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7 *Canis familiaris* as model for non-invasive comparative neuroscience

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28 *Abstract:* There is ongoing need to identify and improve animal models of human behaviour and
29 biological underpinnings thereof. The domestic dog (*Canis familiaris*) is a promising model in
30 cognitive neuroscience. However, before it can contribute to advancements in such science in a
31 relevantly comparative, reliable, and valid manner, methodological questions warrant attention.
32 To base the research on rigorous foundations, we review non-invasive canine neuroscience
33 studies, primarily focusing on 1) variability across dogs and between dogs and humans in cranial
34 characteristics and 2) generalizability across dog and dog-human studies. Arguing not for
35 methodological uniformity but for *functional comparability* in study methods, experimental
36 design, and neural responses, we conclude that the dog may become an innovative and unique
37 model in comparative cognitive neuroscience, one that is complementary to traditional models.

38 **Animal models in comparative neuroscience**

39 Animal model research is grounded in the idea that animals share behavioural, physiological, and
40 other characteristics with humans. Benefits of such research include increased understanding of
41 phenomena that could not be directly studied in humans or without cross-species comparison. The
42 neuroscience of socio-cognition has been extended from traditional primate and rodent models to the
43 domestic dog – an alternative, complementary model that permits for non-invasive measurement of
44 behaviour and its neural correlates. There has been an upsurge in canine neuroscience studies,
45 necessitating establishment of methodological guidelines that ensure scientific rigor. To this end,
46 complementing available reviews that are heavily [1] or solely [2] focused on available fMRI findings
47 [1,2] from a conceptual perspective, we review the non-invasive canine neuroscience literature, focusing
48 on methodology and experimental design. Primarily guided by principles of comparative anatomy, we
49 highlight advantages of and remaining challenges of the dog as an animal model for comparative
50 cognitive neuroscience.

51 We begin with an overview of animal models of human behaviour, then narrow our focus into
52 neuroscience, leading to questions about the domestic dog as a model for comparative neuroscience.
53 Mainly focusing on non-invasive canine fMRI and EEG research, we reflect on such questions in light of
54 three main considerations. These centre on within- and between-species variability, in particular in cranial
55 characteristics, though are also varied in terms of the degree to which they potentiate (1) advantages and
56 disadvantages for the dog as an animal model and, in case of disadvantages, whether solutions (2) have or
57 (3) have not been developed to address those.

58 **Animal models for comparative cognitive neuroscience**

59 A goal of comparative research is to establish principles of **proximate and ultimate causation**
60 (see Glossary), via between-species comparisons and study of individual organisms. Animal models for
61 comparative cognitive science include avian [3–5] as well as rodent and primate models that have
62 emerged as primary models for comparative cognitive *neuroscience* [2]. Advantages of rodents include
63 feasibility of handling the animals under laboratory conditions; cost-efficiency; and utility in pre-clinical

64 and clinical studies [6]. Advantages of primates include similarity to humans in development,
65 neuroanatomy, physiology, and reproduction, as well as in cognition and social complexity and thus
66 suitability for studying a range of mental processes [7]. Yet, use of these models is increasingly
67 problematic for animal welfare and ethical reasons [8]. Conversely, the role of the domestic dog has been
68 becoming increasingly important, with research initially focused on informing treatment for human
69 medical diseases with laboratory dogs [e.g., 4] and more recently involving basic research on sensation,
70 perception, and socio-cognition with family dogs (Box 1). One reason for this increase in importance is
71 that dogs, having been encultured in human society, naturally exhibit *cooperativeness* and *trainability*,
72 *obviating need for fluid and/or food restriction as a motivational tool*. Thus, relative to other species,
73 preparation of the dog for an experiment is more similar to preparation of humans in terms of
74 corresponding physiological and social state and there is less limitation to generalizability of interaction
75 with experimenters and environmental (e.g., lighting and sound) and experimental stimuli [1].
76 *Cooperativeness and trainability also permit for non-invasive methods*; although techniques have been
77 developed for awake scanning of monkeys, pigeons, and rats [1], unlike these animals but like humans,
78 dogs do not need to be restrained (e.g., via surgically implanted posts [10]) but can be trained to hold still,
79 yielding more valid cross-species comparisons. Finally, given their evolutionary history and integration
80 with humans, dogs and humans exhibit a range of socio-cognitive skills that share key behavioural and
81 functional characteristics [11]. It is for ability to study these very skills and corresponding functions (Box
82 1) that the dog may be one of the best model species for study of human socio-cognition [2] in
83 *comparative* neuroscience [11].

84 Together, it stands to reason that the domestic dog is a suitable model for comparative neuroscience
85 and that the non-invasive methods of brain circuits, physiology, and behaviour used with the dog ideally
86 complement the invasive methods appropriate for studying molecules and cells used with traditional
87 models. In combination with over 20 years of canine ethological research [12] and capitalizing on
88 exciting possibilities of the species and non-invasive methods, there has been an increase in the number of

89 canine neuroscience studies, with an overwhelming majority conducted in the past 3 years. (Mostly fMRI
90 and EEG, although other methods have also been used [13]).

91 Basic standards for measures and methods include reliability and validity [14] and, in case of
92 comparative research, for them also to be *relevantly* comparative. Related pressing questions pertain to
93 the degree to which methods are comparable across dog-dog and dog-human studies as well as the degree
94 to which employed methods allow for comparability and generalizability across studies (Table 1, Key
95 Table); with the impetus behind such questions stemming from within- and between-species variability,
96 especially in cranial characteristics. Some of this variability presents advantages for the dog as a model
97 and some may be limiting. In the latter cases, methods to address limitations are either already being
98 developed and evaluated or are in need of development and evaluation.

99 **Differences that present advantages**

100 *Differences in skull formation and brain anatomy.* Across humans, variation in skull formation
101 and brain size is relatively trivial; the average female brain volume is 90% of the male [15] and the
102 average brain volume of a 7-11-year old child is 95% of the volume of a sex-matched adult [16].
103 Conversely, there are large differences across dogs in skull shape and size and brain anatomy. Canine
104 skull length ranges from 7 to 28 cms [17] (i.e., the shortest dog skull is 25% of the longest), making *Canis*
105 *familiaris* the species with most within-species morphological variation in this regard [18].

