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Comparing Social Cognitive, Non-Social Cognitive, and Resting Brain Activity in Chimpanzees (*Pan troglodytes*)

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Comparing Social Cognitive, Non-Social Cognitive, and Resting Brain Activity in Chimpanzees (*Pan troglodytes*)

By

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B.A., Washington University, 2002
M.A., Emory University, 2007

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An abstract of
A dissertation submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy
in Anthropology
2010

Abstract

Comparing Social Cognitive, Non-Social Cognitive, and Resting Brain Activity in Chimpanzees (*Pan troglodytes*)

By Sarah K. Barks

The evolution of the human brain and cognition represents a long-standing question of biological anthropology. Skillful interaction with others has been proposed as a primary mover behind increased intelligence in primates (Dunbar 1998). This study explores the origins of the neural bases of social cognition in humans, asking whether human patterns of social cognitive brain function are unique to our species, or shared with chimpanzees (*Pan troglodytes*). Using [^{18}F]-fluorodeoxyglucose positron emission tomography, chimpanzee brain function was assessed during a social cognition task, a non-social cognition task, and at rest. Two primary aims are to assess the degree to which social cognitive brain function is similar to resting brain function in chimpanzees, and to examine the neural correlates of chimpanzee social cognition. Similar patterns of function to those of humans would suggest that these social cognitive networks were present in our last common ancestor. Conversely, if patterns of activation differ, these species may have diverged in this regard.

Chimpanzees performed a match-to-sample task with videos depicting conspecific behaviors with varying social complexity. Functional neuroimaging data obtained during these task conditions were compared with data from a non-social condition and a resting condition. These conditions were compared both qualitatively and on a voxel-by-voxel basis using paired t-tests.

Like the resting state, social cognition in chimpanzees activates cortical midline structures, including the precuneus, posterior cingulate, and medial prefrontal cortex. Social cognition also activates the insula and amygdala; higher levels of social complexity activate the ventral striatum. At rest, these areas are active to a greater degree. Whole brain averages of each condition examined independently show the same cortical midline areas of greatest activation across all conditions. Rest, however, produces a higher maximum activation and a wider spread of intensity.

This study bolsters previous findings that the resting state in chimpanzees is characterized by similar patterns of brain activity as that of humans, with cortical midline structures highly active, and shows that these areas consistently deactivate in a variety of task conditions much like the human default network. Further, these data demonstrate similarity in brain function during social cognition and at rest in chimpanzees.

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Acknowledgments

This dissertation was produced with the help of many people, including faculty, students, and staff in the Emory University Department of Anthropology and at the Yerkes National Primate Research Center. Research support was provided by the National Science Foundation and the Wenner-Gren Foundation.

My committee members have given me invaluable support and mentoring during my time at Emory. Dr. Jim Rilling provided a rigorous training environment in which I learned the research methods that will serve me well throughout my career. Dr. Lisa Parr supported and encouraged me in the very challenging work of research with chimpanzees, and has taught me how to be both a primatologist and a neuroscientist. Dr. Todd Preuss is one of the smartest people I have ever met, as well as one of the kindest, and I aspire to be a scientist and mentor of his caliber. Finally, Dr. Sally Gouzoules has been a tireless supporter at every step of this process, and I appreciate her reminders that chimpanzees are not the only primates worth studying.

Neuroimaging with great apes is a daunting process that requires the participation and collaboration of many people. This project would not have been possible without the expert chimpanzee-wrangling of Sheila Sterk and Erin Siebert in Dr. Parr's lab, or Erin Hecht's logistic and moral support on scan days. I would like to thank the veterinary and animal care staffs at Yerkes, as well as Margie Jones at the Emory PET Center. I appreciate her patience with the chaos we brought to her. Dr. John Votaw's expertise in analyzing these imaging data is much appreciated.

My fellow graduate students have been a second family at Emory. My cohort in particular—Sarah Davis, Dredge Kang, Brandie Littlefield, Kenny Maes, Michelle Schulein Parsons, and Julie Solomon—has been a source of support and camaraderie, as well as a much-needed social life. I am so proud of how far we've all come. I am immensely grateful to Bethany Turner, Jenny Mascaro, David Goldsmith, Avi Brisman, and Lauren Myers for their friendship, and to Zeia Fanucchi-Brisman for showing up just when I needed her. I don't think I could have done this without all of these phenomenal people, and in any case I wouldn't have wanted to.

My family has given me endless encouragement and unwavering support, and I cannot adequately express my gratitude and appreciation. I would not be the person I am today without the love of my parents, Sandy Watts and Dennis Barks, and my brother, Daniel Barks. Thank you, thank you, thank you. I can't say it enough.

Finally, I want to thank the chimpanzees who were so much more to me than subjects in this research. Working with them has been one of the most difficult experiences of my life, but also one of the most rewarding. I treasure the time I spent with Katrina, Patrick, Scott, Faye, Lamar, and Lucas. This dissertation is dedicated to Jarred and his always-impressive brain.

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Introduction

The evolution of the human brain and cognition presents one of the long-standing questions of biological anthropology. A high degree of intelligence and a greatly expanded brain—three times larger than that of our closest great ape relatives—are hallmarks of our species. Research in this field has sought to identify the unique properties of the human brain (beyond its size), and the specializations of human cognition that might set us apart from other primate species.

The selective pressures that led to expanded brain size in the human lineage are often described as falling into two categories: *movers* and *releasers*. Releasers remove constraints: factors that limit the size of the brain are altered such that an expansion can occur. Some of the proposed releasers in the study of brain evolution include metabolic demands of brain tissue relative to the rest of the body (Aiello and Wheeler 1995), vasculature required to cool the brain (Falk 1990), and cooling temperatures due to global changes in climate (Schwartzman et al. 2009). Movers, by contrast, are selective pressures that make a larger brain adaptive by creating a niche in which greater cognitive abilities are adaptive. For instance, the ability to forage for hard-to-find food opens a dietary niche previously unavailable, and the intelligence to support such foraging would be an impetus for brain expansion (Milton 1988).

Social cognition has been proposed as a primary mover behind increased intelligence in primates as a whole, and in humans in particular (Dunbar 1998). Brothers (2002) defines social cognition as “the processing of any information which culminates in the accurate perception of the dispositions and intentions of other individuals,” and states that “… primates, especially those most closely related to ourselves, have developed a

unique capacity to perceive psychological facts (dispositions and intentions) about other individuals" (p. 367). Most primate species are highly social, and maintain relationships with large numbers of conspecifics in their social groups. This social nature creates many cognitive demands: the ability to recognize and remember individual conspecifics, the ability to understand relationships with and among others, the ability to plan one's own behavior with respect to others' behavior, and so on. There is in fact a general (though not complete) relationship between the degree of social complexity, measured by number of individuals in a group and number of relationships each group member has with others, and brain expansion: the brain's neocortex (responsible for most "higher" cognitive functions) expands as group size expands (Barton 1996, Dunbar 1998).

This study seeks to illuminate the evolutionary origins of the neural bases of social cognition in humans and asks whether the patterns of brain function during social cognition in humans are unique to our species, or shared with chimpanzees (*Pan troglodytes*), our closest living relatives. Direct comparison of human and chimpanzee brains is one of the best ways to examine unique aspects of the human brain; this research employs [^{18}F]-fluorodeoxyglucose positron emission tomography (FDG PET), a functional neuroimaging technique, to do so. If the chimpanzee brain shows similar patterns of function in response to social stimuli as those of humans, it would suggest that a brain that is socially-adapted—to a degree not found in other primates—may have been present in our last common ancestor. Conversely, if patterns of activation are different, it would suggest that the two species have diverged and one or both have become specialized in this regard.

This research is situated at the intersection of two broader fields of study: human social neuroscience and chimpanzee behavior and cognition. Here, the tools of cognitive neuroscience research are applied in a cognitive testing paradigm with great apes, with an aim of bridging the gap between studies of brain function in humans and behavior in non-human primates.

Chapter 1: Background

Human social cognitive neuroscience

Social complexity has been suggested as the driving force behind increased brain size, one of the hallmarks of human evolution: brains become larger as social groups become more complex, providing greater cognitive power to monitor and manipulate relationships (Dunbar 1998). Humans live (and have evolved) in rich social environments, requiring complex reasoning about others' intentions, emotions, relationships, and so on. In fact, recent evidence from neuroimaging suggests that reflection on social interactions and on one's own mental states may be the default state of the human brain. As such, social cognition and the brain processes that underlie it represent a critical area of study in human cognitive neuroscience.

Theory of mind

Perhaps the most salient feature of human social cognition is our capacity for theory of mind (ToM). ToM encompasses an awareness and understanding of others' mental states (Premack & Woodruff 1978), and an ability to make inferences about those mental states, particularly intentions and beliefs. These abilities are a skill set that guides, to some degree, our interactions with other people; its inherent perspective-taking is a foundation for both cultural learning and language. The neural systems and structures that support ToM in humans are well-documented through functional neuroimaging, studies of patients with neurological damage, and studies of social cognitive disorders such as

autism spectrum disorders and Williams syndrome. Further, ToM is known to develop during the first few years of life, suggesting a foundational role in human cognition.

Anatomy of theory of mind

Several brain areas have been identified that support the multiple components of ToM. Most salient of these are the medial prefrontal cortex (MPFC), the temporo-parietal junction (TPJ), the amygdala and surrounding cortex of the temporal pole, and the superior temporal sulcus (STS) (Gallagher and Frith 2003, Saxe and Wexler 2005, Siegal and Varley 2002).

In functional neuroimaging studies of ToM function, the MPFC is the most consistently identified area of activation (Gallagher & Frith 2003). Many structures involved in ToM serve other cognitive functions as well (Gallagher and Frith 2003); unique among these structures, however, the MPFC appears to be exclusively devoted to the representation of one's own and others' mental states (Frith & Frith 1999). First-person and third-person perspective taking—making inferences about both the self and others—show overlapping activations in the MPFC (while also both activating distinct areas) (Vogeley et al. 2001). Another study (den Ouden et al. 2005) takes that result further, replicating the finding that reasoning about self and other mental states activates the MPFC, and also demonstrating that subjects more readily identify intentional causality than physical causality. This result suggests that humans' default approach to the world is social. Finally, the MPFC is activated not just when thinking about mental states and perspectives, but also when actively engaged in real-time social interactions (Rilling et al. 2004).

The STS is involved in detection of biological motion and of agency (Allison et al. 2000, Grèzes et al. 2001); interpreting such motion can aid in inferences about intentions (Frith and Frith 2006). The TPJ, particularly in the right hemisphere, activates for attributing mental states to others and for integrating biographical details about a person with their mental states, forming a coherent perception of others (Saxe and Wexler 2005). The TPJ is also involved in distinguishing the self and others, a capacity that supports empathy and understanding of others (Decety and Grèzes 2006).

The amygdala is critical for modulating and interpreting emotions, which in turn is necessary for interpreting others' social cues. Disrupted amygdala functioning is frequently suggested as an important factor in the social deficits associated with autism spectrum disorders—frequently described as an absent or diminished capacity for ToM. For instance, autistics show lower amygdala activation than controls when they attempt to identify mental states from pictures of eyes (Baron-Cohen et al. 1999). Performance on emotion-identification tasks such as this is very similar in autistic subjects and patients with damage to the amygdala (Adolphs et al. 2001), further bolstering the implication of amygdala dysfunction in autism.

Other studies of ToM function in patients with neurological damage suggest that the right hemisphere is particularly important for these tasks; lesions to the right hemisphere tend to lead to greater ToM deficits than do similar lesions to the left hemisphere (Griffin et al. 2006, Happé et al. 1999). (Note, however, that neuroimaging studies often show bilateral activation for ToM tasks, and sometimes left-lateralized function (Happé et al. 1996).) In a test of several aspects of ToM, right hemisphere lesioned patients perform similarly to controls on non-mentalizing tasks and tests of first-

order belief attribution, but are impaired at recognizing humor that depends on a social inference and at making second-order inferences (Griffin et al. 2006). While these patients had a variety of specific lesions, the areas most likely to result in ToM deficits were in Brodmann's areas 44 and 45—areas associated with mirror neurons and imitative abilities (see below).

A study of patients with frontal lobe lesions—either orbitofrontal cortex (OFC) or dorsolateral prefrontal cortex (DLPFC)—adds further to our understanding of ToM. DLPFC patients do not show ToM deficits; by contrast, OFC patients are impaired to about the same degree as Asperger subjects (Stone et al. 1998). The impairments described for these OFC patients are not profound ToM deficits, but rather an inability to parse subtle aspects of social interactions. The authors suggest that the OFC patients are unable to connect their cognitively-based ToM inferences with an understanding of the emotions underlying typical social interaction.

As a caveat, however, Bird et al. (2004) describe a patient with a highly circumscribed MPFC lesion who does *not* suffer from any impairment to ToM capacities. This patient's neurological damage in the medial frontal lobes is extensive, and she is impaired on executive functions such as working memory, but ToM capabilities are intact. This case seems to demonstrate that, contrary to others' arguments and considerable evidence from functional neuroimaging, the MPFC is not a necessary substrate for ToM functions. The authors note that this patient's lesion might not cover all the parts of MPFC that other studies implicate in ToM, and that there are probably other parts of the network serving ToM functions that are spared in this patient.

Theory of mind and imitation

The human capacity to imitate others supports varied processes such as matching one's own to others' actions, learning motor behavior, understanding facial expressions of emotion, and understanding others' intentions. A growing body of evidence suggests that imitative capacities go beyond motor behavior, affecting several aspects of social cognition. If the primary function of imitation is to understand others' actions, that understanding would in turn serve the ability to understand the intentions behind those actions. We internally simulate others' actions, and that simulation extends to emotions (Gallese et al. 2004): emotions are "mirrored" as well. The experience of the emotion is replicated when we observe it in someone else, providing a mechanism by which we understand others' experiences and mental states.

These imitative capacities, both in humans and other primates, are thought to be supported largely by mirror neurons. Initially identified (through single-cell recording) in macaque cortex, these neurons fire both when an individual performs an action and when it observes the action being performed by another (Rizzolatti 2005). Mirror neurons are found in a distributed network throughout the macaque brain, but they are most abundant in premotor area F5. While methodological constraints prevent the explicit identification of mirror neurons in human cortex, there is considerable circumstantial evidence—primarily from functional neuroimaging—that a similar circuit exists in the human brain. The human mirror neuron system comprises a circuit between inferior frontal cortex (primarily Brodmann's area 44) and rostral inferior parietal cortex, with the STS linking the two (although STS in humans is not thought to be a mirror neuron area itself (Aziz-Zadeh et al. 2006)). Neuroimaging studies show that these areas are consistently activated

in when imitating others' behavior, more so than when performing the same motor action without an imitative component (Iacoboni et al. 1999).

