



# Comparison of bonobo and chimpanzee brain microstructure reveals differences in socio-emotional circuits

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## Abstract

Despite being closely related, bonobos and chimpanzees exhibit several behavioral differences. For instance, studies indicate that chimpanzees are more aggressive, territorial, and risk-taking, while bonobos exhibit greater social tolerance and higher rates of socio-sexual interactions. To elucidate the potential neuroanatomical variation that accompanies these differences, we examined the microstructure of selected brain areas by quantifying the neuropil fraction, a measure of the relative tissue area occupied by structural elements of connectivity (e.g., dendrites, axons, and synapses) versus cell bodies. In bonobos and chimpanzees, we compared neuropil fractions in the nucleus accumbens (NAc; core and shell), amygdala (whole, accessory basal, basal, central and lateral nuclei), anterior cingulate cortex (ACC; dorsal and subgenual), anterior insular cortex (AIC), and primary motor cortex (M1). In the dorsal ACC and frontoinsular cortex (FI) we also quantified numbers of von Economo neurons (VENs), a unique subset of neurons thought to be involved in rapid information processing during social interactions. We predicted that the neuropil fraction and number of VENs in brain regions associated with socio-emotional processing would be higher in bonobos. In support of this hypothesis, we found that bonobos had significantly greater neuropil in the central and accessory basal nuclei of the amygdala, as well as layers V–VI of the subgenual ACC. However, we did not find a difference in the numbers of VENs between the two species. These findings support the conclusion that bonobo and chimpanzee brains differ in the anatomical organization of socio-emotional systems that may reflect species-specific variation in behavior.

**Keywords** Microstructure · Neuropil · Amygdala · Social cognition · Bonobo · Chimpanzee · Von Economo neurons

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## Introduction

Bonobos (*Pan paniscus*) and chimpanzees (*Pan troglodytes*) are African great apes and the closest living relatives of humans. Despite their close genetic relatedness to each other (estimated divergence 1–2 million years ago) and striking phenotypic similarities, it has become increasingly clear that bonobos and chimpanzees exhibit several behavioral differences. Bonobos, like chimpanzees, live in fission–fusion societies where females are the dispersing sex (Goodall 1986; Boesch and Boesch-Acherman 2000; Furuichi 2011). Unlike chimpanzees, however, where males are dominant to females (Goodall 1986; Boesch and Boesch-Acherman 2000), in bonobos there is partial female dominance (Furuichi 1997; Vervaecke et al. 2000; Stevens et al. 2007). Furthermore, some have reported that adult chimpanzees engage in more severe aggression, are more risk-taking, and less socially tolerant toward non-group members relative to

bonobos (Goodall 1986; Hare et al. 2007; Haun et al. 2011; Wilson et al. 2014; Tan and Hare 2013). Bonobos, on the other hand, are neophilic, risk-averse (Herrmann et al. 2011; Haun et al. 2011; Rosati and Hare 2012a, b) and show significantly higher levels of adult social play and socio-sexual behaviors compared to chimpanzees (Palagi and Cordoni 2012; Woods and Hare 2011; Wrangham 1993). Bonobos also outperform chimpanzees on tasks related to their sensitivity in responding to socio-communicative cues and theory of mind, whereas chimpanzees perform better on physical cognition tasks (Herrmann et al. 2010; Hopkins et al. 2017).

Studies have examined the proximate mechanisms underlying the reported behavioral variation between bonobos and chimpanzees by identifying species differences in hormone levels (Wobber et al. 2013; Behringer et al. 2014), neurotransmitter systems, neuropeptides and their receptor genes (Donaldson et al. 2008; Hopkins et al. 2012; Staes et al. 2014; Stimpson et al. 2015), as well as neuroanatomy (Rilling and Insel 1999; Schenker et al. 2005; Hopkins et al. 2009, 2017). For example, bonobos and chimpanzees show differences in the timing of urinary thyroid hormone levels during development that may be linked to the distinct ontogenetic changes found between the two species, and potentially reflect the lower intensity of aggression found in bonobos (Behringer et al. 2014). Chimpanzees show a deletion in the gene coding for the vasopressin receptor 1A, which may be associated with lower levels of sociability and sensitivity to socio-communicative cues compared to bonobos (Staes et al. 2015, 2016; Hopkins et al. 2012, 2017). Bonobo brains have a higher density of serotonin transporter-immunoreactive axons in the amygdala, particularly in the basal and central nuclei, potentially modulating a variety of behavioral responses to stimuli that elicit emotional arousal (Stimpson et al. 2015; LeDoux 2007). Studies comparing brain anatomy have also revealed differences between chimpanzees and bonobos in neural systems supporting social cognition. Relative to chimpanzees, bonobos have larger volumes of the anterior insula, fronto-insular cortex, and lateral nucleus of the amygdala (Bauernfeind et al. 2013; Barger et al. 2007). Coupled with species differences in risk aversion (Haun et al. 2011; Rosati and Hare 2012a, b), novelty avoidance (Herrmann et al. 2011), social sensitivity (Herrmann et al. 2010) and severe aggression (Wilson et al. 2014), these findings point to overall differences in (socio-) emotional control between bonobos and chimpanzees.

To determine further if the organization of brain regions involved in social cognition and emotion differ between bonobos and chimpanzees, in this study we examined neuroanatomical variation by comparing neuronal architecture and distribution in histological sections at the microstructural level. One quantitative approach that has been used in previous studies is to measure the proportion of neuropil space in the gray matter from histological sections (Schenker

et al. 2008; Spocter et al. 2012). The neuropil is defined as the space between neuronal and glial cell bodies, which is comprised by dendrites, axons, synapses, and microvasculature. Therefore, it provides a measure of connectivity within a region. Microstructural indicators of connectivity have been shown to vary in association with disorders that impact social cognition and affect (Dajani and Uddin 2016; Courchesne and Pierce 2005; Alexander-Bloch et al. 2010; Casanova et al. 2002, 2006). Accordingly, quantification of neuropil space may give insight into species differences in the brain regions supporting these behaviors.