106 In addition to skull length, differences across **dolichocephalic**, **brachycephalic**, and
107 **mesaticephalic** dogs include dissimilarities in the craniofacial angle (angle between the **basilar axis** and
108 **hard palate**) [19], in neuroanatomy (e.g., in brachycephalic dogs the brain is rotated with respect to its
109 mediolateral axis) and the anatomy of the cerebral cortex [20], temporomandibular joint (i.e., jaw joint)
110 [21], and **cribriform plate** [22].

111 These differences across dogs *allow for examining the relation among brain structure, function,*
112 *and behaviour within the same species* and the effects of differences in skull- and brain-morphology on
113 neuro-socio-cognition. As the ≥ 400 documented breeds exhibit a variety of genetically fixed morphologic
114 traits that correspond to differences in behaviour, longevity, size, skull shape, and disease susceptibility

115 [20], better understanding of these was proposed to increase understanding of mammalian biological and
116 embryonic development [20]. Although, to date, the number of dog breeds involved in fMRI studies is
117 considerably lower, they include subjects from diverse breeds suggesting that there is no limitation (e.g.
118 in trainability) to between-breed comparisons.

119 In support of stated advantages, differences in dog skull shape are associated with differences in
120 brain organization, e.g., brachycephalic brains are relatively rounded and shortened in the anterior-
121 posterior plane, the brain pitched ventrally at the anterior pole, with a pronounced shift in the position of
122 the olfactory lobe [18] (see Box 2 for additional examples). Differences in skull shape are further
123 associated with differences in behaviour in that brachycephaly, relative to dolichocephaly, is associated
124 with increased ability to focus and rely on human gestures [23]. Conversely, less morphological
125 differences across individuals in other species, such as humans, are less (or not) suitable for addressing
126 these questions and are thus largely overlooked.

127 *Differences in experimental design: sample composition.* Compared to the human neuroscience
128 literature, there is significant overlap in groups of dogs across studies. This is due, in part, to challenges
129 (e.g., limited subject availability and need for extensive training) and, in part, to advantages that make the
130 dog a multi-experiment model (e.g., ability to re-measure dogs as they do not need to be euthanized after
131 participation). For example, in canine fMRI studies, 100% of the sample of [24] was included in [25], and
132 there was a 92% overlap in the samples of [25] and [26], and a 67% overlap in the samples of [25] and
133 [27], and all dogs in [28] came from one of these samples. Similarly, in EEG studies, there was a 100%
134 overlap in the samples of [29] and [30], and a 68% overlap in the samples of [31] and [32].

135 Awake fMRI testing necessitates that dogs are trained to get used to scanner coil; place their heads
136 in-between their paws [34,35,37–39] or on a chinrest [24–28,33,36,40], and hold this position until a
137 release signal and then while wearing canine ear muffs; get used to recordings of scanner noise and being
138 in a mock scanner; and to adhere to these procedures inside the scanner room and ultimately the scanner
139 [25,34]. Training is extensive and typically involves behavioural shaping, conditioning and social
140 learning (e.g., the “**Model/Rival**” training method [34]). Different training methods allow for different

141 lengths of time during which dogs are able to hold a position, which has implications for design. For
142 example, in some studies, consistent with human studies, dogs do not exit the scanner between runs
143 [34,35,37,39,41] whereas in others, they do [24–28,33,36,40]. Movement artefacts are also handled
144 differently: some authors, consistent with human studies, exclude scans with head translation >3mm or
145 rotation >1° [34–36]; whereas others exclude scans with >1% scan-to-scan signal change [24]; >0.1
146 fraction of outlier voxels in each volume or >1% scan-to-scan signal change, in combination with >1mm
147 scan-to-scan displacement [26–28,40,42], and yet others exclude runs with .10mm total displacement
148 [37,41]. As the size of the dog brain is roughly one-third of the human, arguably, a >3mm translation in
149 dogs would approximate an unacceptable >9mm in humans. However, in most studies where the human
150 criteria were used, translation did not exceed 1mm [34,43]. Additionally, it has been shown that changes
151 in the time course of fMRI data are decreased when correlations are examined long-distance but increased
152 when they are examined short-distance, indicating that absolute movement is less and relative movement
153 is more important when pre-processing the data [44]. Finally, depending on study design and research
154 group, dogs need anywhere from five sessions [34] to 18 months of training [25]. For comparison, human
155 adults do not receive training and human children as young as 6 years of age receive minimal (a one-,
156 maximum two-occasion, 30-60-minute familiarization with a mock-scanner and recordings of scanner
157 noise) or no training [45] (Table 1).

158 The overlap in groups of dogs included across studies also has advantages for examination of
159 reliability and validity of measures as it allows for assessment of *within-subject stability vs. change of*
160 *measures of neural function over time* and of *within-subject correspondence of neural correlates and*
161 *performance across social, cognitive, and affective paradigms*. This ability to examine psychometric
162 properties of measures is comparable to research with humans but not most other species, where animals
163 easily habituate or are euthanized following participation. Regarding *within-subject stability vs. change*
164 *over time*, although the reliability, including test-retest reliability, of neuroimaging [14] has, until
165 recently, been a relatively neglected area of research in human neuroscience, the overlap in groups of
166 dogs across canine studies presents a natural opportunity to attend to questions of psychometrics [46].

167 Regarding *within-subject correspondence of neural correlates and performance across paradigms*,
168 it is important that these exhibit convergence and divergence, where expected. Establishing
169 correspondence across different indices of phenomena of interest (e.g., social and cognitive indices of
170 self-regulation) but that these provide unique information about variables examined, is key to the
171 innovative dimensional frameworks that are currently championed (e.g., the Research Domain Criteria
172 [RDoC]; [47]).

173 **Differences that potentiate disadvantages but solutions are available**

174 *Within-species differences in skull formation and brain anatomy.* These within-species
175 variabilities (Figure 1) are relevant for normalization. In fMRI research, advantages of normalization are
176 that when a set of coordinates is referenced, the location to which those coordinates correspond is known
177 and that results can be: generalized to a larger population; compared across studies wherein the same
178 brain is used for normalization; and can be averaged across subjects for group-level analyses.
179 Disadvantages are that it reduces spatial resolution and increases probability of error in identification of
180 anatomical location.