That mechanism has implications for theory of mind. Two major hypotheses about how ToM works are the "theory theory" and the "simulation theory" (Vogeley et al. 2001). According to the theory theory, we understand others' mental states by reference to learned knowledge about mental inferences. There is a system of rules in place for making those inferences, and we carry out interactions with others based on reading their behavior and thus their intentions and beliefs. The understanding is externally directed. By contrast, the simulation theory holds that we understand others' mental states by making reference to our self-awareness; it is internally directed. Unconscious imitation is the foundation of the simulation theory—it is through the simulation of others' emotional experience, for example, that we put ourselves in their place and make inferences based on what *we* might do in the same mental circumstances.

In addition to shared experiences of emotion between self and others, there is evidence in support of the simulation theory from autism. This deficit in theory of mind capacities may result from an impairment of the mirror neuron system's function (Dapretto et al. 2006, Gallese 2006). In a neuroimaging study of emotional imitation, high-functioning autistic children were asked to imitate expressions of emotion (Dapretto et al. 2006). While these children perform the task as well as normal control subjects, the patterns of brain activation between the two groups are strikingly different. Normal controls show activation in inferior frontal areas previously demonstrated to underlie imitative capacities, primarily pars opercularis. Autistic children, however, show very little activation in the inferior frontal gyrus/pars opercularis (roughly corresponding to

Brodmann's area 44), but greater activation outside those areas, suggesting that they are not invoking the mirror neuron system to perform this task. The authors note that autistics' deficit does not lie in their ability to perform the task itself, but rather in the neural basis for that performance. They suggest that autistics develop alternate strategies to serve these functions—strategies that do not rely on imitation or simulation of others' emotional experience. As such, they most likely lack the understanding of that experience that comes so easily to normal controls. Another study demonstrates that high-functioning autistic subjects, in addition to a lack of activation in established imitation areas, do not activate the amygdala and TPJ during an imitation task to the same degree that normal controls do (Williams et al. 2006). The diminished amygdala activation may further bolster support for an imitative role in understanding others emotions. The TPJ is consistently implicated in ToM functions, suggesting that its attenuated activation in autistics in this task may have implications for their impaired ToM capabilities.

Gallese (2006) takes this evidence a step further to posit that the simulation based in mirror neuron mechanisms underlies most of the basic processes of social cognition, and that the wide-ranging deficits in social cognition that characterize autism result from a global breakdown of the mirror neuron mechanism. Understanding others is based on shared experience, representing others' beliefs, intentions, emotions, etc. by reference to our own experience of same. This reference to experience is called "intentional attunement" (Gallese 2006). Intentional attunement is based on physical experience, representing emotions in terms of body states (a visceral experience (Bechara et al. 2000)). Simulated experience of emotions is primarily based in viscero-motor cortical areas (more so than simulated action) (Gallese et al. 2004).

Development of theory of mind

The capacities that support theory of mind begin to develop in infancy. Joint attention, in which a child attends to a stimulus that someone else is also attending to, typically appears around nine to 12 months of age (Tomasello 1999). Children at this age also begin to follow gaze and pointing by others, to direct others' attention with their own pointing, and to imitate others (Tomasello 1999). Full-fledged ToM is typically "online" by four or five years of age, absent any neurological or cognitive disorder. ToM in children is typically assessed using the false belief task (Frith 2001). This experimental task requires the child to understand a character's belief when it contradicts both reality and the child's own belief.

Damage to the structures noted above can result in impairments to ToM and other social cognitive functions; such damage is particular detrimental early in life. Anderson et al. (1999, 2000) compare social cognitive deficits resulting from damage to prefrontal cortex (PFC) in early childhood and in adulthood. Both patient groups are severely impaired in social behavior (although their intellectual abilities are normal). The early-onset patients, however, are further impaired: they do not have the knowledge of correct social behavior—they have not learned the "rules." Patients with adult-onset lesions, by contrast, are aware of what "correct" behavior is; they simply do not act accordingly. These patients are capable of moral reasoning, particularly in a cognitive test situation, although their real-life behavior is abnormal. Adult-onset patients possess the social knowledge that early-onset patients lack. These studies suggest that factual knowledge about social interaction is acquired early in life, and that intact PFC is required for that acquisition.

The extent to which theory of mind (or social cognition as a whole) is a modular, encapsulated function is debated in the literature (Beer and Ochsner 2006). However, it does seem that whatever degree of modularity there is, it develops with age rather than being fully-formed at birth (Johnson et al. 2005). Processes that are fairly widely distributed at birth and in infancy gradually come to be performed by a restricted neural substrate; likewise, parts of the brain that start out serving several tasks come to narrow their function. In this way, relationships between anatomy and function change over time. Johnson et al. (2005) suggest that one of the consequences of atypical development (for instance, in the case of autism) is that parts of the social brain network fail to become properly specialized.

Theory of mind functions may also become automated over time. Satpute and Lieberman (2006) describe two complementary systems that underlie many cognitive functions: the X-system and the C-system. The X-system (reflexive) is more automatic and does not rely on extensive learning; it includes the amygdala, basal ganglia, STS, and ventromedial prefrontal cortex (VMPFC), among other structures. The C-system (reflective) serves more conscious and intentional processes; it relies more on learning and is characterized by slower functioning overall. It includes lateral PFC, memory structures in the medial temporal lobe, posterior parietal cortex, and dorsomedial prefrontal cortex (DMPFC), among other structures. The authors suggest that early development of theory of mind processes relies on the C-system, as the functions are learned (primarily in the MPFC). Over time, however, ToM may become automated, and could then be supported by other parts of the brain, in the X-system. Note that a model by which this process fully occurs—that is, in adulthood ToM functions are *always* carried

out by X-system structures—is not compatible with neuroimaging literature in which the DMPFC (a C-system structure) is consistently activated for ToM tasks. There could, however, be some degree of redundancy built into the theory of mind system.

The patient described above with extensive MPFC damage but spared ToM (Bird et al. 2004) may also bolster a developmental argument by which ToM becomes (or can become) automated with age, in which case it is typically but not *necessarily* supported by MPFC in adulthood. It is possible that in the event of damage to the core structures that support ToM, automated systems can serve the same functions. This case may also parallel those described by Anderson et al. (1999, 2000) in which damage acquired late in life is less detrimental than early-onset damage, because the patient has acquired the necessary factual knowledge to accompany social cognitive functions.

The default mode network

Many functional neuroimaging studies have identified a network of brain regions that are consistently active at rest, more so than during most focused cognitive tasks. These areas have been termed the default mode network (Gusnard and Raichle 2001, Raichle et al. 2001), and are thought to represent the brain's ongoing baseline activities—what the brain defaults to when its attentional resources are not directed elsewhere. Initially described in PET studies, this network comprises areas that show high metabolic activity and oxygen extraction from circulating blood at rest (Raichle et al. 2001). The baseline activity identified in this way was found to consistently decrease when attentional resources are recruited for focused cognitive activity.

Gusnard and Raichle (2001) include and ascribe function to several brain areas in this network. The posterior cingulate cortex (PCC) and precuneus compose a medial posterior component of the default mode network, and are suggested to process emotion and external environmental stimuli. Also in the posterior part of the network, lateral parietal cortices attend to salient external stimuli, particularly biological motion. The anterior default mode network includes VMPFC, associated with integration of cognitive and emotional information and online monitoring of sensory input, and DMPFC, associated with representing states of the self and of others (i.e. processes related to theory of mind). Gusnard et al. (2001) further highlight the distinction between the ventral and dorsal portions of MPFC, describing DMPFC as most active in cognitive processes, and VMPFC as responsible for emotional processes. These medial prefrontal areas are particularly critical in a consideration of human social cognition, as they are consistently implicated in social cognitive and self-related processes as well. The consistent convergence of these areas has been robustly replicated in many imaging studies (Buckner et al. 2008). More recently, medial temporal cortical areas (including the hippocampus) related to episodic memory retrieval have been included in the default mode network as well (Buckner et al. 2008, Greicius et al. 2003).

The functions of the areas comprised by the default mode network can be loosely described as falling into two categories: those related to internal processes, and those focused on external information. Fransson (2005) describes these two components of the default mode network as functioning separately, but in coordination with each other. That is, the network is not a homogeneous whole that is constantly active, but rather a two-part system that toggles between these two broad functions. The anterior areas of the default

mode network fall into the introspective category of function, while the posterior areas are primarily externally focused. (Note, however, other authors' description of the precuneus in particular as involved in emotion processing (Gusnard and Raichle 2001) and autobiographic memory retrieval (Northoff et al. 2006).) Fox et al. (2005) suggest that the brain rapidly switches between these two components—anterior internally-focused areas and posterior externally-focused—so as to monitor both the external environment and the internal milieu (particularly self-introspection).

Note, however, that Raichle and Snyder (2007) and Raichle and Mintun (2006) advise caution in ascribing active function in response to external stimuli for each of the parts of this network. These authors point out that even activity observed in direct response to cognitive tasks likely accounts for a small portion of overall brain activity; most of the brain's metabolic activity relates instead to ongoing intrinsic processes, balance of excitatory and inhibitory tonic activity, and maintenance of a state of readiness for input of information. This focus on readiness for incoming stimuli, facilitating preparation for and expectation of future events, is further reiterated by Buckner et al. (2008). In this sense all parts of the brain do exhibit ongoing intrinsic activity even at rest. The areas described in the default mode network, however, are included on account of their consistently high level of metabolic activity. The critical difference is not so much that between activity at rest and activity during a task, but rather between ongoing intrinsic activity and attentionally-focused activity evoked by external stimuli. It is a physiological distinction, as opposed to behavioral (Raichle and Snyder 2007).

One function proposed for the default mode network is "stimulus-independent thoughts" (Buckner et al. 2008)—thoughts that are not evoked by something in the

external environment, but rather arise internally and are unrelated to any ongoing attention to a task. Such thoughts may be described as day-dreaming or mindwandering, and in fact subjects who report the most frequent mindwandering also show highly active default mode network activity (Mason et al. 2007).

The default mode network and social cognition

Significant overlaps between this default mode and social cognitive processes, particularly those related to the self, have been described. These studies collectively suggest that the brain's default function may in fact be reflection on the self and on social relationships and interactions—that social information and its related mental processes hold a privileged position in human cognition as a whole. Studies of theory of mind in particular consistently demonstrate activation in default mode network areas, particularly MPFC (Amodio & Frith 2006). Further support for this overlap comes from studies noting abnormal default mode network function in disorders of the mind and brain related to social cognitive function, particularly autism (Kennedy et al. 2006, Cherkassky et al. 2006).

Iacoboni et al. (2004) presented subjects with videos of social interactions (as well as videos of single actors), without an attendant task, and compared functional magnetic imaging (fMRI) results with a resting state. Unlike performing tasks (which decreases activity in this network) and passively viewing non-social stimuli (which does not alter its level of activity), watching these social interactions increased activity in cortical midline areas that are active at rest (particularly the precuneus and DMPFC). This result is especially notable in that it shows a rare increase in both the anterior and

posterior portions of the default mode network simultaneously. Modulation of activity in this network, both above and below resting state activity, was also demonstrated in a comparison of a social task (reasoning about moral dilemmas), a non-social task (test of the Stroop effect), and rest (Harrison et al. 2008). Here, the Stroop task deactivates the default mode network as expected, while reasoning about moral dilemmas activates cortical midline structures above resting levels. This result bolsters the supposition that a primary function of the default mode network is social reflection.

The cortical midline structures consistently identified in the default mode network are also active in many studies of self-related cognition and reflection. In a meta-analysis of 27 imaging (PET and fMRI) studies of self-referential activity, Northoff et al. (2006) identify these cortical midline areas as critical in self-related cognition, regardless of the domain or modality of stimuli in each study. They note as well that these areas frequently act in concert, and may be seen as a functional unit dedicated to self-reference and self-reflection. Considering the overlap of these areas with those active at rest, the authors suggest that self-processing forms the baseline of neural and cognitive activity in humans. Wicker et al. (2003) also identify MPFC as an area that is consistently active during self-referential mental processes, and suggest a direct inverse relationship between activity in the MPFC and attention required to attend to external information.

Chimpanzee social cognition

The structure of chimpanzee social groups creates a rich environment to foster the development of complex cognitive capacities, and has been proposed as the driving force behind the sophisticated social cognition and behavior that characterize this species

(Barrett et al. 2003). It is argued that the demands of such groups—for example, the need to identify and recognize a large number of group-mates, to monitor and manipulate relationships, to negotiate a complex and sometimes unstable dominance hierarchy—create a strong selection pressure for intelligence (Dunbar 1998, Humphrey 1975). That these factors involve other intentional agents increases the need for social intelligence because—as Tomasello (2000) puts it—"other animate beings do not just sit around like food waiting to be found and manipulated, but they have social strategies of their own" (p. 354).

Social structure in the wild

Chimpanzees live in large groups with a fission-fusion social structure, in which the entire population is rarely together, but splits apart into small groups of variable composition (Goodall 1986). These groups are highly flexible and change frequently: they may be single- or mixed-sex, kin or unrelated individuals, mother and offspring, etc. A group may stay together for a day or more, or only a few minutes; individuals may also travel alone. The activities of chimpanzee groups vary as well: they may forage or hunt, groom, engage in sexual behavior, play, and so on.

The dominance hierarchy is the central feature of chimpanzee social interactions. Chimpanzees are male-dominant; all males are almost always dominant to all females (Riss and Goodall 1977), and compete for status in their hierarchy. While the males' hierarchy is roughly linear—i.e., there is typically an alpha male dominant to all the rest, a beta who is subordinate to the alpha but dominant to the rest, and so on—it is complicated by the formation of coalitions among individuals and "contextual"

dominance in which one male's dominance over another is contingent on the presence or absence of a third (de Waal 1998, Goodall 1986). Dominance hierarchies are characterized by broad levels (e.g. high, middle, low). Dominance between levels is clear—that is, the lowest-ranking member of the "high" group is clearly dominant to the highest-ranked "middle" member—but within levels may be more ambiguous (Newton-Fisher 2002, 2004). Males typically enter the dominance hierarchy at adolescence; those who achieve alpha status typically do so around age 20-30, with a sharp decline in status after age 30 (Goodall 1986, Riss and Goodall 1977). Younger males who attain and then lose alpha status may still climb the ranks again, more so than older males. Not all males strive for dominance; some seem content to stay lower in the hierarchy (Goodall 1986).

