deviations in the interpretation and organization of speech. In a number of studies, failures in linguistic processing have been demonstrated at the levels of semantic, syntactic and discourse structure. Schizophrenia, a condition which apparently occurs in all societies with approximately the same incidence, may best be understood as an anomaly of the function which is most characteristically human – language.

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How should brain nuclei be delineated? They don’t need to be!

Gahr reviewed three common methods to delineate brain areas in tissue sections: the cytoarchitectural, the connectional and cytochemical delineation. He focused on the HVC (higher vocal center) nucleus of songbirds. He showed that the cytoarchitectural, cytochemical and projection properties of the same HVC brain area change independently both during development and in adulthood, and concluded that a combination of the three delineation methods may give new insights into neural plasticity and the dynamics of brain parcelization in general.

Insight into neural plasticity, however, does not depend on delineation of brain areas, but on estimation of total neuron numbers and glial cells. Total cell numbers of any brain nucleus with circumspect boundaries can be easily determined by multiplying the mean neuronal density with the volume of the nucleus. The volume can be estimated by Cavalieri's principle: multiply the sum of the cross-sections of equidistant sections throughout the whole extent of the nucleus with the intersection distance. When more than ten sections are investigated and more than 100 cells are sampled the coefficient of error of the volume is less than 5%, which is negligible to the coefficient of variation of the group mean. Unfortunately, in Gahr's review no statement on total neuron number or total volume of the HVC nucleus has (or could have been) made.

Delineation of brain structures with indistinct boundaries, however, such as the human basal nucleus of Meynert is impossible and, consequently, so is the volume, but total neuron numbers can still be estimated in normal controls and in disease by using a systematic sampling design also known as the fractionator. Again, the coefficient of error of the estimate is below 5% (Refs 10, 11).

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LETTERS TO THE EDITOR

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on observations made on two-dimensional tissue sections. This integrated set of precise tools is called stereology and may measure volume, area, length and number of arbitrarily shaped, sized and orientated particles in an efficient and unbiased manner. 'Particles' means anything that can be unambiguously identified from the set of profiles produced by a section through them, for example, fibers, somata, nuclei, nucleoli, synapses, receptors. 'Efficient' means 'with a low variability after spending a moderate amount of time' and 'unbiased' means 'without systematic deviation of the true value'. When, as in the cytoarchitectural Nissl delineation of the HVC nucleus, the boundaries are defined on a fluctuating cell-size criterion, one may not interpret this phenomenon as 'dynamics of brain parcellation'. Instead, one should stop delineating, as the self-evident requirement of unambiguous identification of the cells of interest is not fulfilled any longer.

Gahr states that the borders of brain nuclear should be delineated using a combination of different methods, since different methods might provide a different judgment of where the borders of a nucleus lie. Although we are in agreement with this basic thesis, we disagree strongly with Gahr's claim that delineation of the telencephalic nucleus HVC (higher vocal center) in songbirds changes depending on whether cytoarchitectural, cytochemical or projection properties of HVC neurons are used as the criterion for judging the borders of this nucleus. We and others have demonstrated that HVC clearly changes volume as a function of season or hormone treatment, regardless of whether the borders of HVC are judged by the distribution of Nissl-stained neurons, estrogen- or androgen-accumulating cells, neuropeptide expression, neurotransmitter enzymes and receptors, or projection neurons within HVC (Refs 2-8). Thus, although Gahr stresses that Nissl staining can give a different picture of the borders of HVC relative to these other methods based on his own work, he does not cite the numerous studies that have failed to replicate this result.

Although the borders of HVC are apparently not different for different staining criteria, the borders of another song-control nucleus are. Once again, however, relevant papers are not cited by Gahr. Thalamic inputs to the telencephalic song-control nucleus IMAN (lateral magnocellular nucleus of the anterior neostriatum) define a region different from what we (and others) had originally delineated as the borders of this nucleus based on Nissl criteria. However, the original finding that IMAN undergoes substantial regression was supported by the demonstration that

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