181 Normalization requires a “standard” brain, i.e., template. In the adult human literature, the Montreal
182 Neurological Institute (MNI) template (MNI305) is commonly used (Table 1), which is based on
183 combination of 152 healthy adult MRI scans [48]. Given relatively little difference between adult and
184 child brains, the MNI-305 is suitable for use with children over age 6 years [49] and empirical studies
185 have generally followed suit, with some attempts at developing a child template for use with a wider
186 range of ages (e.g., from 2 weeks to 4.3 years [50] and 4.5 years through 19.5 years (on age increments of
187 6 months [51])). Conversely, at present, there is no widely-accepted and used dog template. Authors of
188 canine fMRI studies have addressed this issue by omitting group-level analyses altogether or, where
189 group-level analyses were conducted, by using the brain of a selected individual, or using a template
190 based on the brains of 15 mesaticephalic dogs (Table 1).

191 Besides the said advantages of population-based templates, there are advantages of study-specific
192 templates [52] (a special case of which is use of the brain of a selected individual). Regarding the Datta

193 atlas [53], one limitation is that head length and width may influence cortical folding in a manner that an
194 affine transformation of brain size may not correct for, indicating that the Datta template may not be
195 appropriate for non-mesaticephalic animals.

196 Challenges resulting from within-species differences in skull formation and brain anatomy across
197 dogs have been addressed differently in canine continuous EEG and in event-related potential (ERP)
198 studies. Regarding **continuous EEG**, presumably due to differences in skull morphology (e.g., thickness
199 of the frontal and parietal bones), absolute EEG power (μV^2) varies greatly across dogs (e.g., 3-fold
200 across our samples; [31,32]). As a result, group-level analyses are best conducted using relative EEG
201 spectrum values [31,32], which is common practice in human EEG studies as absolute EEG power is less
202 psychometrically sound than relative EEG power. Regarding **ERP** research, challenges have been
203 addressed either via use of a homogenous group of dogs (e.g., laboratory-bred and -kept beagles, all of the
204 same age and similar weight [29,30]) or via report of results at the level of individual dogs [54].

205 Relevant for both continuous EEG and ERP studies, an additional methodological issue is electrode
206 placement. Despite canine methods having been adopted from human studies, given variability in dog
207 head shape and size, the distance between electrodes placed on anatomical landmarks is different across
208 dogs. Although this difference is difficult to address, such variation in absolute distances are compatible
209 with the **International 10-20 system** used in human studies [55], which keeps not the absolute but the
210 relative distance between electrodes constant.

211 *Between-species differences in skull formation and brain anatomy* (Box 2; Figure 1). In fMRI,
212 these differences highlight consideration related to correction for multiple comparisons (Box 3). Given
213 smaller brain volume of dogs relative to humans, the multiple comparison problem is less relevant in
214 canine fMRI. If correction that takes voxel number into account is used in a human and a dog study or
215 across dog studies, results are comparable. If correction that does not take such number into account is
216 used, it is important that the search area is comparable in size. Both are feasible. Nevertheless, although
217 there are widely used methods for correction in human studies and these are now employed in most (if not
218 all) adult and child studies [56], there is heterogeneity across dog studies (Table 1). No meaningful

219 comparison can be made between results obtained without and with correction, with varying degrees of
220 stringency. If and when the aim is to compare results, consistency across studies will be important.

221 In EEG research, differences between dog and human skull and brain morphology necessitate
222 differences in electrode placement. Because dogs have a smaller but more muscular head than humans,
223 their heads permit less sites for electrode placement. The number of electrode holders in human EEG
224 head caps range from 16 to 256 compared to 3 [54,57], 4 [32], or 5-7 [29–31] electrodes placed on dogs’
225 heads. Nevertheless, as these sites correspond to human electrode sites, a *functional comparison* between
226 species can be made, even if restricted to a small number of EEG channels, which may be further
227 increased with methodological advancements.

228 ***Differences in experimental design: sample composition.*** Available findings having been obtained
229 with a small group of dogs and the noted overlap in included dogs may be disadvantageous for
230 generalizability to larger dog populations. This can be addressed through sample selection that increases
231 generalizability potential, e.g., ensuring that dogs of different ages, breeds, sexes, and level of prior
232 training (e.g., from training-naïve to service dogs), are included and then tested. Selection of a
233 biologically and demographically heterogeneous sample with variation in training history has been
234 attended to with varying degrees, with some variability in laboratory [29,30,37,39,41] vs. family [24–
235 28,31–36,40,54,57] dogs, single [29,30,37,39,41,57] vs. multiple [24–27,31,32,34–36,40,54] breeds (with
236 [28,33] not specified), and ages ranging from 1 to 12 years.

237 The noted small sample sizes and overlap in included dogs also means a very small overall number
238 of tested dogs. The sample sizes of all but one [32] canine neuroscience studies published to date are <15,
239 leaving the research underpowered and effects difficult to detect. Although the obtained results may
240 reflect effects that are so large and robust that they are detectable even with small samples, they may
241 alternatively reflect effects that are fragile, non-generalizable, or spurious. Power analysis indicates that
242 larger samples are needed for confidence in results [58]. Yet, it is also the case that in early and
243 exploratory stages of a research area, small *N* studies are not only warranted but also desired to establish
244 that larger (necessitating more funds and participant and researcher time) studies are indicated.

245 **Differences that potentiate disadvantages and solution need to be identified**

246 *Between-species differences in skull formation, brain anatomy, and physiology.* Although further
247 research is needed about *the degree to which dogs' anatomical structures and circuits correspond to*
248 *humans'*, knowledge about canine brain anatomy and the similarities between such anatomy and that of
249 humans' is encouraging regarding the dog as an animal model in comparative neuroscience. There is
250 evidence of correspondence between the species in, for example, primary sensory areas and associated
251 functions [34]. Yet, whether other areas, especially the frontal and prefrontal cortex are organized in a
252 manner that allows for characterization of structures and circuits as associated with similar cognitive
253 functions across dogs and humans is largely unknown. As such, when a specific human structure is
254 referenced (e.g., rostral anterior cingulate cortex [rACC] or dorsolateral prefrontal cortex [DLPFC]), it is,
255 at present, unclear whether the rACC in dogs is anatomically delineable from other areas of the ACC *and*
256 functionally (e.g., attentional control over emotional conflict or distracters [46,59]) the same or at least
257 meaningfully comparable across the species.