In part because of these coalitions and "political" relationships (de Waal 1998), the most dominant male is not necessarily always the biggest or physically strongest. Rather, dominance may be achieved through manipulation of others (which may entail negative or positive interactions) or other, more cognitive (rather than physical) strategies (de Waal 1998, Goodall 1986). Goodall (1986), for instance, describes a male—Mike—who, although smaller than others, became dominant largely through unique charging displays using cans, branches, and other objects. Goodall notes that Mike was never seen to attack another male as he maneuvered into alpha status, gaining his position instead through behavioral ingenuity in his displays; he maintained that pattern of avoiding aggressive conflict during his tenure as alpha.

Chimpanzee males rarely gain dominance on their own. Rather, they depend on the support of others in the group, both male and female. De Waal (1998) describes shifting power alliances in the large captive colony at Arnhem, in which three males—

Luit, Yeroen, and Nikkie—competed for status over a period of several years. Each male at different times allied with another; two would support each other against a third, but those alliances shifted with changes in dominance. The partnerships were strategic. Also important in these three males' status was the support of the group's females; de Waal describes several instances in which one of the three's actions was thwarted by the females, who supported one of the other males instead. At Gombe, two brothers, Figan and Faben, played an important role in the group's dominance relationships. Although Faben was older, he became subordinate to his brother after being disabled by polio (Riss and Goodall 1997). Faben would typically support Figan, and the two of them together were dominant to other high-ranking males. However, although Figan eventually became alpha, he did so only with his brother's support, and required that support to maintain his own dominance.

When positions in the dominance hierarchy are stable, rates of aggression tend to be low (de Waal 1998, Goodall 1986). An established alpha male controls aggressive encounters in the group, frequently intervening to break up fights. Dominance is maintained much more through threats of aggression than through actual fighting; while threats maintain the social order, fights reverse it. As the hierarchy becomes less stable—when an alpha's status is challenged and his position becomes precarious, or when there is no clear alpha—aggression increases. Periods of change are characterized by fighting as males challenge each other for status (de Waal 1998). Aggression is closely tied to existing coalitions. One coalition member may challenge another male on his partner's behalf, or an individual may direct aggression at two others who may be allying against him, so as to neutralize the partnership (Goodall 1986).

An interesting side effect of these shifting relationships is the behavior of dominant males toward subordinates. Even an alpha male will direct submissive behavior to subordinates under some circumstances, so as not to alienate a potential ally (Boesch and Boesch-Achermann 2000). Chimpanzee males' relationships are necessarily ambiguous, because while they must maintain close affiliations, they are also in near-constant competition with each other (Ihobe 1992). Because of the need to maintain valuable relationships, fights are typically followed by affiliative behavior; such reconciliation repairs the relationship (de Waal 2000). Coalitionary relationships come into play in reconciling fights as well—reconciliation might be facilitated by a third party. Reconciliatory behavior is seen both in captivity (de Waal 1996) and in the wild (Kutsukake and Castles 2004), although there is some evidence that it is less frequent in the wild, possibly because of a decreased need to immediately reduce conflict and tension—animals in captivity are less able to avoid one another.

In light of this complexity, one might easily imagine that a finely honed social cognition would be highly adaptive in chimpanzee social groups. Much as human cognitive activity appears to default to social reflection and rehearsal at rest, it may be advantageous for chimpanzee cognition to do so as well. Such reflection would benefit an individual needing to keep track of changes in dominance and of ongoing coalitions and disputes in the group.

Social learning

Another hallmark of chimpanzee social life (both in the wild and in captivity) is learning complex behaviors from group-mates, particularly kin. Such learning suggests,

in many cases, an understanding of others' intentions and perspectives. Several behaviors have been noted in the wild that vary between populations (frequently referred to as "cultural" variation, but more conservatively described as "traditions" that characterize different groups), even in the absence of ecological factors that might dictate such variation. These behaviors have often been observed to be passed down within groups, especially from mothers to juveniles. Transmission of a behavior depends by definition on learning from other individuals. The form that this learning takes, however, is a matter of considerable debate.

Several mechanisms have been proposed by which social learning might occur, including stimulus enhancement, in which one individual's actions merely draw another's attention to something, usually an object that can be manipulated, and the second individual learns the behavior on its own; emulation, in which one individual copies the end goal of another's action without necessarily using the same actions; imitation, in which one individual exactly replicates another's behavior so as to meet the same goal; and explicit teaching (Biro et al. 2003, Call et al. 2005, Nagell et al. 1993). Emulation and imitation in particular have been explored through studies with both chimpanzees and children. (Note, however, that teaching would be difficult to identify in a non-verbal subject—on the surface, it would likely look very similar to imitation.)

Regarding imitation and emulation as a dichotomy may be an inappropriate view—the two abilities may form a continuum, in which chimpanzees' social learning is flexible according to the situation. While human children use imitation almost exclusively to learn, chimpanzees imitate when it is useful to do so and emulate when it is not (Nagell et al. 1993, Call et al. 2005, Myowa-Yamakoshi and Matsuzawa 1999,

2000, Whiten et al. 2004). Emulation is based on an understanding of causal relations; when causal relations are not evident, chimpanzees can rely on imitation instead because it only requires the ability to replicate actions (Horner and Whiten 2005). In a study that tested emulation in chimpanzees and children, subjects were given a box to open to retrieve a reward (Horner and Whiten 2005). Demonstrators showed the subjects both relevant and irrelevant actions with two types of boxes, clear and opaque. Irrelevant actions could not be identified with opaque boxes, but could with clear. Children and chimpanzees both faithfully imitated the demonstrator's actions with opaque boxes. However, with clear boxes, chimpanzees omitted the irrelevant action (i.e. using emulation, obtaining the goal without regard to the specific means), but children did not (i.e. continuing to imitate). In this case, emulation is the more effective strategy. In using emulation, chimpanzees learn about the physical relationships between the objects in the task, and their relationship to the goal. Imitation requires a focus on the experimenter instead; in that sense, it is a more social process (Nagel et al. 1993)—though not necessarily a more effective one. In fact, Whiten et al. (2009) find that children *over*-imitate; i.e., even when presented with actions that are clearly superfluous and instructed not to imitate those actions, they continue to do so.

Social cognitive capacities

Premack and Woodruff (1978) asked if chimpanzees have the ability to ascribe mental states to others and to the self—theory of mind. This question has been explored through both naturalistic observations in the wild and controlled studies in captivity; studies have examined many dimensions of potential ToM capacities, including

deception and false beliefs, self awareness, and understanding of the relationship between sensory input and mental representations of the world. These studies have encompassed the most thorough assessment of chimpanzees' social cognitive abilities. Studies of non-human primates are by necessity less straightforward than studies with humans, as inferences about their mental states must be made from their behavior rather than from verbal reports. As such, these data must be cautiously interpreted.

Self-awareness

Awareness of the self as an intentional agent is considered a prerequisite for recognizing others as agents. Mirror self-recognition has been used as the litmus test for self-recognition and, therefore—although the link has been challenged (Heyes 1998)—self-awareness. The classic mirror test begins with exposing animals to a mirror and then, after acclimation, sedating a subject, applying an odorless dye to a spot (such as the eyebrow) that is not visible without using the mirror, and monitoring the number of touches to the spot that the subject makes both before and after introduction of a mirror (Gallup 1970). Several studies have consistently demonstrated that chimpanzees (and orangutans (Gallup 1997)) pass this test, but monkeys do not (Eddy et al. 1996, Povinelli et al. 1993). Critiques that the positive results are merely an artifact of chimpanzees waking up from anesthesia (Heyes 1998) have been refuted (Povinelli et al. 1997). Not all chimpanzees show the capacity for mirror self-recognition; in those that do, the ability typically emerges around 5-8 years of age, and decreases in late adulthood (de Veer et al. 2003, Povinelli et al. 1993).

As predicted, young chimpanzees who do not recognize themselves in mirrors also fail to attribute knowledge to others in a guessing/knowing experimental paradigm (in which subjects must choose a baited cup based on indications of two experimenters, only one of which has seen the baiting) (Povinelli et al. 1994). Heyes (1998) has argued that mirror self-recognition requires only a "body concept," not a "self concept," that there is not necessarily a mental component to self-recognition—only a kinesthetic awareness of the boundaries of one's own body. Povinelli and Cant (1995) posit that great apes do in fact have a body awareness that is distinct from that of monkeys, resulting from the combination of large mass and arboreal locomotion. They argue, however, that this is in fact a psychological development, with a direct influence on self-awareness.

Aside from mirror self-recognition, there is evidence from chimpanzees' behavior in the wild that they have some self-awareness. At the Taï site, male chimpanzees have been known to change their own and imitate others' characteristic vocalizations (Boesch and Boesch-Achermann 2000), suggesting that they recognize that aspect of themselves as distinct from others.

Deception and false belief

The most extensive evidence for putative theory of mind in the wild is from intentional deception, whereby an animal acts to create a false belief in a conspecific (de Waal 1992, Whiten and Byrne 1988). There is considerable evidence from many primate species, including chimpanzees, of several types of intentional or tactical deception, including concealment (e.g. of noises, facial expressions, or one's own attention),

distraction (shifting a conspecific's attention away from something of interest), and creating an image (that is, behaving in a way that will be misinterpreted) (Whiten and Byrne 1988). Deceptive acts like these can be interpreted as relying on representations of mental states. The agent, it is argued, understands the target's view of the world and acts to manipulate it. However, because inferences are made from behavior, that interpretation can never be certain. It is also possible that animals are acting only to influence others' behavior, without reference to mental states. Without experimental control, the two alternatives are difficult or impossible to tease apart.

One of the primary tests of theory of mind in humans is the false belief task, in which a child must understand that another person has a belief that differs from her own, and from the true state of the world. Call and Tomasello (1999) studied false belief in chimpanzees with a nonverbal version of this test. In this task, chimpanzees were presented with two containers, one of which was baited with food and marked by an experimenter; the subjects were allowed to choose between them. In the test condition, the containers were baited while the first experimenter watched, and then she left the room; while she was gone a second experimenter switched the containers so that when the first returned, she marked the wrong one. The chimpanzees, having seen the switch, failed to infer that the first experimenter had a false belief about where the food was hidden, and that they should ignore her mark—they did not pass this test. Children, by contrast, passed both this task and a traditional verbal version of the false belief test. The authors note as well that the chimpanzees passed multiple control trials involving each component of the false belief task, indicating that their failure was specific to

understanding the false belief, and not a failure to grasp some procedural aspect of the experiment.

Joint attention

While evidence for the attribution of most mental states by chimpanzees is equivocal, perhaps the best candidate for mental state attribution in that species is knowing what others can see (Tomasello et al. 2003). Human infants follow the gaze of others, and by the time they are toddlers they demonstrate a reliable understanding of the relationship between the eyes and attentional states of others (Povinelli and Eddy 1996). Chimpanzee infants also follow gaze (Okamoto et al. 2002) and prefer to look at faces with a direct gaze, rather than averted (Myowa-Yamakoshi et al. 2003). Like humans, chimpanzees (and other apes) follow gaze geometrically (Tomasello et al. 1999); that is, they follow another's gaze to its endpoint, rather than simply looking in the same direction until they see something interesting, and seem to be able to infer that opaque barriers obstruct another's line of sight (Bräuer et al. 2005, Povinelli and Eddy 1996). Chimpanzees follow the gaze of both humans and conspecifics (Tomasello et al. 1998). But whether chimpanzees extrapolate from gaze and attention to an understanding that seeing leads to knowing—that is, that it influences mental states—is debated.

In many instances, chimpanzees reliably use the gaze direction of human experimenters to obtain food with begging gestures. Presented with an experimenter who is attending either to a desirable food item or an undesirable distracter object, chimpanzees will gesture to the experimenter rather than simply to the food, presumably to influence her attention (Povinelli et al. 2003). Behaviors like this, however, are

significantly influenced by factors other than orientation of the eyes, suggesting that chimpanzees do not have a sophisticated grasp of the relationship between the eyes and subsequent knowledge and mental states—that is, a realization that seeing something is associated with an internal representation of it (Povinelli et al. 2000). A series of experiments show that chimpanzees have a rule-based understanding of others' attention, in which the eyes are a cue but not necessarily the most important cue (as they are for humans). In this paradigm, chimpanzees are presented with two experimenters who both have food, and must gesture to one of them. However, only one can actually see the chimpanzee. Several permutations are used: eyes open and closed, facing forward and backward, blindfolded and not, etc. In each condition the chimpanzees do gesture to the appropriate experimenter, but only after several trials, as if they are learning a rule to guide their behavior (e.g., gesture to the person whose face I can see) (Povinelli et al. 2000). Factors such as orientation of the head or body, body posture, or movements of the head (i.e. species-typical movements that chimpanzees make when attending to something) (Povinelli et al. 2002, Povinelli and Eddy 1996) are at least as important, or possibly more so, to chimps as orientation of the eyes for chimpanzees' understanding of attention.

Some authors suggest that experiments like these, for various reasons, are not ecologically valid ways to test chimpanzees' knowledge. For instance, an experimenter facing forward vs. backward is much more easily distinguished by chimpanzees as experimenters facing forward but only one with eyes open (Kaminksi et al. 2004); these authors note that as chimpanzees do not have a white sclera in their eyes, conspecifics' eyes may be much less salient for them and so are not a reliable signal of attention. Call

et al. (2000) argue that gaze is not an effective cue for chimpanzees to find food (e.g. when given a choice of several containers, only one of which is baited), because in the wild they are more likely to use cues such as vocalizations and physical proximity. They propose a "foraging mode" in which chimpanzees seeking food use many sources of information—gaze direction is one source, but not the most important one. Furthermore, Hare and colleagues (Hare et al. 2000, 2001) note that chimpanzees in the wild are in constant competition for monopolizable food sources, and would never point out food for a conspecific. Therefore, they argue, a seeing/knowing paradigm in which an experimenter indicates a baited container for a chimpanzee to choose is unlikely to produce positive results. A paradigm in which chimpanzees must compete for food, either with a conspecific or a human experimenter, is much more likely to tap into behaviors that reflect an awareness of the relationship between seeing and knowing.