A second approach is to focus on total numbers of specific neuron types. For example, studies have examined von Economo neurons (VENs), which are large bipolar projection neurons located in the fronto-insular cortex (FI) and anterior cingulate cortex (ACC) (Allman et al. 2010). In humans, VENs are hypothesized to be involved in processing networks associated with empathy, social awareness, and self-control (Allman et al. 2005; Kim et al. 2011; Senatorov et al. 2014). Across primates, VENs have been identified in humans, great apes, and macaques (Allman et al. 2010; Evrard et al. 2012; Stimpson et al. 2011), with the greatest densities in humans and African great apes (Nimchinsky et al. 1999). Based on available data, it may be speculated that greater numbers of VENs are associated with specializations for social cognition within and between species (Watson et al. 2006; Butti et al. 2009). For example, quantification of VENs in small samples of captive orangutan brains has revealed the highest numbers in female Sumatran orangutans (*Pongo abelii*) compared to Sumatran males and Bornean males and females (Allman et al. 2010). Given that within orangutans, in the wild females represent the philopatric sex (Singleton and Van Schaik 2002) and are more gregarious with more spatial overlap in Sumatra (Galdikas 1985; Wich et al. 2004; Delgado and van Schaik 2000, 1999), it is possible that variation in numbers of VENs is related to these different levels of sociability. In humans, lower VEN counts are linked to diseases that involve impairments to emotional expression and social cognition, including the behavioral variant of frontotemporal dementia (Kim et al. 2011), agenesis of the corpus callosum (Kaufman et al. 2008), autism spectrum disorder (Butti et al. 2013; Santos et al. 2011), and early-onset schizophrenia (Brüne et al. 2010).

The goals of the present study were to test the hypothesis that bonobos and chimpanzees differ in microstructure of brain regions supporting socio-emotional function, by measuring neuropil fraction, and to test whether bonobos have higher numbers of VENs than chimpanzees. The neuropil fraction was determined for the anterior cingulate cortex (ACC; dorsal and subgenual), anterior insular cortex (AIC) and amygdala (whole and accessory, basal, central and lateral nuclei), as these regions are implicated in empathy, anxiety, and affect (Devinsky et al. 1995; Gu et al. 2013;

Lovero et al. 2009; Davis 1992). We subdivided the ACC because a number of fMRI studies have found that the dorsal and subgenual components are differentially activated during cognitively demanding and affective tasks, respectively (Margulies et al. 2007; Gray and Braver 2002; Holroyd et al. 2004). We hypothesized that a higher neuropil fraction in bonobos would be found in the subgenual compared to the dorsal ACC. We also analyzed the nucleus accumbens (NAc; whole, core, and shell). The NAc, as a whole, is a central generator of motivated behaviors (for review see Floresco 2015). The core of the NAc is most associated with risk-taking (Knutson et al. 2001), whereas the shell is more involved with behavioral control, spatial learning, and memory (Barrot et al. 2002; Ito et al. 2008; Heysieattalab et al. 2016; Kerfoot and Williams 2018). Given the reported species differences, with greater risk-taking and the spatial memory abilities of chimpanzees (Haun et al. 2011; Menzel 1973; Rosati and Hare 2012a, b, but see; Herrmann et al. 2010), we predicted that bonobos might have a higher neuropil fraction in the NAc core, while chimpanzees would have relatively greater neuropil in the NAc shell. The primary motor cortex (M1) and the putamen were also included in the current analysis as they are principally involved in motor control, which is not thought to differ considerably between these two species (Marchand et al. 2008; Graziano 2005; Holdefer and Miller 2002). VENs were quantified in both the ACC and FI.

## Materials and methods

### Subjects

This study compared postmortem brain samples from 7 bonobos (*Pan paniscus*) and 7 chimpanzees (*Pan troglodytes*) that were age and sex matched (see Table S1). Brains were collected opportunistically after necropsy from apes that died of natural causes at various zoos and research facilities. For some chimpanzees, sections were not available for all brain regions; therefore, data from brain regions of a total of 14 individuals (6 females: mean age at death = 28.3 years; standard deviation (SD) 12.5; range 12–45, and 8 males: mean age at death 20.4 years; SD 5.3; range 11–28) were included to compare to the 7 bonobos (3 females: mean age at death = 29.9 years; SD 16.4; range 12–52, and 4 males: mean age at death = 19.7 years; SD 11.0; range 4–34).

