local contacts. We found no significant difference in axonal conduction velocity between rat and human, and conclude that differences in dendritic properties may underlie the differences we observed in pairer recordings. Subsequently we used dendritic patch clamp recordings to determine the speed of propagation of electrical signals from the dendrite to the cell body and from the soma to the dendrite, and human dendrites conducted faster in both directions. Since we found a significant correlation between the velocities measured in the two directions, we performed our further pharmacological experiments by investigating the propagation of back propagating action potentials, as the elicitation and measurement of these signals is technically simpler. Our pharmacological studies suggest that higher HCN channel expression in human cortical pyramidal cells may contribute to faster signal propagation speeds, but this alone is not sufficient to explain the difference between the two species. After blocking dendritic voltage-dependent channels in passivated dendrites, it was also observed that electrical signals travel significantly faster through human dendrites. Therefore, we conclude that there may be differences in the parameters determining the passive cable properties of the dendrites in the

two species. First, we examined the specific membrane capacitance of the cells and found no significant difference between the two species. This was confirmed by an independent method, electron microscopy of the membrane thickness, as our measurements showed no significant difference in membrane thickness between the two species. However, we found a significant difference in the thickness of the dendrites, which strongly influenced axial resistance. The human cortical cells having thicker dendrites than those of the rodent, and a significant positive correlation between the average diameter of the dendrites and their conduction velocity was observed. To explore the causality of our latter observation, we conducted modelling experiments showing that increasing the dendritic thickness alone, while holding other parameters in the model fixed, also increased conduction velocity.

In summary, we have shown that information propagation velocity in the recurrent excitatory network of human cortical layer II/III pyramidal cells is higher than in rodents, and that this is due to dendritic properties such as higher HCN channel expression and larger dendritic diameter, which is typical of human neurons. These processes may therefore underlie our ability to process stimuli from the outside world at similar speeds to other species around us, despite the fact that the cells that make up our brains are significantly larger, allowing them to make more connections and perform more complex computations.

Puplications

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*: co-first author

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