In this paradigm, dominant-subordinate pairs must compete for food, some hidden, some visible (the subordinate individuals are the subjects in these studies). Two primary advantages of these studies over others are that chimpanzees are dealing with conspecifics rather than human experimenters, and that they do not require training to perform the task (that is, they do not have to learn the task during testing) (Hare et al. 2000). Subordinate subjects and dominant competitors are both released into a room with two pieces of food. In various permutations of the study conditions (Hare et al. 2000, 2001), food is hidden where only the subordinate can see it or where the dominant can see it; food is placed either behind an opaque barrier (hidden) or a behind a transparent barrier (not hidden); the subordinate is released before the dominant, forcing a choice independent of the dominant's behavior; or the dominant who has seen the hiding of the

food is replaced with a dominant who has not seen it. The authors report that subordinates successfully retrieve more hidden food than visible when the dominant has not seen its hiding, suggesting that they take into account what the dominant has seen.

In a similar paradigm, but with human experimenters instead of conspecifics, chimpanzees successfully obtained food from a competitive experimenter by concealing their actions (Hare et al. 2006, Melis et al. 2006). Given a choice between reaching through a clear or opaque tunnel to get food when a competitive experimenter is present, chimpanzees will preferentially choose the opaque tunnel. Similarly, they will choose a silent tunnel over one that makes a loud noise, presumably so as to avoid alerting the experimenter to their presence. These experiments go beyond asking whether chimpanzees understand that a competitor can see something, determining instead of chimpanzees will manipulate that information (Hare et al. 2006). Like the subordinate-dominant paradigm, these tests required no training or learning—the effects were present from the beginning of the experiments.

The competitive paradigm, then, does indeed produce positive evidence for chimpanzees' understanding of seeing and knowing, more so than paradigms that require chimpanzees to interpret cooperative signals from experimenters. However, two important critiques of this paradigm have been raised by Povinelli and colleagues. The first is methodological. In an attempt to replicate the findings of Hare et al. 2000, Karin-D'Arcy and Povinelli (2002) found that although subordinate chimps do indeed obtain more hidden food than visible, they do *not* preferentially approach the hidden food initially—instead, they take hidden food only after the dominant competitor has already taken the visible food. Their subjects also did not seem to distinguish between barriers

that did and did not actually obscure the competitor's view, suggesting that they simply prefer food that is not out in the open. Overall, they argue that postulating visual perspective taking on the part of the chimpanzees does not contribute any significant predictive power to interpreting their behavior.

The second critique is of the nature of the competitive paradigm itself. While it is true that this paradigm is more naturalistic and ecologically valid for chimpanzees, Povinelli and Vonk (2003) argue that these conditions do *not* provide better evidence than less natural studies for mental state attribution, because "these are the contexts for which evolution is most likely to have sculpted special-purpose, highly-focused behavioral representations for use by the organism" (p. 159). In this case, behavioral and mental explanations of the chimpanzees' response to the task will always be conflated.

Theory of mind in chimpanzees

As described above, two forms of theory of mind in humans are proposed: "theory theory" and "simulation theory." Evidence for either system in chimpanzees, however, is unclear. Again, the best evidence for any sort of mental state attribution in chimpanzees is from seeing and attention, but it is inconclusive. In their test of one chimpanzee's ability to attribute intentions, Premack and Woodruff (1978) explicitly rule out the use of empathy (which would fit with simulation theory)—the subject's choices in the test (matching videos of actors solving problems to that problem's solution) depend on the actor, and she is not simply choosing what she would do.

In the study of non-human primate social behavior, parsimony dictates that mentalistic explanations of behavior should not be invoked when simpler, non-

mentalistic explanations can also account for the data. At the same time, however, that rule leads to differing explanations for similar behaviors in humans (theory of mind) and non-humans (behavioral abstractions) (de Waal 1992). Tomasello and colleagues (2003) argue that mentalistic descriptions of chimpanzee behavior should not be dismissed "by noting that simpler explanations are hypothetically possible with no supporting evidence" (p. 24)—parsimony for parsimony's sake is insufficient for denying theory of mind in chimpanzees. However, although the differences are subtle, such low-level explanations are either equivalent to or better than high-level models for accurately predicting chimpanzees' behavior in a wide array of experimental tasks (Povinelli et al. 2000); Povinelli and colleagues explain the discrepancy with the reinterpretation hypothesis (Povinelli et al. 2000, Povinelli and Vonk 2003). By this hypothesis, the complex social behaviors that are seen in both chimpanzees and humans evolved early in their lineage, and were present in the last common ancestor. It was after they were already in place that humans evolved the means to mentally interpret those behaviors—the introduction of theory of mind. Mentalistic interpretation did not create drastically changed behavior, but rather provided a subtle (and more effective) means of re-organizing existing behaviors. Premack and Woodruff (1978) claimed that "the ape could only be a mentalist . . . he is not intelligent enough to be a behaviorist" (p. 526). However, while it is in fact very difficult for humans to interpret social behavior without reference to mental states, the same is not necessarily true of chimpanzees.

Comparative research methodology

Several methodological issues have constrained the comparative study of cognition and brain function in primates, including humans. First, invasive methods such as single-cell recording and surgical lesions cannot ethically be used on humans or great apes. Monkey models of brain function using these methods are often extrapolated to humans, but with the caveat that there is almost certainly not a one-to-one equivalence across species (Preuss 2000). Second, tests of cognition are difficult to employ in non-verbal species; their results are much more ambiguous than those of human experiments. Inferences must be made from behavior, which involves a layer of interpretation and bias that is far less prominent in studies of human cognition in which subjects can give verbal reports of their experience (although these reports cannot be entirely objective). In humans, functional neuroimaging has helped to bridge the gap between cognition and physiology, allowing researchers to correlate behavior with brain function. The most commonly used functional neuroimaging method, fMRI, has recently been used with monkeys trained to be restrained during scanning, but cannot be safely used with great apes due to their size and strength. The application of FDG PET to such studies represents one way to overcome some of these limitations.

Non-human primate models of brain function

Work with rhesus macaques (*Macaca mulatta*) has formed the foundation of non-human primate models of neuroanatomy and physiology. As described above, single-neuron experiments in macaques identified mirror neurons in this species (Rizzolatti 2005). These experiments place highly specific neural function (e.g. responding to a

particular and narrowly-constrained type of visual stimulus) within a framework that describes cognition on a larger scale. Brothers and Ring (1992) describe the collective function of such neurons as an “ensemble” of responses, adding up to a coherent whole. A social cognitive ensemble would be expected to contain neurons that respond to specific features of conspecific stimuli (such as recognizing biological motion or identifying faces), to somewhat more complex features such as the category of action or the identity of a particular individual, and to higher-level syntheses of these stimuli such as the intention behind actions (Brothers and Ring 1992). Such results are interpreted at a system level, though their components are dissociable and distinct (Brothers 2002).

A second approach to the study of social cognition (as well as other domains) in monkeys is experimental lesions placed in structures thought to be particularly important for these processes. Limbic structures are described as key in many social behaviors and interactions (Brothers and Ring 1992). The amygdala and surrounding temporal cortex in particular, in concert with the OFC, appear from lesion studies in monkeys to be critical for development of normal social behavior (Butter et al. 1970, Machado and Bachevalier 2003).

Functional neuroimaging of non-human primates

Invasive methods such as those described above cannot be used with either humans or endangered great ape species (chimpanzees, bonobos, gorillas, and orangutans). As these apes—chimpanzees and bonobos in particular—are the closest living relatives to humans, exploration of their cognition and brain function is likely the best way to elucidate the evolutionary history of our own. FDG PET represents a novel

method to bridge that gap between humans and great apes, in that it is uniquely feasible with these non-human primate species and able to reveal functional aspects of neurobiology. Briefly, FDG PET measures brain activity during an awake subject's behavior in a condition of interest. A radioactive isotope is taken up in the brain during this period of behavior, and trapped in active neurons. The decay of this isotope is then measured in the scanner after that period. During scanning, the subject can be sedated; this sedation does not affect the pattern of the trapped isotope. The image collected is of brain activity during the uptake period, *not* of brain activity while the sedated subject is in the scanner. (Note that sedation is not necessary for the scanning procedure itself, but rather only for the safety of the animal subject and of experimenters. As such this method can be used the same way in human subjects, allowing direct comparison across species.) These procedures, including the molecular processes that underlie the FDG PET methodology, are described in detail in the Methods section below.

FDG PET has an established history of use in monkeys (e.g. Eberling et al. 1995, Perlmutter et al. 1991), and recent studies have used this method in great apes (Parr et al. 2009, Rilling et al. 2007, Taglialatela et al. 2008, 2009). A key difference between FDG PET and other functional neuroimaging methods (such as fMRI) is that it measures glucose metabolism directly, rather than blood flow as a proxy for metabolism. This measurement is particularly informative as the relationship between blood flow and brain function—that is, the actual neuronal activity that underlies cognitive activity—is not necessarily a direct one-to-one correspondence. The associated consumption of glucose likely supports multiple ongoing processes, and comprises both oxidative phosphorylation and glycolysis in both neurons and astrocytes (Raichle and Mintun

2006). Raichle and Mintun (2006) caution against considering the signals observed in functional neuroimaging methods, particularly those measuring blood flow, as a direct representation of neuronal spiking activity. They suggest rather that it is *input* to neurons in advance of spiking (i.e. local synaptic activity) that accounts for much of the brain's glucose metabolism. These authors further argue that observed changes in blood flow or glucose metabolism in response to a task or other input should not be thought to reflect the majority of the brain's activity at that moment; instead, such changes represent a very small (no more than 5% – 10%) adjustment to the brain's overall metabolic activity. That is, changes in metabolic activity directly related to cognitive function are quite small relative to the brain's resting activity.

Chapter 2: Research Design and Methods

Research design

This study employs [^{18}F]-fluorodeoxyglucose positron emission tomography (FDG PET), a functional neuroimaging technique, to compare brain function in chimpanzees during two social cognitive tasks, a non-social cognitive task, and at rest. FDG PET is uniquely able to reveal brain function in awake and behaving great apes, and as such is a valuable tool for the study of chimpanzee neurobiology and cognition. Using a match-to-sample paradigm with video stimuli, chimpanzee subjects were tested on their ability to discriminate categories of behaviors, some social and some non-social. The neuroimaging data collected in these task conditions were compared to previously-collected images of a similar task with non-social stimuli, and of a resting state.

Hypotheses

Three hypotheses were developed, based on human functional neuroimaging studies and previous research on resting state brain activity in chimpanzees.

H1: The cortical midline areas (specifically, dorsal and ventral medial prefrontal cortex and medial parietal cortex) that are active at rest in chimpanzees should also be highly active during social cognitive tasks. However, because these tasks do involve an attentionally-focused state, some deactivation in these areas relative to rest is expected.

H2: These same cortical midline areas should be much *less* active during a non-social cognitive task than they are at rest, as well as somewhat less active during non-social cognition than they are during social cognition.

H3: Compared to a non-social cognitive condition, the social cognitive conditions should also active other areas—outside the default mode network—that are active during social cognition in humans. These areas include the insula, the amygdala, the superior temporal sulcus, and the temporo-parietal junction.

Subjects

Six adult chimpanzees (two female, age 14 – 21) at the Yerkes National Primate Research Center (NPRC) were trained for this study. Subjects were selected by availability in coordination with other studies being performed in the Chimpanzee Cognition Laboratory, and by training for the procedures involved in match-to-sample joystick testing. These chimpanzees have been extensively trained in the match-to-sample (MTS) paradigm and are familiar with the general structure of this method of testing (Parr et al. 2000). Most had been previously tested in tasks using video stimuli; one, however, was naïve to the use of videos in a task. The subjects have also been trained to accept injections by hand, minimizing the need for darting with sedatives.

These subjects are housed in adjacent enclosures with indoor and outdoor access, with auditory, visual, and limited physical contact with other chimpanzees in the Yerkes NPRC great ape wing. All subjects were raised in peer groups by humans at Yerkes, and were later transferred to permanent social groups with older animals. These rearing and

living conditions provide the necessary environment for normal social and cognitive development (Parr 2004). Two subjects (a male and female) were paired in one enclosure. Others shared enclosures with a single peer animal.

Creation of stimulus set

The videos used in these tasks were collected at the Yerkes NPRC field station, in Lawrenceville, GA. The field station houses two large chimpanzee social groups, and both were filmed. Wide arrays of behaviors, both social and non-social, were captured. Non-social behaviors included walking through the enclosure, climbing on the various structures in the enclosure, eating, manipulation of objects (e.g. toys), and self-grooming. Social behaviors included play, grooming, agonistic interactions (e.g. bluff displays), and sex.

The raw video footage was edited and standardized using Adobe Premiere software. Several hundred 5-second clips were produced, each 620 x 418 pixels. Still images were also captured from these videos, representing the full range of behaviors. These images were cropped and standardized at 300 x 300 pixels, using Adobe Photoshop.

From these videos and images, five tasks were created using custom software for MTS written in Visual Basic. In these tasks, only grooming, playing (social), walking, and climbing (non-social) videos and images were used, as these are very unambiguous behaviors and were well-represented in the available stimuli.

The first task, the *training* condition, paired videos with a still image from the same video (the match, or correct choice) and a still image from a different behavior

category (the foil, or incorrect choice). The trials in this condition represented a mix of all behavior types, both social and non-social. This condition was used to familiarize the subjects with the format of the task, specifically the use of video stimuli and still image choices.

The second task, the *transfer* condition, followed the same format, but with the match choice an image from a different video than the sample. For instance, a grooming sample video would be matched with a grooming still, but from a different video. The foil choices represented different behaviors from the sample and match. Again, social and non-social behaviors were mixed.

The remaining tasks—two *high social*, one *low social*—were used exclusively during PET scans, and used only social or non-social behaviors, respectively. (The condition using non-social behaviors is referred to as "low social" on the grounds that any stimuli involving conspecifics are likely to elicit some degree of social cognitive response from the chimpanzees, regardless of the behavior involved.) Previous research (Parr 2001) indicates that chimpanzees do in fact see videos as a representation of a real situation, validating the choice of video stimuli as a means of displaying conspecific behaviors.

In addition to the high social and low social study conditions, data were available in two additional conditions from previous studies: rest (subjects resting in the home cage without an experimenter present) and non-social (MTS using clip art with no social content).