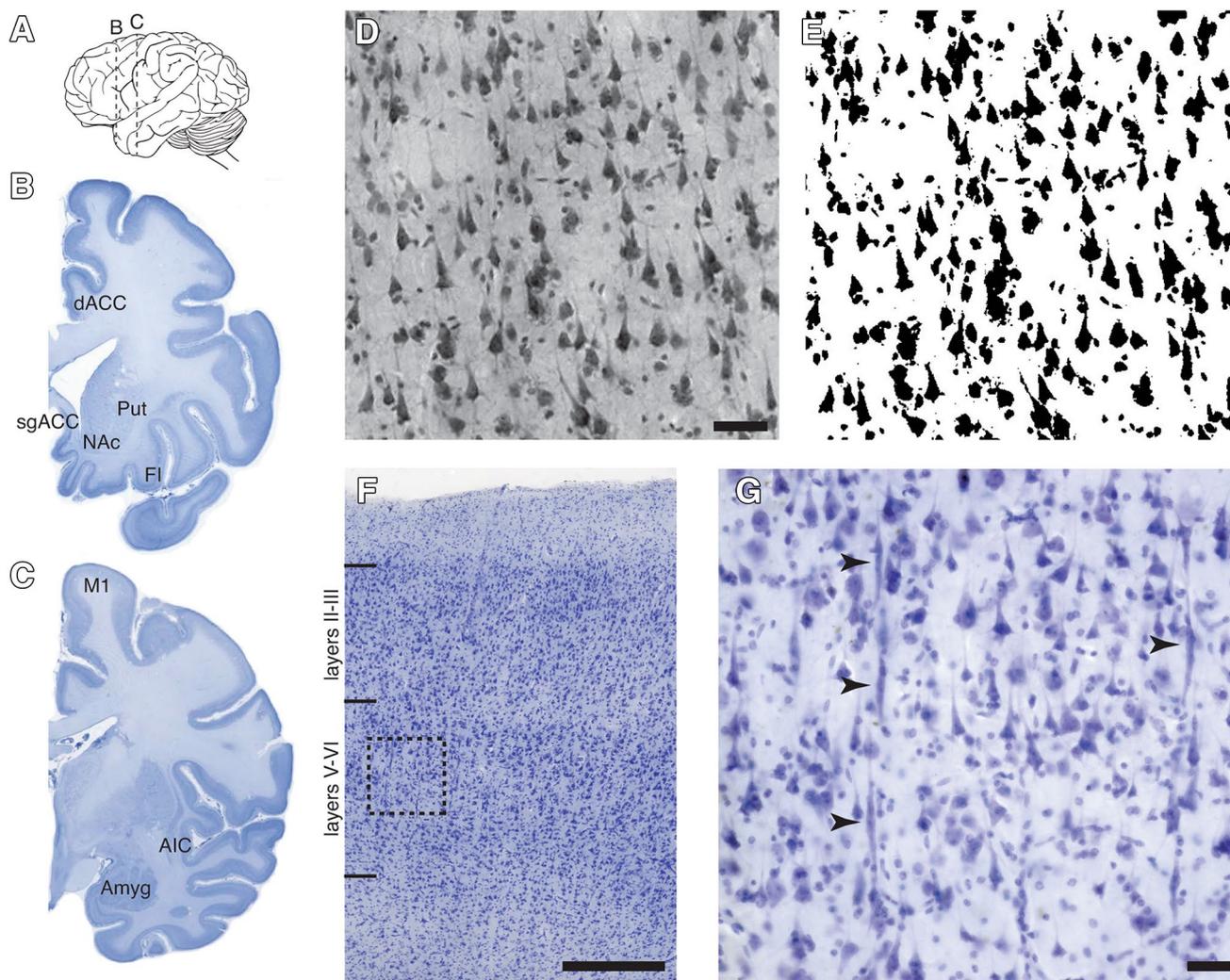
### Tissue preparation and Nissl stain

All brains were obtained after death and immersion fixed in 10% formalin within a 14-h postmortem interval. Brain hemispheres were blocked into three large slabs coronally and cryoprotected by immersion in graded sucrose solutions (up to 30%) in PBS, pH 7.4. Tissue blocks were frozen

on dry ice, and sectioned at 40  $\mu\text{m}$  on a freezing sliding microtome, with the exception of one bonobo brain that had been sectioned at 100  $\mu\text{m}$  thickness. From these blocks, adjacent sections were collected for histological staining and stored in anatomical order. Every 10th section (spaced 400  $\mu\text{m}$  apart) from each block was mounted on chromalum-subbed slides, stained using 0.5% cresyl violet to visualize cytoarchitecture, and coverslipped with DPX. For this study, only the left hemisphere was analyzed, as right hemisphere samples were not available for all individuals. Therefore, our results should be interpreted with the understanding that hemispheric asymmetry in function has been reported for autonomic processing (for review see Craig 2005), although often such activity is complementary or bilateral with regard to socio-emotional processing (Duerden et al. 2013; Oberlin et al. 2015; Craig 2005).

### Neuropil fraction

Neuropil fraction was measured using high-resolution images of Nissl-stained sections. Imaging of the regions of interest was performed with a Zeiss Axioplan 2 photomicroscope (Zeiss, Thornwood, NY) equipped with a Ludl XY motorized stage (Ludl Electronics, Hawthorne, NY), Heidenhain z-axis encoder and an Optronics MicroFire color video camera coupled to a Dell PC using StereoInvestigator software (MBF Bioscience, Williston, VT). Area identification was based on published regional and cytoarchitectural definitions (Bauernfeind et al. 2013; LeDoux 2007; Paus 2001; Groenewegen et al. 1996; Fig. 1a). For each bonobo or chimpanzee brain, three evenly spaced coronal sections were sampled throughout the region of interest (Fig. 1b, c). For each section, regions of interest were contoured under low magnification (2.5 $\times$  objective lens) underneath a representative portion of the area (for cortical regions this was approximately 3 mm in length along the cortical surface). At least 30 systematic random sampled (SRS) images were taken within the contours of each section using a 20 $\times$  objective lens, resulting in images at 0.53 pixels/ $\mu\text{m}$  resolution (Fig. 1f). Each image was imported into Image J (v.1.32j) and subjected to background subtraction with a rolling ball radius of 50 pixels and then converted to binary by an automated threshold routine (Spocter et al. 2012) (Fig. 1g). Before calculation of the neuropil fraction, images that contained artifacts were removed from the batch and the remaining images were blind-coded to avoid observer bias. We considered the one bonobo brain that was sectioned at 100  $\mu\text{m}$  acceptable for inclusion in neuropil fraction analyses because it has been previously shown that values for imaging of cell profile areas in brain sections reach asymptote around 15  $\mu\text{m}$  (Wree et al. 1982). Furthermore, we ran all analyses both including and excluding this individual and it did not have an impact on the overall pattern of results.