258 The solution to this challenge is unclear as from a biological perspective, there is no "reference
259 species" that is uniformly appropriate for addressing pertinent questions. Would it be prudent to take
260 rodents as a reference? Although rodent brains are more dissimilar from human brains than dog brains,
261 evidence obtained via invasive methods indicates correspondence in certain structures across rodents and
262 humans [60]. Alternatively, would it be useful to take humans as a reference and identify areas of
263 activation to stimuli, present dogs with comparable stimuli and search for correspondence in the canine
264 brain? Then again, in addition to or instead, is there need for research that identifies parallels through
265 ontogeny? For example, although there are differences between birds and apes in neural structures, e.g.,
266 birds do not have a cerebral cortex for processing complex mental tasks [5], both species have prefrontal
267 structures that control comparable executive functions [5]. It has been argued that these similarities either
268 originated from the last common ancestor passing down neuronal bases of executive functions or evolved
269 independently due to the species facing similar challenges [5].

270 Between-species differences in skull formation and brain anatomy are also source of
271 methodological shortcomings in fMRI as the obtained images are of poor quality due to use of
272 radiofrequency (RF) coils (human head/neck coils [24–28,33] or knee coils [34–39]) whose geometries
273 have been optimized for different purposes and have not been tailored to dogs' heads and neuroanatomy,
274 making them less than ideal for canine fMRI. Together, as was the case with other species (e.g.,
275 marmosets, rats, mice, and rhesus monkeys) where use of dedicated animal coils has been shown to
276 improve signal-to-noise ratio (SNR) [10], there is need for development of dedicated dog coils that satisfy
277 the anatomical constraints imposed by these animals. Until such coils are available, it will be important
278 for research to determine which coil type is best for performing fMRI in awake dogs with sensitivity,
279 specificity, and large functional contrast-to-noise ratio [1].

280 Between-species differences in cranial musculature and size are relevant for artefact rejection in
281 EEG (Box 4). In human studies, artefact rejection includes correction for ocular artefacts and quantitative
282 procedures (e.g., removing artefacts with voltage step between sample points that is greater than e.g.,
283 $50\mu\text{V}$; with voltage difference of e.g., $300\mu\text{V}$ within a trial; and maximum voltage difference within e.g.,
284 100msec intervals of e.g., $<0.5\mu\text{V}$ [61]) and rejection via visual inspection. In dog studies, there are no
285 well-established quantitative procedures, given difficulty in distinguishing muscle artefact from EEG
286 signal and artefact rejection is typically done using simpler methods. The authors of ERP studies used
287 only a single crude method [62] for rejecting trials with artefacts, in which a trial is rejected if the voltage
288 during the epoch exceeds a user-defined threshold (amplitudes higher than $100\mu\text{V}$ [54,57] or $200\mu\text{V}$
289 [29,30]) and the authors of sleep EEG studies conduct artefact rejection by visual inspection only [31,32].

290 Although the user-defined method works for rejection of artefacts resulting from blinks, it is
291 inadequate for detecting more subtle artefacts, such as those resulting from eye (or ear) movements [62].
292 As such, the used methods are problematic for awake continuous EEG measurement and ERP data
293 collection where there is need for more stringent artefact rejection, given greater canine cranial muscle
294 mass; another example where methodological uniformity between human and dog studies is neither
295 possible, nor warranted. As an example, if the dog moves its eye (or ear) every time there is an event (i.e.,

296 stimulus), it is difficult to determine whether what appears to be a voltage change reflects the movement
297 or differential neural activation. It may be for this reason that there are no established methods for non-
298 invasive measurement of ERPs in dogs, albeit some non- [29,30] and semi-invasive studies suggest
299 progress [42,44].

300 Potential solutions to the artefact problem in non-invasive canine ERP research is to collect data
301 from dogs with less cranial muscle and/or in a state of drowsiness (i.e., canine equivalent of light sleep) or
302 sleep. In support, the Mismatch Negativity (MMN) component can be elicited during light sleep in
303 humans [63,64], indicating an auditory ERP method may be useable with drowsy dogs. Notably, dogs
304 spend at least 30 minutes in drowsiness during a 3-hour-long spontaneous EEG recording [32]. Not unlike
305 sleep, drowsiness is characterized by lowered muscle tone, indicating it permits a considerable amount of
306 artefact-free EEG data that ERP studies could potentially capitalize upon.

307 Between-species differences are pertinent beyond skull formation, brain anatomy and include
308 differences in resting state physiology. Specifically, normal respiratory rate in newborn puppies may be as
309 low as 15 breaths/minute and in an average adult dog it is 24 breaths/min [65]. Conversely, respiratory
310 rate in human neonates (<1 year old) is 30-40 breaths/min, in older children/young adolescents (5-12-
311 year-olds) it is 20-25 breaths/min [66] and in a healthy adult it is 12–20 breaths/min [67]. With regard to
312 heart rate, <2-week-old puppies have 160-200 beats/min (bpm), \geq 2-week-old puppies have up to 220
313 bpm, and adult dogs have 60-140 bpm [65,68]. For comparison, human neonates (<1 year old) have 110-
314 160 bpm and older children and young adolescents (5-12-year-olds) have 80-120 bpm [66]. The heart rate
315 of a healthy adult is between 50–90 bpm [69].