Training of subjects

Each subject was tested two to three times each week with its cage mate present for most sessions, beginning with the training task. (Subjects and cage mates were separated for some training sessions, so as to replicate the conditions of scan days and habituate subjects to those procedures.) After reaching an arbitrary performance criterion of 75%, subjects were advanced to the transfer task. After reaching the same criterion on the transfer tasks, subjects were scanned once each in the *high social #1*, *high social #2*, and *low social* conditions. The order of these conditions was counter-balanced across subjects. While all subjects met the performance criterion on the training task, two (including the subject who had not previously been exposed to video stimuli) failed to reach performance levels above chance on the transfer task after several months of training. These two subjects were dropped from the study, leaving a sample size of n = 4 for the imaging study. In order to minimize stress from the scanning procedures (particularly the use of anesthesia) for the chimpanzees, subjects were scanned no more than once in a 30-day period. Every effort was made to maximize the elapsed time between scans for each subject, but these intervals varied across subjects based on their performance levels in the transfer task (i.e. subjects did not reach the criterion at the same rate, and some were scanned twice before others were ready to be scanned at all).

FDG PET methodology

FDG PET is a neuroimaging method that is uniquely able to capture functional imaging data in non-human primate species that cannot be safely scanned using fMRI; as such, it is a critical tool in the comparative study of brain function in humans and non-

human primates. Unlike other imaging methods that measure blood flow in the brain and correlate it with neural (and thus cognitive) activity, FDG PET measures glucose metabolism in neurological tissue directly.

Deoxyglucose (DG) is a glucose analog whose molecular structure has been altered so that it cannot be fully metabolized by neurons; it competes with both glucose and with hexokinase (the enzyme required for glucose metabolism, or phosphorylation) for uptake by active cells, and then becomes trapped in those cells when the metabolic process cannot be completed (Phelps 1979). For PET imaging, DG is labeled with a radioactive tracer (^{18}F) to create fluorodeoxyglucose (FDG); the decay of this tracer can be detected and measured by the scanner. The chemical properties that allow DG to become trapped in neurons are also present in FDG (Reivich 1978). The use of FDG requires that a number of assumptions be true (Huang et al. 1980). First, overall rates of glucose consumption in tissue must be constant across time. Second, FDG and glucose must be evenly distributed in tissue (that is, FDG should not be more or less abundant than glucose in any particular area). Finally, because it is not fully metabolized, the proportion of FDG to normal glucose in tissue must be small enough to not interfere with normal metabolic processes in a way that would be harmful to the subject.

Prior to a PET scan, FDG is administered to the subject (orally, intravenously, or intramuscularly) and is then taken up preferentially by the most active neurons during an uptake period in which the subject performs the task under study. The rate of uptake varies by administration method, and is largely complete at 50 – 60 minutes after oral dosing (Parr et al. 2009). Because of the chemical properties of FDG that prevent its metabolism in cells, it remains trapped in these active neurons. Thus, the functional

image collected in the scanner represents not current brain activity, but rather the activity during the uptake period; this allows the subject to be sedated if necessary during the scan itself without affecting the functional neuroimaging data collected. Note that in addition to the rates of glucose metabolism, the quantity of FDG that the subject absorbs will also influence the end data obtained (Raichle 1983).

The subject is scanned at the end of this uptake period. ^{18}F has a half-life of 110 minutes (Reivich 1978), providing an ideal timeframe for scanning following administration of FDG to the subject and the uptake period. The method does, however, become less accurate as more time is allowed to elapse between uptake and scanning (Huang 1981). As the ^{18}F trapped in the brain begins to decay, positrons are released that annihilate upon impact with electrons, releasing two 511-keV photons (Reivich 1978). These photons travel away from the annihilation site in approximately opposite directions, and are measured by radiation detectors in the scanner (Raichle 1983). The distance that the emitted positrons travel in tissue before annihilation varies from one to six mm, depending on the energy generated as the isotope decays, and this distance limits the ultimate resolution of the scan that can be obtained (Raichle 1983). However, ^{18}F decays with low energy relative to other isotopes used in PET imaging, allowing for comparatively high-resolution images (Lubberink et al. 1999).

It is the possibility of sedation that makes FDG PET a useful technique for studying non-human primates, particularly great apes. Apes are too strong to be safely imaged while awake; they cannot be restrained to prevent either movement artifact or potential injury to investigators. Therefore, methods such as fMRI that measure activity during the scanning period cannot be used with these species.

Acquisition of PET images

For each task-related PET scan, the subject was separated from its cage mate and locked inside alone in its home cage. (Cage mates were left together during rest scans.) Food was withheld, so that no glucose in the subject's bloodstream would compete with the radioactively-labeled glucose in the tracer. Testing for the scans was performed at a time of day when the great ape housing wing was typically quiet, after the animal care staff had finished any morning work. The road behind the housing wing was blocked off so that traffic outside would not disrupt testing.

A 15 mCi dose of FDG was administered to the subject at 11:30 AM for each scan. The FDG was administered orally, mixed with sugar-free Kool-Aid. After dosing, the subject was tested for 45-60 minutes. During testing, as with training, correct answers were reinforced with small amounts of sugar-free Kool-Aid. As the majority of FDG uptake occurs in the first 15 minutes after dosing, it was necessary for the subject to begin working within a few minutes of receiving the dose and to continue working steadily during that critical uptake period. If the subject did not test well, the scan was canceled. Performing fewer than 50 trials within the first 15 minutes of the uptake period was a rough criterion for cancelation. However, in almost every case the subjects tested readily and continued testing throughout the uptake period, with minimal disruptions. Three scans were canceled and rescheduled due to the subjects' reluctance to test; a fourth was canceled and rescheduled because of a computer malfunction.

At the end of the uptake period, Yerkes NPRC veterinary staff accessed the subject for sedation with 5 mg/kg Telazol. As these chimpanzees are trained to accept hand injections, in most cases the subjects were willing to present for an intramuscular

injection. When subjects would not present after a reasonable interval, they were darted with the sedative by the veterinary staff. One subject was darted for each of her three task-related scans; another subject was darted for one scan only. All others took injections by hand. After sedation, the veterinary staff prepared the subject for the scan. The subject was then transported by van to the Emory PET Center for image acquisition using a Siemens High-Resolution Research Tomograph (HRRT) (CPS, Knoxville, TN), with an approximate spatial resolution of 2.2 mm FWHM. (At the start of this research, the HRRT PET scanner was located in the Emory University Hospital; the majority of the scans were collected there. The scanner was later moved to a facility at the Wesley Woods center at Emory University. Both of these locations are approximately a five minute drive from the Yerkes NPRC main station.) Upon arrival at the scanner, the subject was intubated by the veterinary staff and given an IV bolus of propofol anesthesia (10 – 40 mg/kg/hour) via a catheter placed in the cephalic vein. The administration of propofol was maintained for the duration of the scanning procedure. The subject was then positioned in the scanner and two scans were collected: a transmission scan (duration of approximately 10 minutes) and an emission scan (approximately 20 minutes). Transmission data were collected with a Cs-137 point source. An attenuation image was reconstructed, segmented into air, tissue (water), and bone, and the Cs-137 attenuation coefficients were replaced with the appropriate 511-keV attenuation coefficients. Attenuation correction factors were determined by foreprojecting this image. The reconstructed image was produced in the Vinci file format.

At the conclusion of these scans the subject was removed from propofol anesthesia and transported back to the Yerkes NPRC. The subject was then allowed to

recover from sedation in its home cage under the veterinary staff's supervision, and remained alone in the home cage for 24 hours. The subject remained separated from its cage mate for two reasons: one, for the subject's safety during recovery from sedation, and two, to minimize the cage mate's exposure to radiation. On the morning after the scan, the subject, its cage, and the testing area were surveyed to ensure that all radiation was clear. After this survey, the subject and cage mate were reunited.

Acquisition of MR images

An anatomical magnetic resonance image (MRI) was collected from each subject for coregistration with the functional PET images and for improved anatomical localization of functional activations. Subjects were sedated in the home cage with 5 mg/kg Telazol (either by injection or darting, as described above) and transported by van to a Siemens Trio 3T scanner at Emory University Hospital. Upon arrival at the scanner, an IV propofol drip (10 mg/kg/hour) was administered through a catheter placed in the cephalic vein. A T1-weighted Magnetization Prepared Rapid Gradient Echo (MPRAGE) scan was acquired from each subject (repetition time (TR) 2,300 ms, echo time (TE) 4.4 ms, inversion time (TI) 1,100 ms, flip angle 8, three signals averaged) with voxel sizes ranging from 0.60 mm isotropic to 1.0 mm isotropic. Duration of the scans ranged from 20 to 40 minutes.

Analysis of PET images

Each PET image was converted from Vinci to Analyze format, using XMedCon. Each image was coregistered to that individual's structural MR image, using SPM5 (http://www.fil.ion.ucl.ac.uk/spm/) (Friston et al. 1995). All non-brain voxels were masked out of the PET image using a mask created from the subject's MRI. The subject's MRI was then spatially normalized to a template created from 11 (six female, age 14 – 22) chimpanzees' MR images; this spatial transformation was then applied to the masked PET image (Friston et al. 1995). This spatially normalized PET image was then masked a second time, using a mask created from all subjects' MR images that included only voxels representing brain tissue in all subjects. These procedures ensured that each PET image from each subject would be aligned to the same space, and would contain only brain voxels common to all subjects, so that later analyses would not entail comparison across subjects of brain to non-brain voxels. Each spatially normalized and masked PET image was then divided by its mean intensity value, setting the mean of each scan to one. Therefore, comparisons of regional cerebral glucose metabolism could be made across subjects, eliminating variation created by differential levels of FDG uptake, differing elapsed time between dosing and scanning, varying body mass, etc. These intensity-normalized images were smoothed at four mm FWHM. This smoothing kernel was determined by doubling the voxel size (in this case, 2 x 2 x 2 mm) of the original images, a standard practice for functional neuroimaging data (Worsley et al. 1992).

T-tests

Normalized and smoothed images were analyzed using a t-statistic contrast model in SPM5. Two main effects, condition (high social, low social, non-social, and rest) and subject, were assessed in this model. An explicit mask was included, eliminating both non-brain voxels and the cerebellum and brain stem. Initial results showing large activations in the cerebellum and brain stem motivated this masking, as these activations were thought to obscure any cortical or subcortical areas more relevant to the study's hypotheses about social cognition. Because of the small sample size, no corrections for multiple comparisons were included. A priori hypotheses justified relatively liberal thresholds of $p < 0.05$ and $p < 0.01$. In addition to contrasts comparing two conditions (e.g. high social #1 > rest), the social conditions were lumped together for comparison with the rest and non-social conditions (e.g. both high social and low social > rest).

A second t-test model was constructed with the same parameters (independence, variance, scaling, etc.) as the first, but with an explicit mask showing only voxels within a region of interest (ROI) defined by activation in the resting state, without a contrast. This ROI was created using the top 5% most active voxels in the average of all subjects' resting state images, as described by Rilling et al. (2007). This model allowed for more fine-grained analyses of the areas specifically hypothesized to vary according to the degree of social content in each study condition. In each of these models, functional activations were localized in the brain with reference to human brain atlases (Duvornoy et al. 1999, Roberts & Hanaway 1971).

Whole brain averages

In addition to analyses contrasting conditions, the four subjects' scans in each condition were averaged to create images representing only that condition's activity. These images were then thresholded to show the 5% most active voxels in each condition, as done in Rilling et al. 2007. These areas in each condition were compared both qualitatively (i.e. the anatomical extent of activation) and quantitatively (i.e. the absolute levels of activity in those voxels).

Subtraction contrasts

Within-subject comparisons were made via simple subtractions in SPM5, using the ImCalc function. For each subject, every condition was contrasted with every other condition by subtracting the intensity-normalized images (non-smoothed). For instance, Subject 1's normalized non-social scan was subtracted from that subject's normalized rest scan to create a rest > non-social contrast image, in which each voxel's value represented the difference in activity between the two conditions in that voxel. These contrast images were thresholded above zero to show only positive voxels—that is, those that had higher activity in the first condition—and again above an arbitrary value (e.g., 0.5) to show the voxels with the greatest difference between the two conditions.

In order to compare the aggregate of these contrasts in all subjects, the thresholded contrast images were then converted to binary maps in which each voxel with a difference value above the arbitrary threshold value was set to equal one, and all other voxels were set to equal zero. For each contrast, all subjects' binary contrast images were summed to create an overlap image. In this image, the value of each voxel

represented the number of subjects with a contrast value above the arbitrary threshold at that voxel. Thus, a voxel value of four indicated that all four subjects showed a difference at that voxel in the two conditions being compared.

Chapter 3: Results

Behavioral results

Six subjects were trained on the match-to-sample (MTS) task used in this study, and varied in their acquisition of task proficiency. Subjects were evaluated on their percentage of trials correct on the first training session, the number of training sessions to reach 65% correct (significantly above chance), and the number of training sessions to reach 75% correct (an arbitrary performance criterion) (Table 1). After reaching 75% correct on the training task, subjects were advanced to the transfer task (Table 2). After reaching 75% correct on the transfer task, subjects were considered eligible for scanning. When performance was assessed across stimulus categories, one subject (Patrick) showed a bias for grooming (i.e., was more likely to choose a grooming image than any other stimulus category). That bias was corrected by creating a new transfer task for him that did not include grooming foils. Otherwise, each type of stimulus was equally salient to the subjects. Two subjects (Faye and Lamar) failed to reach 75% correct in the transfer task after several months of training, and were subsequently dropped from the study. Scans were not collected from these subjects.

Table 1: Testing results, training task

Training task	Faye	Jarred	Katrina	Lamar	Patrick	Scott
% on first session	50%	62%	67%	58%	67%	54%
# of sessions to 65%	10	3	1	3	1	3
then # of sessions to 75%	4	0*	3	1	1	15

65% = significantly above chance. 75% = arbitrary criterion for advancement to next task.
*89% on day 3

Table 2: Testing results, transfer task

Transfer task	Faye	Jarred	Katrina	Lamar	Patrick	Scott
% on first session	60%	53%	67%	50%	60%	65%
# of sessions to 65%	16	2	1	3	8	1
then # of sessions to 75%	-	0*	3	-	13	11

65% = significantly above chance. 75% = arbitrary criterion for scanning eligibility.
*81% on day 2

In PET scan sessions, subjects were evaluated on percentage of trials correct and number of trials completed (Table 3). As each scan's testing session was of approximately equal duration (mean duration = 51 minutes), the number of trials completed is indicative of the subjects' latency in choosing a response in each trial. Increased latency, resulting in fewer number of trials completed, may be taken as a rough index of the subject's attentional state while testing. However, the number of trials completed and the percentage correct were not significantly correlated ($r^2 = .46$, $p = .14$), suggesting that a lower level of attention did not result in impaired performance. All

subjects performed at lower levels on the scanning tasks than during training. This effect is likely due to the presentation of all-novel stimuli in the scanning tasks. In this respect a scanning test session is similar to the first session of the transfer task, in that the task itself is familiar but the stimuli are not.