**Fig. 1** **a** Lateral view of chimpanzee brain showing location of sections B and C. **b, c** Coronal sections showing regions in the study. **d** An image captured for neuropil fraction measurements from a chimpanzee M1 layers II–III. **e** The binarized output of image D. **f** Fronto-

insular cortex in a bonobo. The box indicates the location of higher magnification view of layer V in **g** arrowheads indicate VENs. Scale bars in **f** 1 mm, **d, g** 100  $\mu$ m

In cortical regions, layers II–III and V–VI were contoured separately. In addition to the whole amygdala, measurements from the accessory, basal, central and lateral nuclei were also collected using anatomical boundaries as previously described (Sah et al. 2003; Stimpson et al. 2015). The ACC was also subdivided into dorsal and subgenual components, which are separated by the corpus callosum (Allman et al. 2001). Finally, the nucleus accumbens was measured whole and subsequently subdivided into its ventromedial and dorsolateral components, which approximately correspond to the shell and core in primates (Friedman et al. 2002). An estimate of inter-rater reliability (IRR) was performed by a second rater retracing at least 3 slides per region of interest from 3 different regions to recalculate the neuropil fraction independently. IRR was calculated in R using the intraclass coefficient in a two-way mixed model measuring consistency. The IRR cutoff

was 0.70, and IRR across all regions was greater than 0.72. Additionally, an analysis of variance (ANOVA;  $\alpha = 0.05$ ) revealed no significant differences between raters.

### Von Economo neuron quantification

For each individual, every 10th section that spanned the region of interest was sampled. We examined FI and dorsal ACC. VENs were identified as having a spindle-like shape with a thin cell body giving rise to a single apical and basal dendrite extending in opposite directions. Since VENs are most dense in cortical layer V, only this layer was contoured in each section (see Fig. 1d, e). Within each contour, systematic random sampling (SRS) placement of counting frames was used to quantify neurons using the optical fractionator in StereoInvestigator (software version

11, MBF Bioscience, Wiliston, VT). To quantify VENs, a  $100 \times 100\text{-}\mu\text{m}$  counting frame was used with a  $320 \times 320\text{-}\mu\text{m}$  SRS grid. To quantify other layer V neurons, a  $40 \times 40\text{-}\mu\text{m}$  counting frame was used with a  $320 \times 320\text{-}\mu\text{m}$  SRS grid. A counting frame height of  $6\text{-}\mu\text{m}$  was used and mounted section thickness was measured at every 10th sampling site. Each type of neuron—VEN and “other neuron”—was quantified using a different marker. Glial cells were identified and excluded based on a combination of criteria, including smaller soma size and the absence of stained proximal neurites. The estimated population of total layer V neurons allowed for a calculation of the percentage of VENs within the regions of interest. The Gundersen coefficient of error was obtained for counts of both VENs and “other” neurons and the cutoff was set to 0.1 (Gundersen et al. 1999). A few cases of 0.11 and 0.12 were tolerated for VENs in the ACC due to the scarcity of these cells overall. All slides were blind-coded to avoid observer bias. To increase the sample size, data for two bonobo individuals were taken from Allman et al. 2010 and included in our analysis.

## Statistical analysis

We calculated statistical differences in neuropil fraction and VEN numbers between bonobos and chimpanzees using ANOVA models with the EZ ANOVA function of the R package EZ (version 3.3.3, R Core Team 2015). A repeated measures design took into account multiple measures across brain regions per individual. For analysis of neuropil fraction in cortical regions (AIC, dACC, sgACC, and M1) the overall

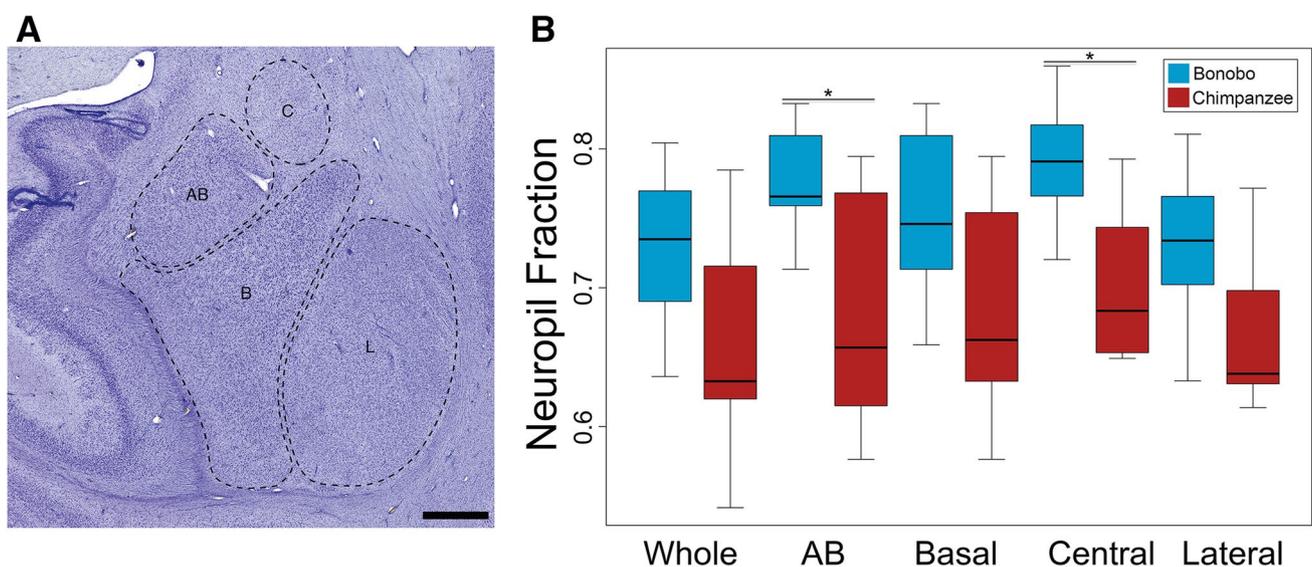
model tested for the effects of region, species, sex and layers (layers II–III versus layers V–VI) and all interactions. If there was a significant interaction effect of species by region, simplified models were run per region to determine those that differed. The follow-up models included species, sex and layers and all two-way and three-way interaction terms. Given the relatively small sample size in relation to the complexity of these models, we reran models excluding sex or layers when they showed no significant main effects or interactions. For subcortical regions (NAc and putamen) the overall model tested for the effects of species, sex and region and all interactions between these terms. If a species by region interaction was significant, follow-up models were analyzed per region including species and sex as factors and their interactions. The amygdala was tested separately from cortical and other subcortical regions and separate models were run for total amygdala and its separate nuclei, testing the effects of species and sex and the interaction between the two. Finally, ANOVA models were analyzed for VEN numbers and percentages in dACC and FI testing for effects of species and sex.