316 These between-species differences are important as differences in brain shape and size also results
317 in between-species differences in the hemodynamic response function (i.e., the course of the
318 hemodynamic response to an external stimulus – the most common functional imaging signal; HRF) [1]
319 and respiratory rate and heart rate are major sources of fMRI confounds as they are correlated with
320 changes in BOLD signal [70]. The shape of the canine HRF is currently unknown [1] potentially due to
321 the temporal resolution in canine fMRI studies, where repetition time (TR) varies between 1-2secs, which

322 is insufficient to sample respiratory or heart rate in dogs. Related, the number of acquired datasets is
323 limited by how long dogs are able to hold still (with experiments necessitating 5- [24], 6- [27,34,40], 7.5-
324 [35], 10- [71], and some 14-minute-runs [26]) (no information is provided in [28,36,39]). As such, the
325 measurement duration that maximizes data quality is unknown. To identify an optimal parameter setup,
326 different anatomical and functional sequence parameters should be tested with phantom and ex-vivo
327 measurements. Similarly, protocols should be optimized with respect to signal- and contrast-to-noise ratio
328 in pilot samples sufficiently similar to the intended experimental samples, but without the constraints on
329 measurement time and motion of in vivo measurements. The ultimate goal of adapting sequence
330 parameters to the dog brain is combination of high spatial and high temporal resolution. Such adaptation
331 will have account for the smaller size of the dog brain, differences in dog compared to human physiology,
332 and limits on run length by how long dogs are able to hold still. Importantly, there are methodological and
333 ethical advantages to shorter runs as these minimize image deterioration due to motion artefacts and
334 prevent rises in specific absorption rates (SAR) of radio frequency levels (see *Ethics and Safety*) [1].

335 ***Differences in skull formation and brain anatomy: within- and between-species.*** Combined,
336 differences across dogs and between dogs and humans in cranial characteristics will make it difficult to
337 determine whether measured electrocortical signal originates from a meaningfully comparable population
338 of neurons across dogs and dogs and humans. Even the human source localisation literature is in its early
339 stages, with only a few studies on the association between BOLD signal and ERPs recorded during the
340 same session [72]. As the human literature advances, it will be important for canine research to make
341 parallel progress. As noted, little is known about the degree to which certain neural structures in dogs are
342 anatomically *and* functionally the same as humans' and advancing the literature in this domain will also
343 be important for source localization.

344 ***Differences in experimental design: active vs. passive paradigm.*** In the human neuroscience
345 literature, there are examples of studies where no behavioural response is required (passive task) and
346 where a response is required (active task). From the perspective of introducing additional movement that
347 results in additional motion artefact, as passive tasks do not involve movement, they are not problematic.

348 In humans, active tasks are also feasible with behavioural responses like a button press. In dogs, requiring
349 an active response would mean that images obtained following an active condition have to be discarded.

350 Indeed, in all but one of canine fMRI studies, the functions that have been examined are ones that
351 do not necessitate an active response, including in *passive auditory paradigms* [34,35], *passive visual*
352 *paradigms* [24,27,28,36,42], *passive olfactory paradigms* [37] or, finally, probing resting state activity. In
353 the only canine fMRI study, with an active, go/no-go paradigm, a “go” signal indicated an active
354 behavioural response is to be executed, which, in this case involved dogs touching a target with their
355 noses while in the scanner. When analysing human go/no-go data, go trials are typically compared to no-
356 go trials [73]. Here, however, activation during inhibition trials was compared with activation during
357 neutral trials as successful “go” trials could not be analysed due to the head motion produced by the nose-
358 touch. This is an important limitation to the current state of the canine neuroscience field as there are
359 socio-cognitive functions that are best probed in active paradigms.

360 In addition, the likelihood of prematurely attributing connections between brain structure and
361 function is enhanced when the aim is to separate active and passive processing in dogs, as in the absence
362 of concurrent behavioural response, the relevant cognitive processes are unknown. Being able to
363 differentiate between active and passive processing in dogs will be key, as there are differences in
364 activation to these two forms of processing in humans. One solution to ameliorate risk of reverse
365 inference (i.e., *post hoc* attribution of presence of a certain cognitive process given activation) is ensuring
366 that dogs have pre-fMRI training on a behavioural paradigm that probes the same cognitive process the
367 fMRI task in question is intended to probe [1] (see, for example, [27]). On a related note, as discussed in
368 relation to the overlap in groups of dogs included across studies, the most ideal assessment battery will
369 comprise measurement methods representing different levels of the measurement continuum (ranging
370 from micro level measurement of brain circuits via fMRI, through less micro level measurement of
371 physiology through EEG, to macro level measurement of observable behaviour via observation or rating
372 scales; [74]) as data obtained at these different levels provide unique information on characteristics of
373 interest [46,61,75–77].

374 Ethics and safety

375 As noted, a main advantage of dogs is that being a domestic animal they can be tested without
376 need for laboratory breeding, raising and keeping. As such, focus on family dogs is what makes the
377 advantage of the dog model ethically permissible. Nevertheless, as aptly discussed by others [1], care
378 should be exercised that no harm is caused, e.g., that scanner noise and high sound pressure levels do not
379 lead to discomfort and hearing damage or that specific absorption rates (SAR) of radio frequencies do not
380 reach harmful levels of rise in tissue temperature [1].

381 During tests, dogs' well-being should be continuously monitored and undue stress eliminated
382 both for reasons of ethics and because stress can lead to increases in physiological activity such as
383 increased respiration and tachycardia, which, as noted, may introduce non-neural noise. The techniques
384 used by canine neuroscience laboratories address stress reduction via use of sound-attenuating earmuffs
385 and in training [1]. Stress reduction can be further improved through careful selection of sequence
386 parameters combined with pre- and post-scanning measurement of physiological indices (e.g., cortisol) of
387 stress such as from saliva or urine [1]. SAR should be measured throughout MR scans and in the absence
388 of established guidelines for nonhuman animals, researchers may adhere to standards established for
389 humans.

390 Concluding remarks

391 There has been a notable, recent increase in canine neuroscience studies, necessitating
392 establishment of methodological guidelines and standardisation to inform the next generation of studies in
393 the area. We discussed foremost questions related to methodology and experimental design in the canine
394 neuroscience literature. As a result, we identified areas for further empirical inquiry. Capitalizing on
395 advantages of the dog such as its cooperativeness and trainability, further areas of exploration include the
396 relation among brain structure, function, and behaviour in dogs, within-subject temporal stability of
397 neural measures, and within-subject correspondence of neural correlates. In addition, we suggest to
398 evaluate and performance across social, cognitive, and affective paradigms, in particular probing socio-
399 cognitive skills that share key behavioural and functional characteristics across dogs and humans.