Table 3: Testing results, scanning sessions

Scanning sessions	Jarred	Katrina	Patrick	Scott
High social #1 percent correct	61%	57%	55%	55%
High social #1 number of trials	252	276	200	204
High social #2 percent correct	54%	57%	54%	n/a*
High social #2 number of trials	150	152	206	170
Low social percent correct	61%	62%	65%	63%
Low social number of trials	172	186	276	273

* Computer error prevented collection of task performance for this scan.

Overview of imaging results

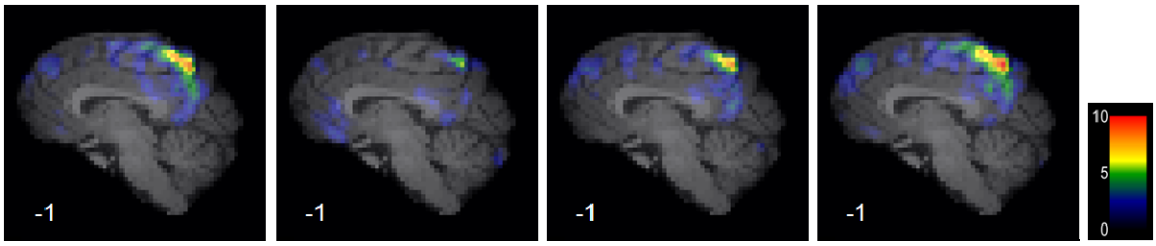
Three approaches were taken in analyzing the functional neuroimaging data in this study. First, paired t-tests were used to compare each condition to every other condition, and to compare the social conditions as a group to both the non-social and rest conditions. These t-tests were conducted across the whole brain, within the brain exclusive of the cerebellum and brain stem, and within a region of interest (ROI) encompassing the areas most active at rest, as determined by Rilling et al. (2007). Second, whole-brain activity in each condition (not contrasted with others) was explored,

revealing the overall most active areas in each. Third, simple subtraction contrasts were performed as a validation of the t-test models. The results of these analyses are reviewed in detail below, followed by a summary of the main findings.

T-tests in whole brain

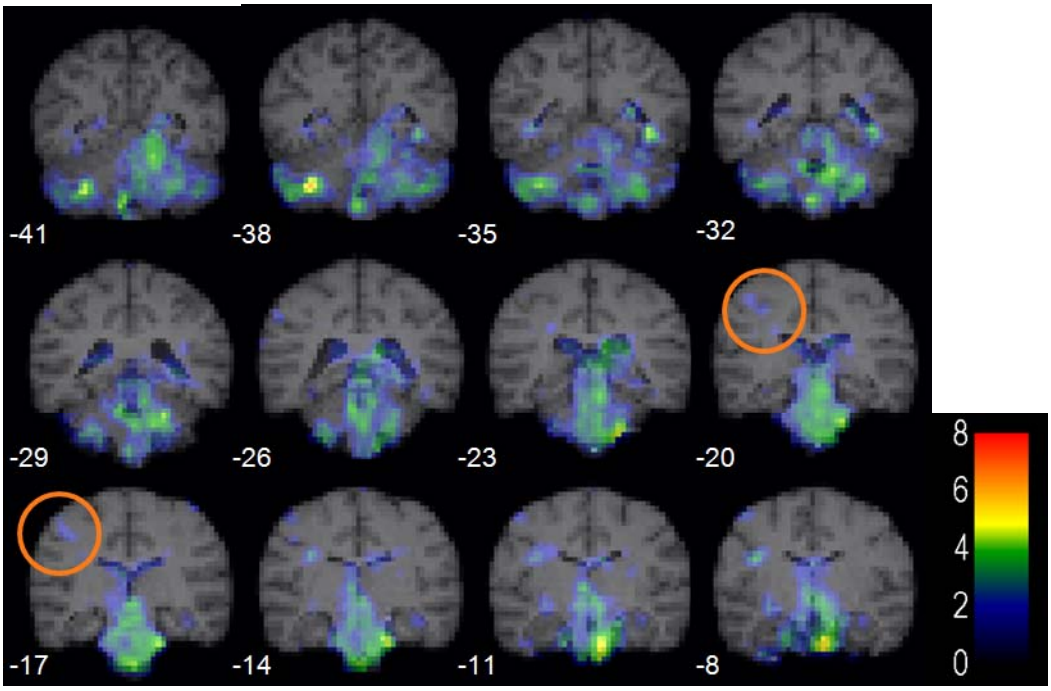
T-tests comparing the resting state with the task-related conditions within the whole brain primarily reflect the robusticity of the brain activity at rest described by Rilling et al. (2007). In contrasts in which any task is subtracted from rest, the active areas largely fall along the midline cortical areas (Figure 1). The activations during the task-related conditions relative to rest seem to reflect the visuo-motor demands of the task. Very large activations appear in the cerebellum, which is frequently implicated (in both human and non-human primate studies) in visual tracking of motor behavior (Miall & Reckess 2002, Miall et al. 1987), an apt fit for the subjects' matching of their motor control of the joystick with the visual stimulus of the cursor. Most subjects primarily used their right hands during scan testing sessions, and there is a corresponding (but small) active area in the left primary motor cortex for the contrast of all tasks > rest (Figure 2).

Figure 1: Whole brain contrasts, rest > each task



Left to right: rest > high social #1, > high social #2, > low social, > non-social.
Whole brain contrast (t-test, $p < 0.05$, uncorrected).
Color bar indicates value of t-statistic.
X-coordinates in millimeters from midline.

Figure 2: Whole brain contrasts, all tasks > rest



All tasks > rest.
Whole brain contrast (t-test, $p < 0.05$, uncorrected).
Primary motor cortex activation is circled in orange.
Color bar indicates value of t-statistic.
Y-coordinates in millimeters from anterior commissure. Left = left.

T-tests in whole brain, exclusive of cerebellum and brain stem

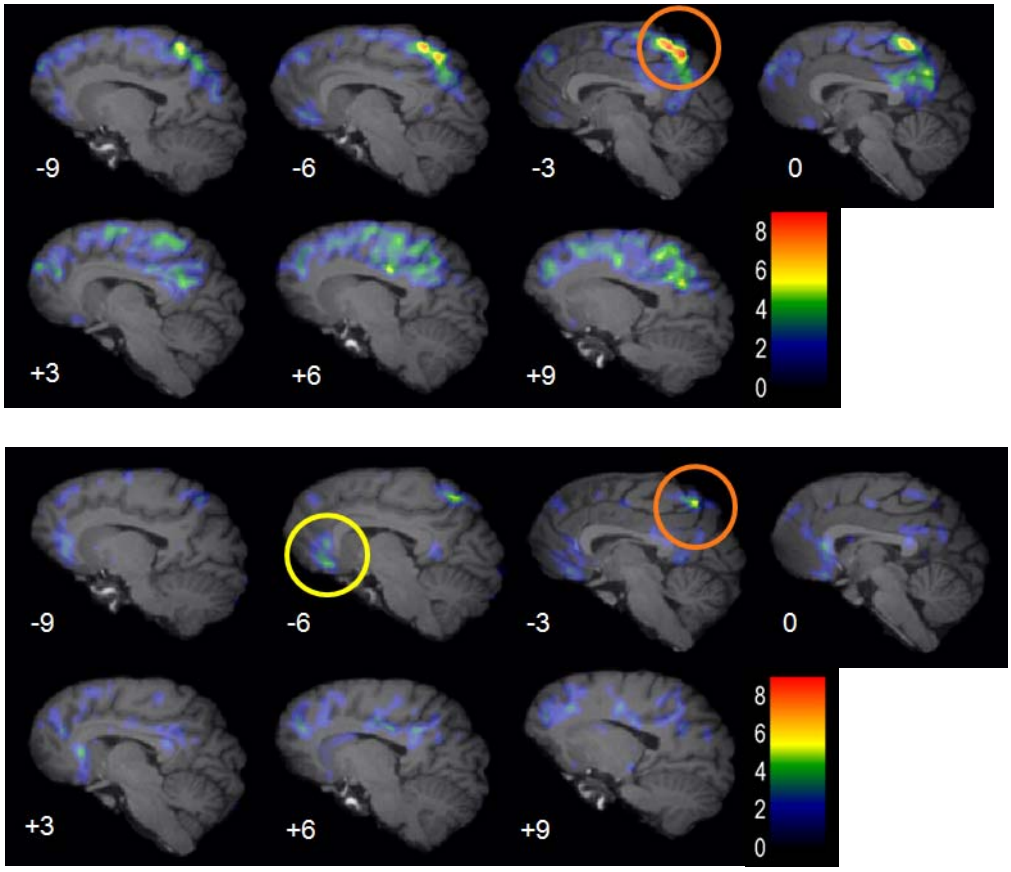
The large activations observed in the cerebellum and brain stem in whole-brain t-tests motivated a more constrained exploration within the cortex and subcortical structures including the basal ganglia, thalamus, amygdala, hippocampus, and hypothalamus. For these contrasts the cerebellum and brain stem were masked out so as to eliminate that activity's obscuring of other results. Unless stated otherwise, all results are thresholded at $p < 0.05$, uncorrected for multiple comparisons. This unusually liberal threshold has been used on account of the small sample size of the study ($n = 4$) and *a priori* hypotheses focusing on particular brain regions. Complete results for each contrast are presented in the Appendix, Table A1 and Figures A1 – A32.

Rest-related activity

The rest condition compared to the task conditions in this analysis (i.e. rest > high social #1, rest > high social #2, rest > low social, and rest > non-social) (Figures A17 – A20) shows much the same pattern of activation as in the whole brain analyses: cortical midline structures, including precuneus, posterior cingulate cortex (PCC), and anterior medial prefrontal cortex (MPFC), are most active. In addition, lateral parietal and lateral temporal activations appear in these contrasts. Rest > high social #2, however, shows some differences relative to the other task contrasts. First, one of the highest areas of activation in this contrast is in ventral medial prefrontal cortex (VMPFC) and orbital frontal cortex (OFC); other contrasts' activity in the MPFC is more dispersed from ventral to dorsal cortex, and is of a lower intensity. Second, while the voxel cluster of highest activation is in the precuneus as it is in other contrasts, it is smaller and has very

few nearby active voxels (Figure 3). Finally, there is more lateral activation in this contrast, in bilateral frontal, temporal, and parietal cortices. In addition to these anatomical differences in active areas, the rest > high social #2 contrast has a lower maximum t-statistic value (6.2) than do the other single task contrasts (9.2 for rest > high social #1, 8.6 for rest > low social, and 10.6 for rest > non-social), suggesting an overall greater similarity in these two conditions.

Figure 3: Rest > each high social condition



Rest > high social #1 (top) and rest > high social #2 (bottom).
T-test, $p < 0.05$, uncorrected.
Color bar indicates value of t-statistic.
X-coordinates in millimeters from midline.
Precuneus activations circled in orange; VMPFC activation circled in yellow.

High social-related activity

In high social #1 > low social (Figure A2), the area of highest activation is in the left ventral striatum. Other active areas include the right insula; left lateral temporal cortex; right inferior temporal gyrus (ITG), inferior temporal sulcus (ITS), middle temporal gyrus (MTG), and superior temporal sulcus (STS); and right inferior frontal sulcus (IFS). High social #1 > non-social (Figure A3) shows greatest activations in the precuneus, left lateral temporal and inferior frontal cortex, left ventral striatum, and bilateral primary visual cortex. High social #2 relative to both low social and non-social is similar to rest when contrasted with those tasks, with the most active voxels in the medial parietal cortex (particularly precuneus). In high social #2 > low social (Figure A6), this medial parietal activation extends laterally into the bilateral intraparietal sulcus and postcentral gyrus. In addition there are small activations in the left ventral striatum and left middle frontal gyrus (MFG). In high social #2 > non-social (Figure A7), the precuneus activation shows a similar, but less extensive, spread into lateral parietal cortex.

The differences between the two high social conditions are best illustrated by comparing them directly, and by examining each contrasted with rest (Figures 3, A4, A8). Each high social condition > rest shows active voxels in the fusiform gyrus and other complex visual processing areas (bilateral, but stronger on the right). The most active areas in high social #1 > rest, however, are overwhelmingly concentrated in limbic areas, particularly the hippocampus, hypothalamus, and left amygdala, as well as the thalamus. By contrast, while high social #2 > rest has a small thalamic activation, its

most active areas are in the left central sulcus, right precentral gyrus, and left ventrolateral prefrontal cortex (VLPFC).

High social #2 > high social #1 (Figure A5) is similar in the location and extent of its activations to high social #2 > low social and > non-social: the greatest activation is in the precuneus, and this activity extends bilaterally into lateral parietal cortex. High social #1 > high social #2 (Figure A1) shows the greatest level of activation in limbic areas, particularly the left amygdala (see also Figure 5c). Overall, the high social #2 > high social #1 contrast is very similar to rest > high social #1, rest > low social, and rest > non-social; the high social #1 > high social #2 contrast is similar to high social #1 > rest. These results further highlight the similarity of high social #2 and rest.

Low social-related activity

Low social > high social #1 (Figure A9) yields active voxels in the left insula and anterior superior temporal gyrus (STG); left MFG; medial superior frontal gyrus (SFG), precentral gyrus, and postcentral gyrus; right superior parietal gyrus (SPG), IPS, and IPG; and the dorsal extreme of the head of the right caudate, extending into white matter. This caudate/white matter region is also the most active area in low social > high social #2 and is highly active in low social > rest; in each of these contrasts, it is present at $p < 0.001$. The same activation is present in low social > non-social as well, but weaker (present at $p < 0.05$, but not at $p < 0.01$). Other active areas in low social > high social #2 (Figure A10) include medial subcortical structures (hypothalamus, septum, and anterior fornix) at $p < 0.01$, extending into medial temporal cortex (including hippocampus and amygdala) at $p < 0.05$. Low social > non-social (Figure A11), much like the high social conditions

contrasted with non-social, shows activation in the precuneus, although more limited in its extent than in the high social conditions. Low social > rest (Figure A12) is most active in the same medial subcortical areas as low social > high social #2, including the medial temporal lobe; it is also highly active in the fusiform gyrus and the extreme posterior precuneus. Overall, the pattern that emerges in the low social contrasts again suggests a similarity between high social #2 and rest (as these two conditions, when subtracted from low social, produce midline limbic activations), and the distinction between rest and the other task conditions. Its activity when compared to the non-social condition is similar but less extensive than the high social conditions contrasted with non-social, suggesting a real effect of varying degrees of social content in these tasks.