## Results

### Neuropil fraction

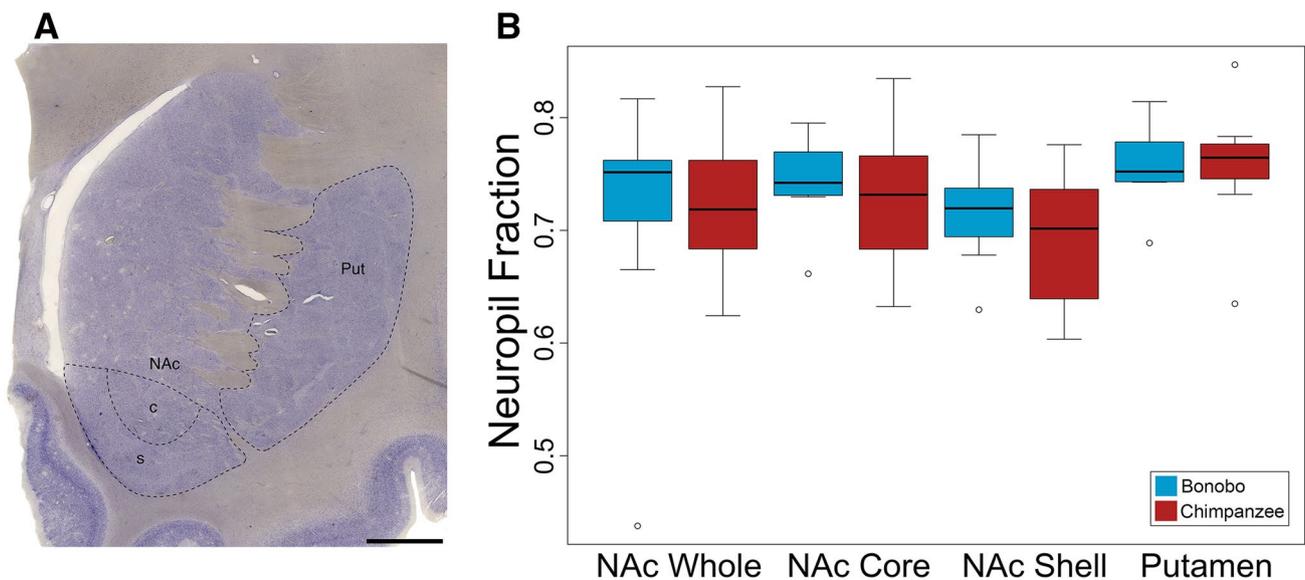
#### Subcortical regions

Significant species differences in neuropil fraction were found in certain nuclei of the amygdala (Fig. 2). Specifically,



**Fig. 2** Amygdala neuropil fraction. **a** Photomicrograph showing amygdala nuclei. *C* central, *AB* accessory basal, *B* basal, *L* lateral. Scale bar = 1 mm. **b** Neuropil fraction results are shown in the whole amygdala as well as its separate nuclei in bonobo (blue) and chim-

panzee (red). Bars indicate the interquartile range, whiskers represent range and horizontal lines represent the median. Significant effects are indicated by an asterisk



**Fig. 3** Basal ganglia neuropil fraction. **(A)** Photomicrograph showing basal ganglia. *Put* putamen, *NAc* nucleus accumbens, *c* core, *s* shell. Scale bar = 2 mm. **(B)** Neuropil fractions for the whole, core and shell

of the NAc in bonobos (blue) and chimpanzees (red) and the putamen. Bars indicate the interquartile range, whiskers represent range and horizontal lines represent the median. Open dots signal outliers

bonobos had significantly more neuropil than chimpanzees in the central ( $F(1, 11) = 7.82, p = 0.017$ ) and accessory basal ( $F(1, 11) = 5.22, p = 0.043$ ) nuclei. Bonobos also had higher neuropil fraction in the lateral ( $F(1, 12) = 3.44, p = 0.088$ ) and basal nuclei ( $F(1, 12) = 3.05, p = 0.106$ ) as well as the whole amygdala, ( $F(1, 12) = 2.78, p = 0.123$ ), though none of these results reached conventional levels of statistical significance. No significant species or interaction effects were found for neuropil fraction differences in any of the other subcortical regions that were tested (whole NAc:  $F(1, 12) = 0.09, p = 0.769$ ; NAc shell:  $F(1, 12) = 0.586, p = 0.459$ ; NAc core:  $F(1, 12) = 0.209, p = 0.656$ ; putamen:  $F(1, 12) = 0.00, p = 0.971$ ) (Fig. 3). No significant sex differences were found (Table S2).