400 Regarding challenges for which solutions are already being employed, it will be important that such
401 solutions are adopted and used in a reasonably standardised fashion. Regarding unresolved challenges, it
402 will be important to ensure that samples of dogs reflect variation in the larger population to increase
403 generalizability. Specific to fMRI, it will be key to improve sensitivity of imaging protocols and image
404 quality including via improved spatial and temporal resolution that also allow for sampling heart and
405 respiratory rate as well as development of sequence parameters and dog coils and that are tailored to the
406 specifics of dogs and their neuroanatomy. It is unknown whether non-invasive ERP research is possible
407 with dogs. Addressing this question may necessitate more sophisticated methods either for minimizing
408 eye-movement and muscle artefact during experiments and/or for artefact rejection (e.g., filtering) that is
409 appropriate to the magnitude and type of artefact that occurs in dogs. The degree to which neural
410 structures in dogs are anatomically *and* functionally comparable to those of humans will need to be
411 established, including to set the stage for future studies with simultaneous neuroimaging and
412 electrophysiological measurement aimed at source localisation. Source localisation will, in turn, help
413 uncover the degree to which what appears to be meaningfully comparable electrode placement across
414 dogs (and across dogs and humans) reflects signal from a meaningfully comparable population of
415 neurons. Regarding difficulty with active behavioural paradigms, methods need to be identified that either
416 permit for dogs to exhibit a behavioural response without data loss or, alternatively, passive paradigms
417 that probe functions that currently can only be manipulated in active paradigms need to be developed.

418 In closing, we argue that, carefully considering inherent advantages, the domestic dog may become
419 an innovative and unique model for comparative cognitive neuroscience. This becomes relevant if the
420 highlighted advancements take place as these will be necessary for measuring the neural bases of canine
421 socio-cognition in a relevantly comparative, reliable, and valid manner. Addressing the noted challenges
422 with dogs appears appreciably more feasible than addressing those with traditional models, such as their
423 non-cooperativeness, them not sharing a social environment with humans, and, in case of primates, cost-
424 inefficiency and paucity.

Glossary

- 425
- 426
- 427 **Basilar axis:** the axis corresponding to the base of the skull
- 428 **Bradicephalic:** short skulled
- 429 **Calvaria:** the bone that covers the cranial cavity containing the brain, i.e., the skullcap
- 430 **Continuous EEG:** continuous measurement of electrocortical signal, i.e., not measurement of
- 431 change in such signal in response to a stimulus
- 432 **Cribriform plate:** a structure that forms the caudal boundary of the nasal cavity
- 433 **Dolichocephalic:** long skulled
- 434 **ERP:** measurement of negative and positive voltage changes in electrocortical signal in response
- 435 to specific events (e.g., stimuli)
- 436 **Gyrencephalic brain:** with brain folds (gyri) and grooves (sulci), i.e., folded brain
- 437 **Hard palate:** a thin horizontal bony plate of the skull, located in the roof of the mouth
- 438 **Homology:** shared ancestry between a pair of genes or structures, in different taxa. A common
- 439 example is the vertebrate forelimb, where bat wings, primate arms, whale front flippers, and dog
- 440 forelegs are all derived from the same ancestral tetrapod structure. The opposite of homologous
- 441 genes or structures are analogous ones, i.e., ones that serve a similar function across two taxa but
- 442 were not present in their last common ancestor but evolved independently. For example, the
- 443 wings of a bird and a sycamore maple seed are analogous (but not homologous), as they
- 444 developed from different structures.
- 445 **International 10–20 system:** a method used to describe the location- and guide the application
- 446 of scalp electrodes in an EEG examination or experiment, based on the relation between
- 447 placement of an electrode and underlying cortex. The 10-20 system was developed to ensure
- 448 reproducibility and standardisation. The “10” and “20” refer to the distances between adjacent
- 449 electrodes being 10% and 20% of the total front–back or right–left distance of the skull,
- 450 respectively.
- 451 **Lissencephalic brain:** without brain folds (gyri) and grooves (sulci), i.e., smooth brain
- 452 **Mesaticephalic:** a mesaticephalic skull is neither markedly dolichocephalic or brachycephalic
- 453 and is of intermediate length and width
- 454 **Model/Rival method:** a social learning training method where during the training of an
- 455 individual, another individual can be present and when the model is rewarded and praised for the
- 456 wanted behaviour the rival is ignored
- 457 **Prehensile organ:** an organ adapted for seizing or grasping especially by wrapping around
- 458 **Proximate causation:** an explanation of biological functions and traits in terms of the effects of
- 459 immediate environmental forces
- 460 **Somatotopic organization:** various portions of the body are represented topographically on
- 461 specific regions of the cerebral gyri
- 462 **Somesthetic cerebral cortex:** the primary cortical processing mechanism for sensory
- 463 information originating at the body-surfaces (e.g., touch) and in deeper tissues such as muscle,
- 464 tendons, and joint capsules (i.e., position sense).
- 465 **Ultimate causation:** an explanation of biological functions and traits in terms of the effects of
- 466 evolutionary forces
- 467