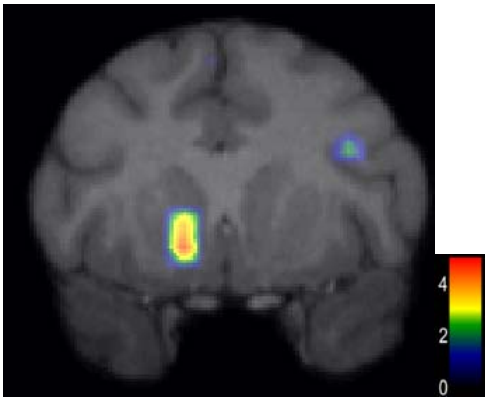
Non-social-related activity

Non-social contrasted with high social #2 (Figure A14) and with rest (Figure A16) are similar in patterns of activation, with midline subcortical structures and medial temporal lobe most active. In non-social > high social #1 (Figure A13), the right posterior STS is active, as well as the right IFG. The right cingulate sulcus is active from its posterior terminus to the approximate level of the anterior commisure. Non-social > low social (Figure A15) has a large activation in right precentral gyrus, extending ventrally into the lateral fissure and STG, and anteriorally into the IFG. Separate small activations appear in the right insula and bilateral marginal segment of the cingulate sulcus.

Combined social-related activity

In addition to these individual condition contrasts, the social conditions—high social #1, high social #2, and low social—were lumped together to form a social condition to compare with non-social and with rest. The two high social conditions were also lumped together and compared with low social, non-social, and rest. When both high social conditions are compared with non-social (both high social > non-social) (Figure A23), the dominant activation is the precuneus. Additional active voxels appear in the left lateral parietal cortex. Both high social > rest (Figure A25) is largely active in the hypothalamus and left amygdala. Relative to low social (both high social > low social) (Figure A21), the two high social conditions are active in the left ventral striatum (Figure 4), as well as bilateral SFG and left precentral gyrus. In low social > both high social (Figure A22), the greatest activity by far is in the right dorsal aspect of the head of the caudate, extending into white matter, as in other contrasts with this condition (e.g. low social > rest). Non-social > both high social (Figure A24) is primarily active in the right precentral gyrus. Rest > both high social (Figure A26) is strongly active in the precuneus and posterior cingulate, with additional activity in the anterior MPFC (particularly ventral) and right posterior STG.

Figure 4. High social > low social



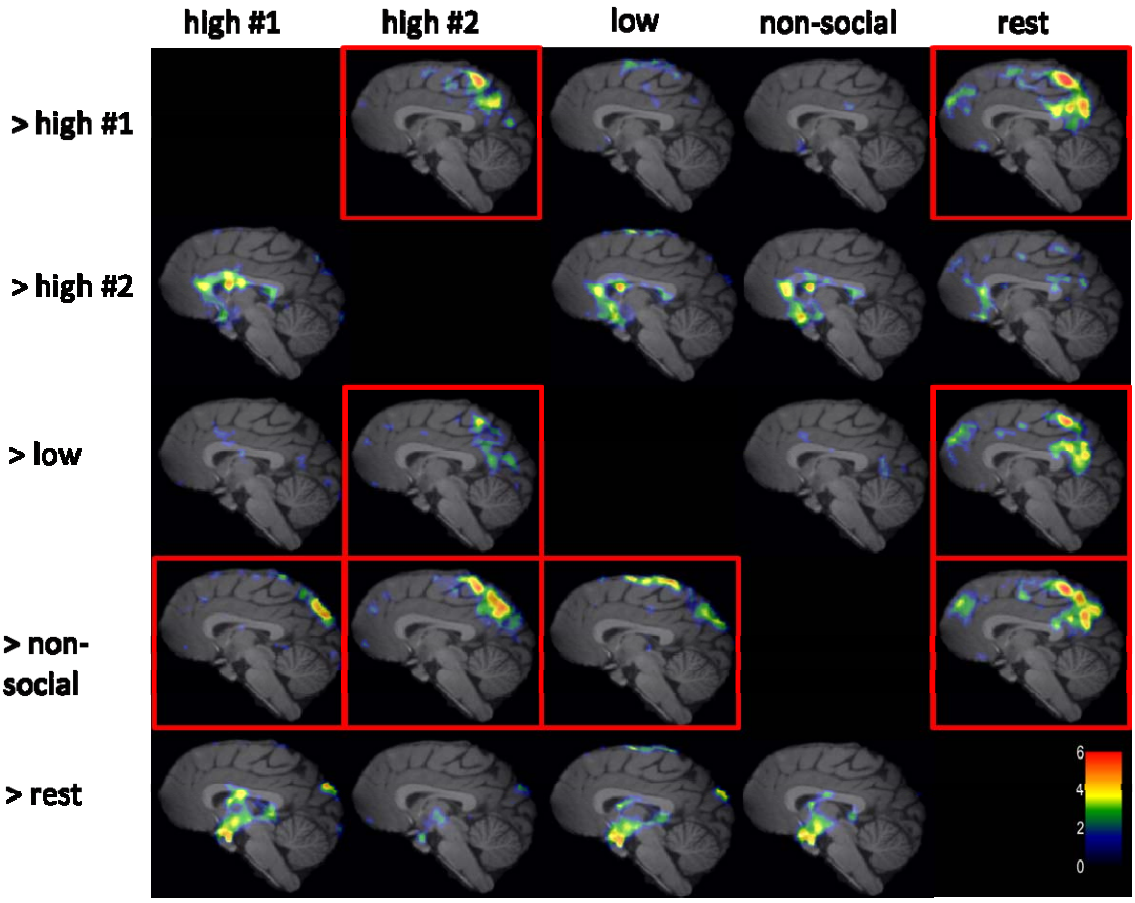
T-test, $p < 0.05$, uncorrected.
Color bar indicates value of t-statistic.
Y = 10 mm anterior to anterior commissure.

When all social conditions are compared with non-social (all social > non-social) (Figure A27), the dominant activation is again in the precuneus and posterior cingulate. Additional activations appear in the left dorsolateral prefrontal cortex (DLPFC) and IFS, and bilateral superior and inferior frontal gyri. Much like other contrasts between task conditions and rest, all social > rest (Figure A29) shows primarily medial subcortical activations (particularly the hypothalamus) and left amygdala and hippocampus. The fusiform gyrus is also active bilaterally, but much more strongly on the right. Rest > all social (Figure A30) does not differ significantly from rest > both high social.

Summary of t-tests

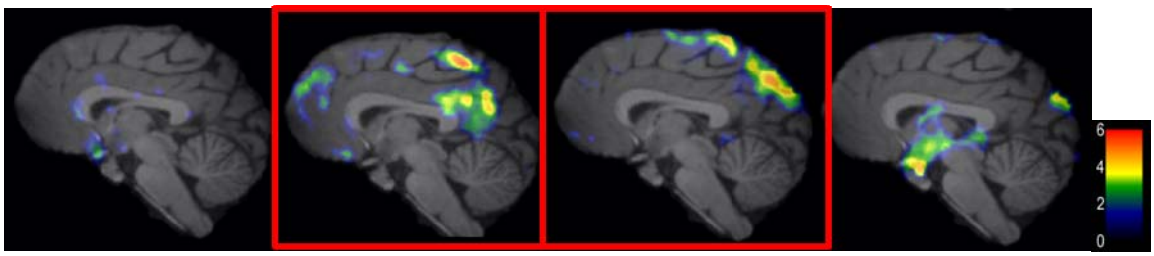
Overall, two distinct patterns of activation emerge from these results: one in which cortical midline structures, particularly the precuneus, are most active, and a second in which limbic midline structures and medial temporal lobe, particularly the amygdala, are most active (Figures 5a, 5b, 5c, 5d, 5e). In this second pattern, the amygdala activity is typically left-lateralized. While not every contrast fits one of these patterns of activity, and each has distinctive activations, the two patterns suggest a way to broadly categorize these study conditions.

Figure 5a: Cortical midline activations in individual contrasts



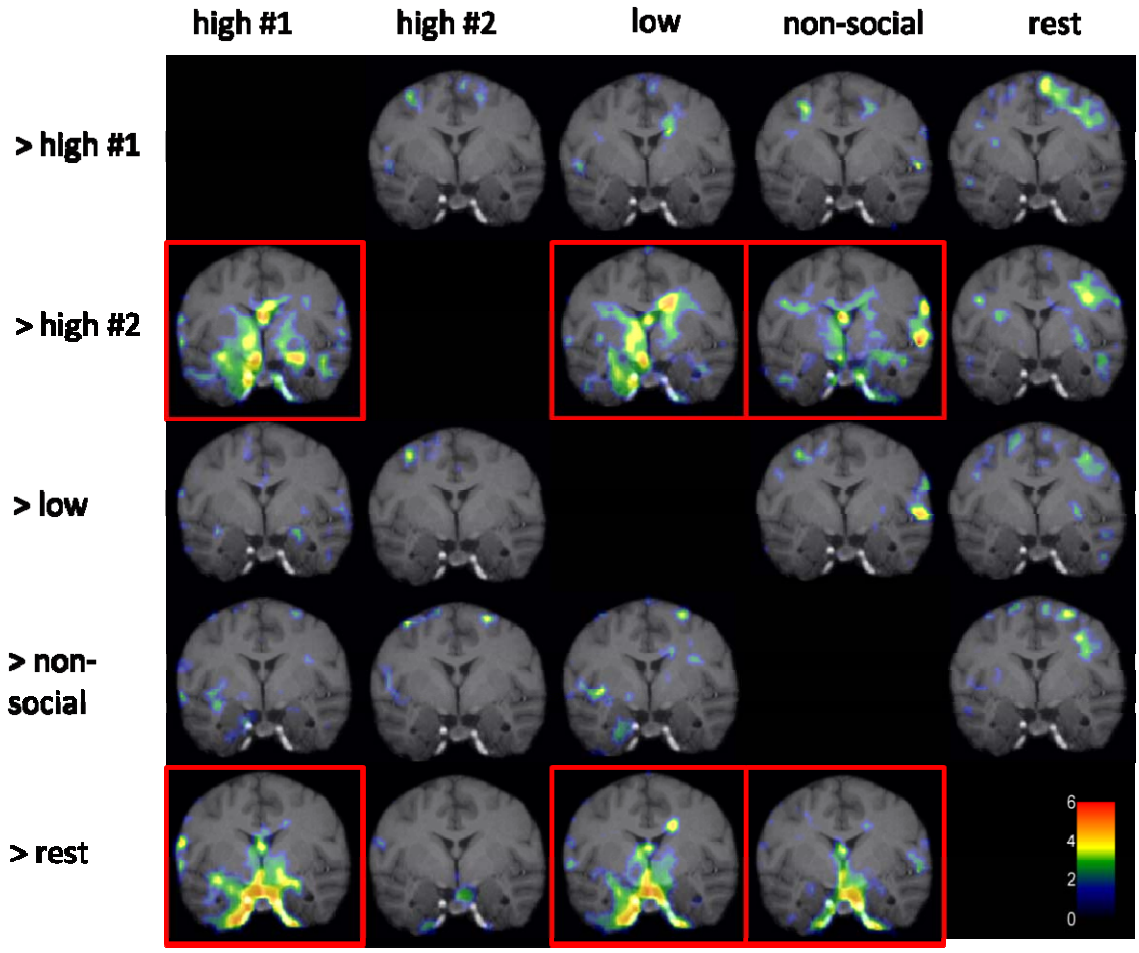
T-test, $p < 0.05$, uncorrected. Contrasts presented as row > column.
Contrasts with cortical midline structures most active are highlighted in red.
Color bar indicates value of t-statistic. For clarity of presentation, all t-statistic values above 6.0 are presented as red. See Appendix, Table A1, for maximum t-statistic values in each contrast.
X = 0 (midline).

Figure 5b: Cortical midline activations in combined social conditions contrasts



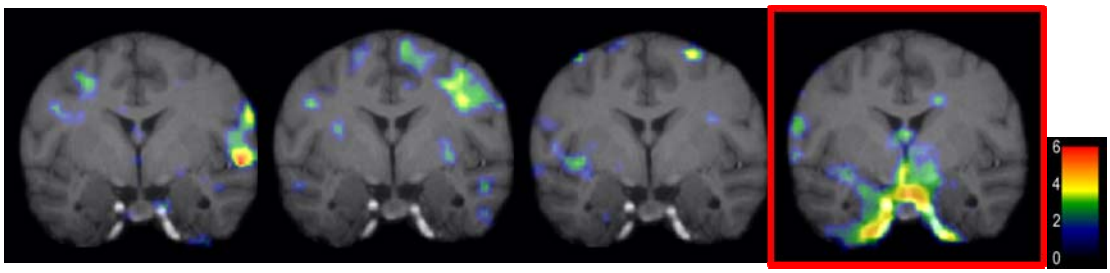
Left to right: non-social > all socials; rest > all socials; all socials > non-social; all socials > rest.
T-test, $p < 0.05$, uncorrected.
Contrasts with cortical midline structures most active are highlighted in red.
Color bar indicates value of t-statistic. For clarity of presentation, all t-statistic values above 6.0 are presented as red. See Appendix, Table A1, for maximum t-statistic values in each contrast.
X = 0 (midline).

Figure 5c: Limbic midline activations in individual contrasts



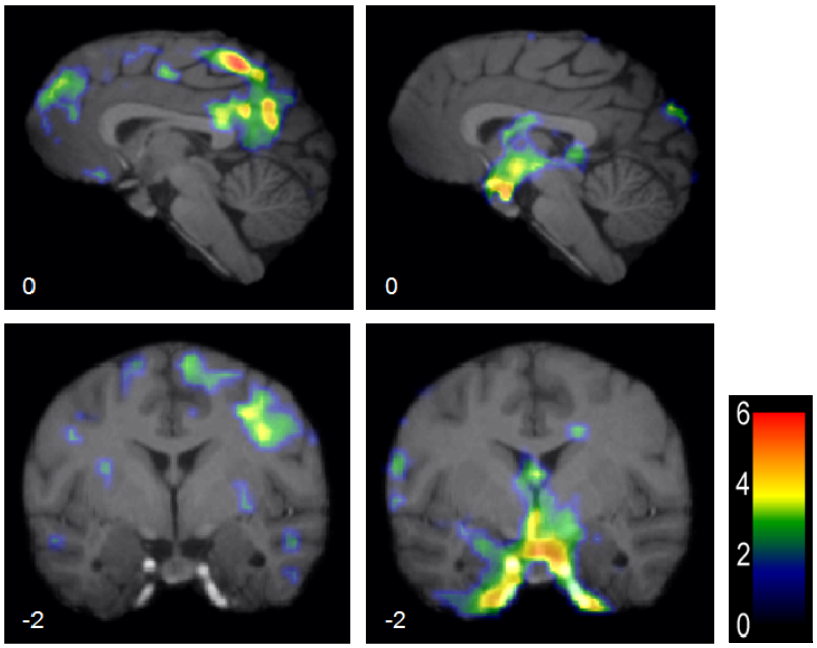
T-test, $p < 0.05$, uncorrected. Contrasts presented as row > column.
Contrasts with limbic midline structures most active are highlighted in red.
Color bar indicates value of t-statistic. For clarity of presentation, all t-statistic values above 6.0 are presented as red. See Appendix, Table A1, for maximum t-statistic values in each contrast.
Y = 2 mm posterior to anterior commissure. Left = left.