### Cortical regions

The overall model for the cerebral cortex revealed a significant three-way interaction between region, species and layer ( $F(3,40) = 5.24, p = 0.004$ ). Follow-up analyses within each region revealed a significant species by layer interaction for sgACC ( $F(1, 10) = 7.52, p = 0.021$ ) and M1 ( $F(1, 10) = 8.38, p = 0.016$ ) (Fig. 4). In sgACC, there was relatively greater neuropil in layers V–VI of bonobos, whereas in chimpanzee layers V–VI had comparatively less neuropil than layers II–III. Conversely, in M1, chimpanzees had more neuropil in layers V–VI than layers II–III. No significant species or interaction effects were found in any of the other regions (Table S3). No significant sex differences were found.

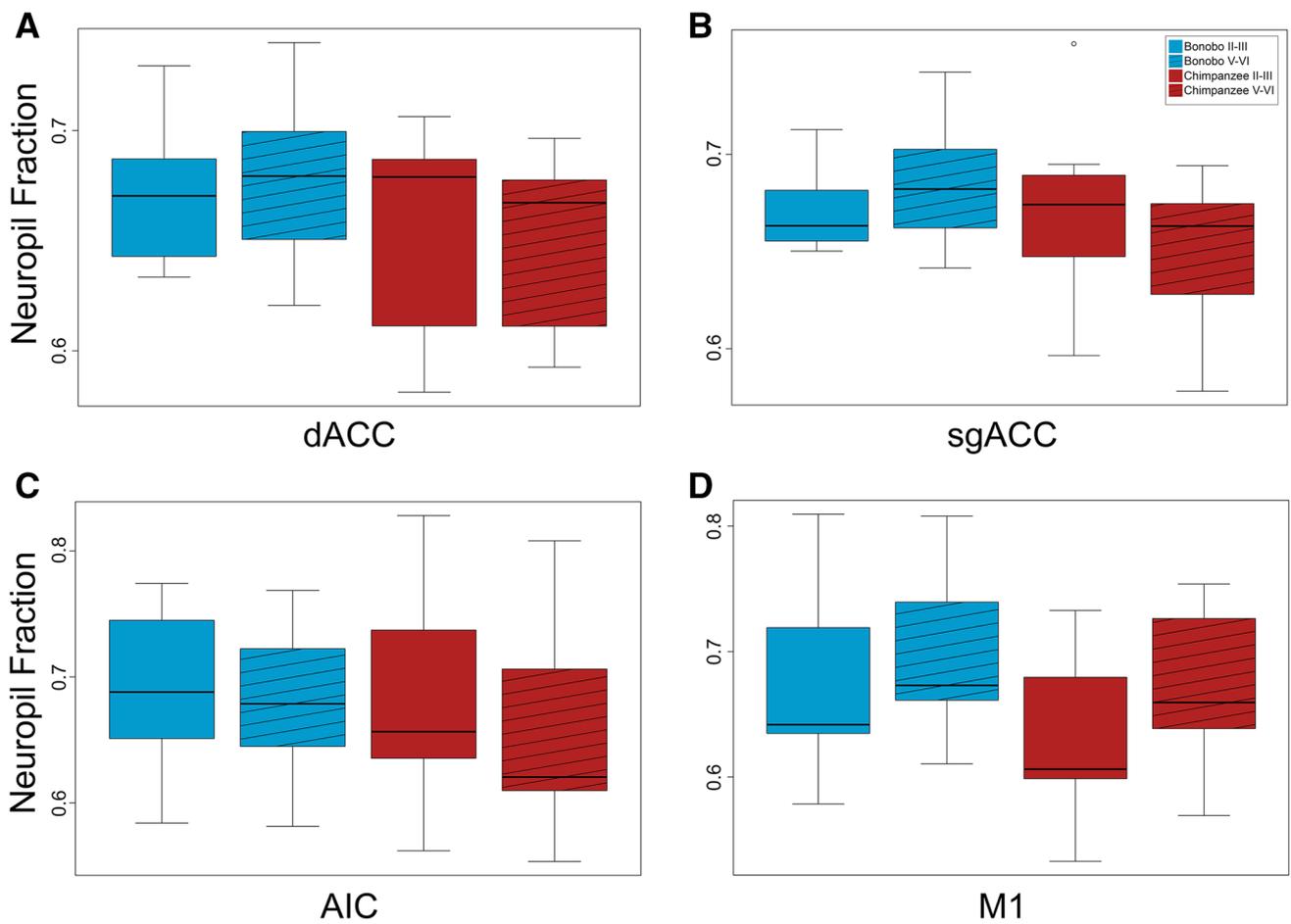
### Von Economo neurons

The total number of VENs did not differ significantly between species (ACC:  $F(1,11) = 0.11, p = 0.743$ ; FI:  $F(1, 17) = 0.03, p = 0.857$ ) (Fig. 5a). No significant sex differences were found (Table S4). The percentage of VENs also did not differ significantly between bonobos and chimpanzees in any of the regions sampled (ACC:  $F(1,10) = 3.13, p = 0.107$ ; FI:  $F(1, 11) = 2.24, p = 0.163$ ) (Fig. 5b).