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References

- 1 Thompkins, A.M. *et al.* (2016) Functional Magnetic Resonance Imaging of the Domestic Dog: Research, Methodology, and Conceptual Issues. *Comp. Cogn. Behav. Rev.* 11, 63–82
- 2 Berns, G.S. and Cook, P.F. (2016) Why Did the Dog Walk Into the MRI? *Curr. Dir. Psychol. Sci.* 25, 363–369
- 3 Seed, A.M. *et al.* (2006) Investigating Physical Cognition in Rooks, *Corvus frugilegus*. *Curr. Biol.* 16, 697–701
- 4 Prior, H. *et al.* (2008) Mirror-induced behavior in the magpie (*Pica pica*): evidence of self-recognition. *PLoS Biol.* 6, e202
- 5 Güntürkün, O. and Bugnyar, T. (2016) Cognition without Cortex. *Trends Cogn. Sci.* 20, 291–303
- 6 Vandamme, T.F. (2014) Use of rodents as models of human diseases. *J Pharm Bioallied Sci* 6, 2–9
- 7 Phillips, K.A. *et al.* Why primate models matter. , *American Journal of Primatology*, 76. (2014) , 801–827
- 8 Jennings, C. *et al.* (2016) Opportunities and challenges in modeling human brain disorders in transgenic primates. *Nat. Neurosci.* 19, 1123–1130
- 9 Gaspo, R. *et al.* (1997) Functional mechanisms underlying tachycardia-induced sustained atrial fibrillation in a chronic dog model. *Circulation* 96, 4027–4035
- 10 Papoti, D. *et al.* (2013) An embedded four-channel receive-only RF coil array for fMRI experiments of the somatosensory pathway in conscious awake marmosets. *NMR Biomed.* 26, 1395–1402
- 11 Miklósi, Á. and Topál, J. (2013) What does it take to become “best friends”? Evolutionary changes in canine social competence. *Trends Cogn. Sci.* 17, 287–294
- 12 Miklósi, Á. (2014) *Dog Behaviour Evolution and Cognition*, Oxford University Press.
- 13 Gygax, L. *et al.* (2015) Dog behavior but not frontal brain reaction changes in repeated positive interactions with a human: A non-invasive pilot study using functional near-infrared spectroscopy (fNIRS). *Behav. Brain Res.* 281, 172–176
- 14 Siegle, G.J. (2011) Beyond depression commentary: Wherefore art thou, depression clinic of tomorrow? *Clin. Psychol. Sci. Pract.* 18, 305–310
- 15 Cosgrove, K. *et al.* (2007) Evolving knowledge of sex differences in brain structure, function, and chemistry. *Biol. Psychiatry* 62, 847–855
- 16 Caviness, V.S. *et al.* (1996) The human brain age 7–11 years: a volumetric analysis based on magnetic resonance images. *Cereb. cortex* 6, 726–736
- 17 McGreevy, P. *et al.* (2003) A Strong Correlation Exists between the Distribution of Retinal Ganglion Cells and Nose Length in the Dog. *Brain. Behav. Evol.* 63, 13–22
- 18 Roberts, T. *et al.* (2010) Human induced rotation and reorganization of the brain of domestic dogs. *PLoS One* 5, e11946
- 19 Regodon, S. *et al.* (1993) Craniofacial angle in dolicho-, meso- an brachycephalic dogs: radiological determination and application. *Ann. Anat.* 175, 361–363
- 20 Schoenebeck, J.J. and Ostrander, E.A. (2013) The genetics of canine skull shape variation. *Genetics* 193, 317–325
- 21 Dickie, A.M. and Sullivan, M. (2001) The effect of obliquity on the radiographic appearance of the temporomandibular joint in dogs. *Vet. Radiol. Ultrasound* 42, 205–217
- 22 Schwarz, T. *et al.* (2000) Radiographic anatomy of the cribiform plate (Lamina cribosa). *Vet. Radiol. Ultrasound* 41, 220–225
- 23 Gacsi, M. *et al.* (2009) Effects of selection for cooperation and attention in dogs. *Behav. Brain Funct.* 5, 31

- 24 Berns, G.S. *et al.* (2012) Functional MRI in awake unrestrained dogs. *PLoS One* 7,
- 25 Berns, G.S. *et al.* (2013) Replicability and heterogeneity of awake unrestrained canine
fMRI responses. *PLoS One* 8, e81698
- 26 Berns, G.S. *et al.* (2015) Scent of the familiar: An fMRI study of canine brain
responses to familiar and unfamiliar human and dog odors. *Behav. Processes* 110, 37–
46
- 27 Cook, P.F. *et al.* (2014) One pair of hands is not like another: caudate BOLD response
in dogs depends on signal source and canine temperament. *PeerJ* 2, e596
- 28 Dilks, D.D. *et al.* (2015) Awake fMRI reveals a specialized region in dog temporal
cortex for face processing. *PeerJ* 3, e1115
- 29 Kujala, M. V *et al.* (2013) Reactivity of dogs' brain oscillations to visual stimuli
measured with non-invasive electroencephalography. *PLoS One* 8, e61818
- 30 Törnqvist, H. *et al.* (2013) Visual event-related potentials of dogs: A non-invasive
electroencephalography study. *Anim. Cogn.* 16, 973–982
- 31 Kis, A. *et al.* (2017) The interrelated effect of sleep and learning in dogs (*Canis
familiaris*); an EEG and behavioural study. *Sci. Rep.* 7, 41873
- 32 Kis, A. *et al.* Development of a non-invasive polysomnography technique for dogs
(*Canis familiaris*). *Physiol. Behav.* 130, 149–156
- 33 Cook, P. (2016) Awake canine fMRI predicts dogs' preference for praise versus food.
Soc. Cogn. Affect. Neurosci. 11, 1853–1862
- 34 Andics, A. *et al.* (2014) Voice-sensitive regions in the dog and human brain are
revealed by comparative fMRI. *Curr. Biol.* 24, 574–578
- 35 Andics, A. *et al.* (2016) Neural mechanisms for lexical processing in dogs. *Science*
(80-.). 353, 1030–1032
- 36 Cuaya, L. V. *et al.* (2016) Our faces in the dog's brain: Functional imaging reveals
temporal cortex activation during perception of human faces. *PLoS One* 11, 1–13
- 37 Jia, H. *et al.* (2014) Functional MRI of the olfactory system in conscious dogs. *PLoS
One* 9, e86362
- 38 Jia, H. *et al.* (2015) Enhancement of odor-induced activity in the canine brain by zinc
nanoparticles: A functional MRI study in fully unrestrained conscious dogs. *Chem.
Senses*
- 39 Kyathanahally, S.P. *et al.* (2015) Anterior-posterior dissociation of the default mode
network in dogs. *Brain Struct. Funct.* 220, 1063–1076
- 40 Cook, P.F. *et al.* (2016) Neurobehavioral evidence for individual differences in canine
cognitive control: an awake fMRI study. *Anim. Cogn.* DOI: 10.1007/s10071-016-
0983-4
- 41 Jia, H. *et al.* (2015) Enhancement of odor-induced activity in the canine brain by zinc
nanoparticles: A functional MRI study in fully unrestrained conscious dogs. *Chem.
Senses* 0, 1–15
- 42 Berns, G.S. *et al.* (2013) Replicability and heterogeneity of awake unrestrained canine
fMRI responses. *PLoS One* 8, e81698
- 43 Andics, A. *et al.* (2016) Neural mechanisms for lexical processing in dogs. *Science*
(80-.). 353, 1030–1032
- 44 Power, J.D. *et al.* (2012) Spurious but systematic correlations in functional
connectivity MRI networks arise from subject motion. *Neuroimage* 59, 2142–2154
- 45 de Bie, H.M. *et al.* (2010) Preparing children with a mock scanner training protocol
results in high quality structural and functional MRI scans. *Eur. J. Pediatr.* 169, 1079–
1085
- 46 Bunford, N. *et al.* (2017) Threat distractor and perceptual load modulate test-retest
reliability of anterior cingulate cortex response. *Prog. Neuro-Psychopharmacology*