### Discussion

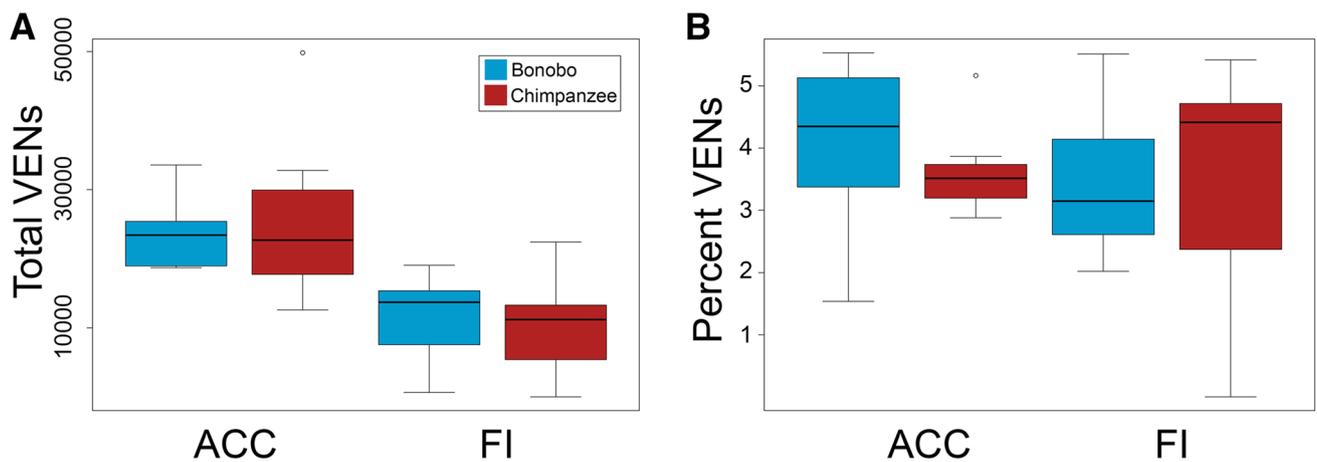
Our results show that, compared to chimpanzees, bonobos have significantly higher neuropil fractions in certain nuclei of the amygdala, as well as relatively greater neuropil in layers V–VI of sgACC. We did not find species differences in the total number or percentage of VENs.

The bonobo amygdala had more neuropil than chimpanzees in the central and accessory basal nuclei. It has been suggested that while the amygdala is involved in emotion generation and behavioral responses in a global sense (Aggleton 1992; Whalen et al. 1998), its individual components are highly functionally distinct (Savonenko et al. 1999; Saygin et al. 2011; Roozendaal and McGaugh 1997; Campbell-Smith et al. 2015; Butler et al. 2017). Central and accessory basal nuclei of the amygdala are involved in generating emotional, physiological, and behavioral responses to fear



**Fig. 4** Cortical neuropil fraction. Neuropil fraction for layers II–III followed by layers V–VI in bonobos (blue) and chimpanzees (red) in **a** the dorsal ACC, **b** subgenual ACC, **c** AIC and **d** M1. Bars indicate

the interquartile range, whiskers represent range and horizontal lines represent the median. Open dots signal outliers



**Fig. 5** Von Economo neurons in the ACC and FI. Both **a** total and **b** percentage of VENS were compared in bonobos (blue) and chimpanzees (red). Bars indicate the interquartile range, whiskers represent range and horizontal lines represent the median. Open dots signal outliers

and stress-inducing stimuli (LeDoux et al. 1988; Moga and Gray 1985; Pitkänen et al. 1997; Kalin et al. 2004). The central nucleus is considered the major output center of the amygdala (Yu et al. 2016; Han et al. 2017; for review see; Fadok et al. 2018). Patterns of intra-amygdaloid connections indicate that it integrates sensory and internal-state information primarily from basolateral nuclei (Hrybowski et al. 2016; for review see; Ledoux 2007), and reciprocal connections are found with areas such as the parabrachial nucleus, periaqueductal gray, and dorsomedial nucleus of the hypothalamus, suggesting an autonomic role involved in generating visceral and internal-state stress responses (Veenig et al. 1984; Moga and Gray 1985; Rizvi et al. 1991; Amaral and Price 1984). The accessory basal nucleus is an input center, providing information about internal states via projections from the hypothalamus (Pitkänen et al. 1997). The differences in neuropil of these particular amygdala nuclei are especially interesting since they may be associated with variation in sympathetic-autonomic activation related to the reported behavioral differences between these species (Herrmann et al. 2011; Rosati and Hare 2013).

We found no significant variation in neuropil fraction between bonobos and chimpanzees in the lateral and basal nuclei of the amygdala. Nevertheless, bonobos did have higher neuropil fractions in both these nuclei, with statistical differences that approached conventional levels of significance. The relatively small sample size available for the current study should be noted. The lateral nucleus is considered the major input center to the amygdala and is responsible for relaying sensory information from external stimuli (Romanski and LeDoux 1993; Turner and Herkenham 1991; for review see; LeDoux et al. 1990). Neurons in the basal nucleus project to brain regions outside the amygdala, with the responses generated by its connections to striatal areas resulting in active (e.g., running) rather than reactive (e.g., freezing) behaviors, which can oppose central nucleus function and decrease the likelihood of fear-based emotional arousal (Lázaro-Muñoz et al. 2010; Moscarello and LeDoux 2013; Ramirez et al. 2015). Previous studies examining species differences in bonobos and chimpanzees have found significant volumetric differences and variation in serotonergic innervation in these nuclei (Barger et al. 2007; Stimpson et al. 2015). Neuropil fraction, however, may be more reflective of the integrated interconnectivity within the amygdala, complicating precise one-to-one mapping of our results to the function of specific nuclei (LeDoux 2007; Aggleton and Mishkin 1986). For example, the accessory basal nucleus is thought to attenuate central nucleus responses to external stimuli based on internal states via projections to the lateral nucleus (Pitkänen et al. 2002). Thus, the trend for greater neuropil in the lateral nucleus of bonobos might be related to its participation in the overall network of connections among other nuclei of the amygdala, which also show increased neuropil in bonobos.

Recent studies on the functional heterogeneity of the ACC have found its dorsal and subgenual components are involved in “cognitive” versus “affective” information processing, respectively (Margulies et al. 2007; Gray and Braver 2002; Holroyd et al. 2004). While we did not predict species differences in the dorsal subdivision, we did hypothesize that differences would be evident in the sgACC. Interestingly, the greatest species difference was found in layers V–VI of the sgACC, where bonobos had relatively higher neuropil fraction than chimpanzees. Diffusion tensor imaging has previously shown that relative to chimpanzees, bonobos have a larger white matter tract connecting the sgACC to the amygdala (Rilling et al. 2012). Because only the sgACC is directly connected to the amygdala (Etkin et al. 2011; Koski and Paus 2000) and layers V–VI preferentially project to subcortical regions, our results provide further support for the conclusion that there are neural specializations in bonobos selectively localized to the pathway connecting ACC to the amygdala.