- Biol. Psychiatry* 77, 120–127
- 47 Morris, S.E. and Cuthbert, B.N. (2012) Research Domain Criteria: cognitive systems, neural circuits, and dimensions of behavior. *Dialogues Clin. Neurosci.* 14, 29–37
- 48 Evans, A.C. *et al.* (1993) , 3D statistical neuroanatomical models from 305 MRI volumes. , in *Proc. IEEE-Nuclear Science Symposium and Medical Imaging Conference*, pp. 1813–1817
- 49 Muzik, O. *et al.* (2000) Statistical parametric mapping: assessment of application in children. *Neuroimage* 12, 538–549
- 50 Sanchez, C.E. *et al.* (2011) Neurodevelopmental MRI brain templates for children from 2 weeks to 4 years of age. *Dev Psychobiol* 54, 77–91
- 51 Sanchez, C.E. *et al.* (2012) Age-specific MRI templates for pediatric neuroimaging. *Dev. Neuropsychol.* 37, 379–99
- 52 Grabner, G. *et al.* (2014) A study-specific fMRI normalization approach that operates directly on high resolution functional EPI data at 7 Tesla. *Neuroimage* 100, 710–714
- 53 McGreevy, P.D. *et al.* (2013) Dog behavior co-varies with height, bodyweight and skull shape. *PLoS One* 8,
- 54 Howell, T.J. *et al.* (2011) Development of a minimally-invasive protocol for recording mismatch negativity (MMN) in the dog (*Canis familiaris*) using electroencephalography (EEG). *J. Neurosci. Methods* 201, 377–380
- 55 Jasper, H.H. (1958) Report of the committee on methods of clinical examination in electroencephalography. *Electroencephalogr. Clin. Neurophysiol.* 10, 370–375
- 56 Wu, M. *et al.* (2016) Age-related changes in amygdala-frontal connectivity during emotional face processing from childhood into young adulthood. *Hum. Brain Mapp.* 37, 1684–1695
- 57 Howell, T.J. *et al.* (2012) Auditory stimulus discrimination recorded in dogs, as indicated by mismatch negativity (MMN). *Behav. Processes* 89, 8–13
- 58 Arden, R. *et al.* (2016) A Review of Cognitive Abilities in Dogs, 1911 Through 2016: More Individual Differences, Please! *Curr. Trends Psychol. Sci.* 25, 307–312
- 59 Bunford, N. *et al.* Neurofunctional correlates of behavioral inhibition system sensitivity during attentional control are modulated by perceptual load.
- 60 Wallis, J.D. (2012) Cross-species studies of orbitofrontal cortex and value-based decision-making. *Nat. Neurosci.* 15, 13–19
- 61 Bunford, N. *et al.* (2016) Neural Reactivity to Angry Faces Predicts Treatment Response in Pediatric Anxiety. *J. Abnorm. Child Psychol.* DOI: 10.1007/s10802-016-0168-2
- 62 Luck, S.J. (2014) *An Introduction to the Event-related Potential Technique*, (2nd edn) MIT Press.
- 63 Loewy, D.H. *et al.* (1996) The mismatch negativity to frequency deviant stimuli during natural sleep. *Electroencephalogr. Clin. Neurophysiol.* 98, 493–501
- 64 Näätänen, R. *et al.* (2007) The mismatch negativity (MMN) in basic research of central auditory processing: A review. *Clin. Neurophysiol.* 118, 2544–2590
- 65 Peterson, M.E. and Kutzler, M. Small animal pediatrics: the first 12 months of life. , *Small animal pediatrics: the first 12 months of life.* (2010)
- 66 Fleming, S. *et al.* (2011) Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: A systematic review of observational studies. *Lancet* 377, 1011–1018
- 67 Barrett, K. *et al.* (2016) , *Ganong’s Review of Medical Physiology.* , New York, NY: McGraw-Hill.
- 68 Klein, B.G. (2013) *Cunningham’s textbook of veterinary physiology*, Elsevier Health Sciences.

- 69 Spodick, D.H. (1993) Survey of selected cardiologists for an operational definition of normal sinus heart rate. *Am. J. Cardiol.* 72, 487–488
- 70 Murphy, K. *et al.* (2013) Resting-state fMRI confounds and cleanup. *Neuroimage* 80, 349–359
- 71 Berns, G.S. *et al.* (2013) Replicability and heterogeneity of awake unrestrained canine fMRI responses. *PLoS One* 8,
- 72 Liu, Y. *et al.* (2012) Neural Substrate of the Late Positive Potential in Emotional Processing. *J. Neurosci.* 32, 14563–14572
- 73 Falkenstein, M. *et al.* (1999) ERP components in Go/Nogo tasks and their relation to inhibition. *Acta Psychol. (Amst).* 101, 267–291
- 74 Nigg, J.T. (2010) Attention-deficit/hyperactivity disorder endophenotypes, structure, and etiological pathways. *Curr. Dir. Psychol. Sci.* 19, 24–29
- 75 Wheaton, M.G. *et al.* (2014) Perceptual load modulates anterior cingulate cortex response to threat distractors in generalized social anxiety disorder. *Biol. Psychol.* 101, 13–17
- 76 Bunford, N. *et al.* (2016) Correspondence between Heart Rate Variability and Emotion Dysregulation in Children, Including Children with ADHD. *J. Abnorm. Child Psychol.* DOI: 10.1007/s10802-016-0257-2
- 77 Bunford, N. *et al.* (2016) Attenuated neural reactivity to happy faces is associated with rule breaking and social problems in anxious youth. *Eur. Child Adolesc. Psychiatry* DOI: 10.1007/s00787-016-0883-9