No significant species differences were found in the AIC, a region that also plays a role in regulating social emotion and communication (Seeley 2010; Nestor et al. 2003), as well as anxiety (Paulus and Stein 2006; Klumpp et al. 2012; Simmons et al. 2011). Given reported species differences in social affiliative and communication behaviors (Clay et al. 2015; Pollick and de Waal 2007; de Waal 1988; Wrangham 1993; Palagi and Cordoni 2012), we hypothesized that bonobos would also have higher neuropil fractions in this region, but this was not the case. In addition, the stereological quantification of VENs in the present study did not reveal significant differences between bonobos and chimpanzees in numbers or percentages of VENs in the ACC or FI (which is the anterior portion of AIC defined by the presence of VENs).

VENs are a unique subpopulation of cells, hypothesized to be involved in the rapid processing of social information (Allman et al. 2005, 2010). In the absence of an animal model and specific biomarkers, their function and connectivity has been difficult to study directly (Evrard et al. 2012). VENs were initially thought to be uniquely present in only humans and great apes (Nimchinsky et al. 1999; Allman et al. 2005), but have since been identified in elephants and cetaceans (Hakeem et al. 2009; Butti et al. 2009; Hof and Van der Gucht 2007) among several other mammalian species (Evrard et al. 2012; Butti et al. 2014; Raghanti et al. 2015). This has led to the suggestion that their occurrence may be due to convergent evolution for this neuronal phenotype in certain mammalian lineages with large brain sizes (Hof and Van der Gucht 2007). It is possible that they play a role in socio-emotional behaviors in some of the species where they are found (Allman et al. 2005). Interestingly, a comparison of these neurons in hominoids has found that humans have significantly higher proportions of VENs that

express the proteins ATF3 and IL4Ra than other ape species (Stimpson et al. 2011). Such neurochemical variation of VENs may be involved in social and emotional processing capabilities across primates (Nawa and Takei 2006; Dijkstra et al. 2018). It remains a possibility, therefore, that there are differences between bonobo and chimpanzee VENs in terms of gene or protein expression profiles. It should also be noted that due to limitations of tissue availability, our study only analyzed the left hemisphere. Thus, an additional possibility is that greater species differences may be present in the right hemisphere, which has significantly more VENs in humans and great ape species (Allman et al. 2010), consistent with sympathetic-autonomic asymmetry in function in ACC and FI for processing emotion (Wittling et al. 1998; Lorberbaum et al. 2002). In any case, a more comprehensive survey of the biochemical, gene expression, and developmental profile of these neurons in bonobos and chimpanzees is needed, since many of the current hypotheses surrounding VEN function rely only on data from neuronal morphology (Watson et al. 2006; Allman et al. 2005). It should be noted, however, that recent work has shown VEN expression of transcription factors and neurotransmitter-related genes indicative of subcortical projection and monoaminergic function respectively (Cobos and Seeley 2013; Dijkstra et al. 2018).

In the NAc, we observed no significant species difference, in the region as a whole, or in subdivisions (core and shell). The NAc is involved in a diverse range of functions including attention, risk–reward evaluation, and motor control (Mikhailova et al. 2016; Morrison et al. 2017; Cole and Robbins 1989; Groenewegen et al. 1996). While no major species differences in neuropil fraction were found in the NAc, other studies have reported interesting species-specific variation in this region in the expression of neuropeptides and their receptors that are known to play important roles in regulation of aggression, anxiety (Bosch and Neumann 2012; Neumann and Landgraf 2012), and affiliative behaviors (Campbell 2008; Bales and Carter 2003). For example, variation in oxytocin and vasopressin 1A receptor densities in the NAc have been shown to be associated with social affiliative behaviors in different species of voles (Ross et al. 2009; Keverne and Curley 2004), and interactions between oxytocin and dopamine in the NAc are crucial for pair bonding in female voles (Liu and Wang 2003). Previous studies have shown that bonobos and chimpanzees differ in the genes coding for the OXTR and AVPR1a (Staes et al. 2014), but to date receptor distribution patterns in these brain regions has not been investigated.

No significant species effect was observed in the putamen, which served as a subcortical control in our study. However, there was a significant species by layer effect in the primary motor cortex. Interestingly, chimpanzees had a relatively greater neuropil fraction in layers V–VI compared to layers II–III; this effect might be related to species

differences in performance on spatial and motor tasks. While captive bonobos demonstrate skilled tool use capability, only chimpanzees are known for frequent tool use in the wild (Gruber et al. 2010; Goodall 1986). Compared to bonobos, chimpanzees also perform better at tool use and spatial memory tasks (Rosati and Hare 2012a, b; Herrmann et al. 2010) and neuroimaging comparisons between species indicate relative expansion of regions such as M1, the cerebellum, and hippocampus in chimpanzees (Rilling et al. 2012; Hopkins et al. 2009).

In summary, our results demonstrate important differences between bonobos and chimpanzees in the microstructure of brain regions implicated in socio-emotional processing, with the most pronounced species differences found in the amygdala (Pitkänen et al. 1997; Veening et al. 1984). Consistent with previous studies, our results suggest that the amygdala is a major focal point of evolutionary differences in the brain underlying affective behaviors of bonobos and chimpanzees (Barger et al. 2007; Stimpson et al. 2015; Gruber and Clay 2016; Hopkins et al. 2017; Woods and Hare 2011). Further comparative studies between bonobos and chimpanzees concerning the neuromodulation, gene expression and cytoarchitecture of brain regions that regulate emotion will further our understanding of how social systems drive changes in primate brain evolution.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.

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