Figure 5d: Limbic midline activations in combined social conditions contrasts



Left to right: non-social > all socials; rest > all socials; all socials > non-social; all socials > rest.
T-test, $p < 0.05$, uncorrected.
Contrasts with limbic midline structures most active are highlighted in red.
Color bar indicates value of t-statistic. For clarity of presentation, all t-statistic values above 6.0 are presented as red. See Appendix, Table A1, for maximum t-statistic values in each contrast.
Y = 2 mm posterior to anterior commissure. Left = left.

Figure 5e: Rest vs. all tasks



Left column: rest > all tasks. Right column: all tasks > rest.
T-test, $p < 0.05$, uncorrected.
Color bar indicates value of t-statistic. For clarity of presentation, all t-statistic values above 6.0 are presented as red. See Appendix, Table A1, for maximum t-statistic values in each contrast.
X = 0 (midline). Y = 2 mm posterior to anterior commissure. Left = left.

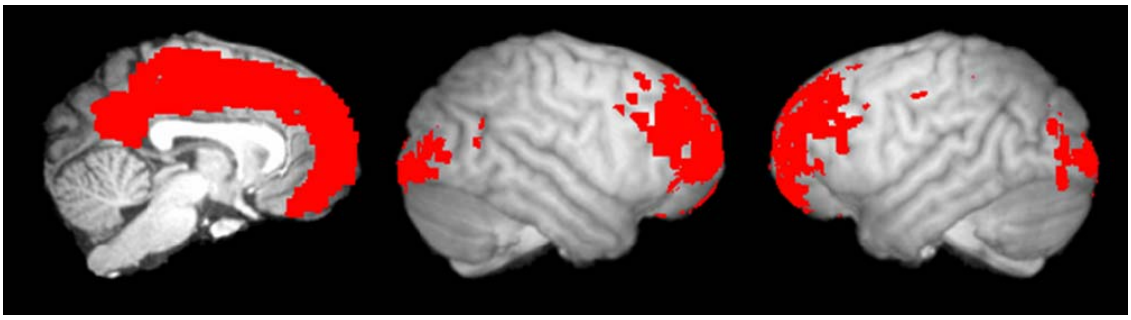
In these figures, note the similarity between rest contrasted with each task condition and high social #2 contrasted with the other task conditions. The second pattern of activation—limbic midline structures most active—primarily maps on to task-related activity, and may represent a general "task-positive" network in chimpanzees. By contrast, the rest-related activation seen in the first pattern—cortical midline structures most active—suggests a "task-negative" network. Further, social stimuli often (but not always) pull the functional activity seen here closer to this "task-negative" state. This is most clearly seen when high social #2 is compared to other tasks, and when all the social

conditions are compared together to the non-social task. It is here that the second high social task's similarity to rest is most evident.

T-tests within resting state ROI

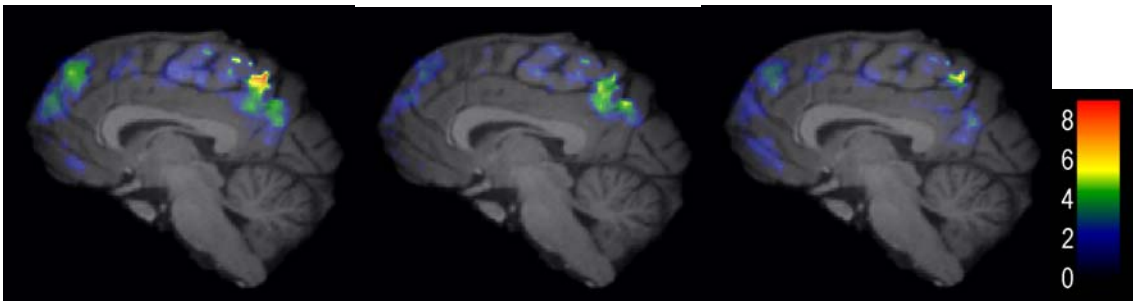
A priori hypotheses based on human default mode network literature predicted similar activity in the chimpanzee brain at rest and during social cognition, or possibly even greater activity in social cognition in the cortical midline structures associated with the default mode. Thus, it stands to reason that if those conditions are in fact quite similar, a contrast of social cognition greater than resting activity would be misleading: rather than showing the areas most active during social cognition, it would instead simply show the areas that are *least* active during rest. To examine this effect, contrasts between conditions were viewed only within a region of interest (ROI) created from the top 5% most active voxels at rest. This ROI encompasses medial cortex including anterior PFC (both ventral and dorsal), the cingulate gyrus and adjacent cortex, posterior cingulate cortex, and the precuneus; bilateral dorsolateral frontal cortex; and small clusters of bilateral parietal cortex (Figure 6). Complete results for each contrast are presented in the Appendix, Figures A33 – A64.

Figure 6: Resting state ROI.



Within this ROI, the contrasts rest > non-social, rest > all social, and all social > non-social (Figures A52, A62, A60) show highly similar patterns of activation. However, both the anatomical extent of activation (at $p < 0.05$) and the intensity values of the active voxels are greatest in rest > non-social, and least in rest > all social. The most active areas in each of these contrasts are midline cortical structures; in particular, the precuneus is the most active area in each, followed by the dorsomedial prefrontal cortex (DMPFC) extending toward the frontal pole. This frontal activation is both more extensive and has a greater intensity value in rest > non-social than in social > non-social, although the active areas in each contrast overlap (Figure 7). In addition, each contrast shows small clusters of active voxels in bilateral DLPFC.

Figure 7: Rest and social activity in the resting state ROI



Left to right: rest > non-social, rest > all social, all social > non-social.
T-test within resting state ROI, $p < 0.05$, uncorrected.
Color bar indicates value of t-statistic.
Precuneus activations circled in orange; DMPFC activation circled in yellow.
X = -3.

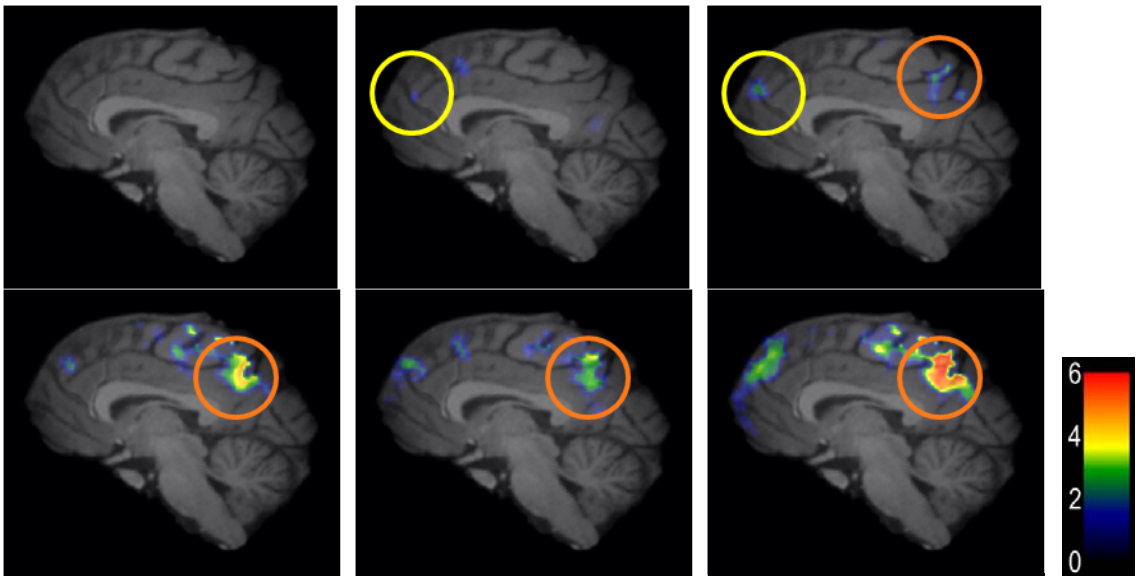
Other contrasts within the rest ROI reflect the same pattern: the task conditions with highly social content generally show higher activity than either the low social or non-social tasks, and the low social task condition shows higher activity than non-social. The levels of activity at rest are greater than in all other conditions. See Appendix figures for detailed results.

High social #1 > low social (Figure A34) shows a small cluster of active voxels in PCC, and a smaller cluster in the cingulate sulcus, superior to the corpus callosum. High social #1 > non-social (Figure A35) shows small clusters of activation in the precuneus and anterior MPFC. There are no results in high social #1 > rest.

The patterns of activation in high social #2 are similar in many ways to those in high social #1, but also show significant differences (Figure 8). Overall, its activations relative to both low social and non-social are similar, but more extensive. High social #2 > low social (Figure A38) shows active voxels in anterior MPFC and PCC, extending into the precuneus. High social #2 > non-social (Figure A39) shows activity in these

same areas, but to a greater extent. In addition, this contrast shows activity in left dorsolateral frontal cortex. A comparison of the two high social conditions themselves shows striking differences between the two. While high social #1 > high social #2 (Figure A33) has only a few active voxels—and none in cortical midline structures—high social #2 > high social #1 (Figure A37) has the same precuneus activation that is seen in that condition contrasted with low social and non-social, as well as a small cluster in anterior DMPFC. Again, it appears that high social #1 is much more similar to the two other task conditions than it is to high social #2.

Figure 8: High social #1 vs. high social #2 in resting state ROI



Top, left to right: high social #1 > high social #2, > low social, and > non-social.
Bottom, left to right: high social #2 > high social #1, > low social, and > non-social.
T-test within resting state ROI, $p < 0.05$, uncorrected.
Color bar indicates value of t-statistic.
Precuneus activations circled in orange; DMPFC activations circled in yellow.
X-coordinates in millimeters from midline.

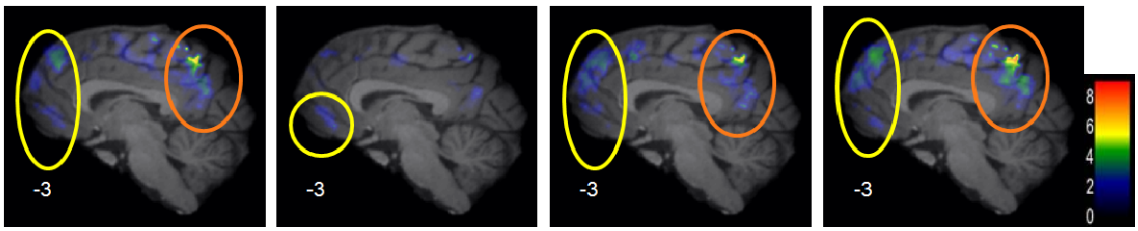
The low social > high social #1 (Figure A41) contrast has a few scattered active voxels, primarily in the medial precentral gyrus. Low social > either high social #2 or rest, or greater than both high social conditions lumped together, has no results. Low social > non-social (Figure A43) has activations in the precuneus, but these clusters are not as extensive as those seen in the high social > non-social contrasts.

The non-social task contrasted with low social (non-social > low) (Figure A47) shows a small cluster of activity in PCC, bordering the precuneus. The non-social condition shows very little activation relative to the three social conditions lumped together (non-social > all social) (Figure A60) at $p < 0.05$ (one small cluster in right

dorsolateral frontal cortex), and none relative to rest or to either high social condition alone.

Rest, when compared to each task condition (Figures A49 – A52), is highly active in midline cortical areas, particularly anterior MPFC (both dorsal and ventral), precuneus, and PCC (Figure 9). These activations are similar in each task's contrast (rest > high social #1, rest > high social #2, rest > low social, and rest > non-social), but much less extensive relative to high social #2 than to the others. In that contrast, the most active voxel clusters are in VMPFC and the precuneus.

Figure 9: Rest > each task in the resting state ROI



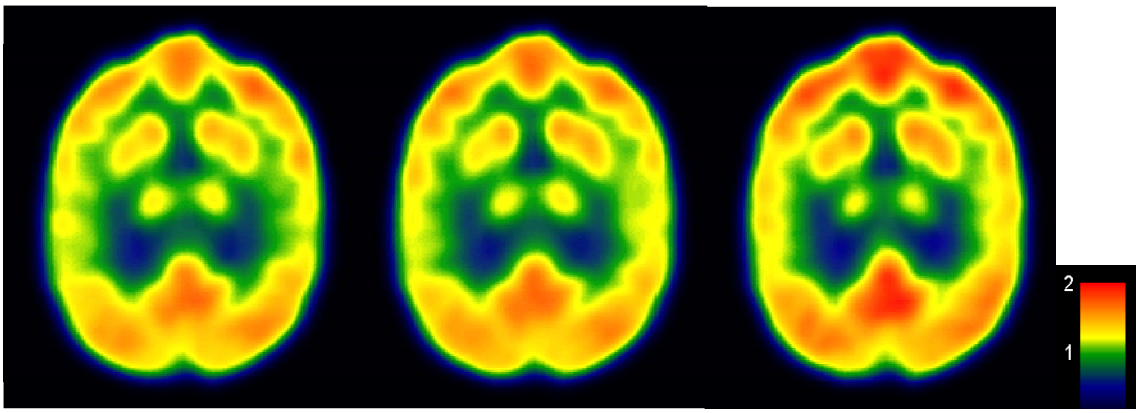
Left to right: rest > high social #1, > high social #2, > low social, and > non-social.
T-test within resting state ROI, $p < 0.05$, uncorrected.
Color bar indicates value of t-statistic.
Precuneus activations circled in orange; MPFC activations circled in yellow.
X-coordinates in millimeters from midline.

Whole brain averages

For each condition, activity in the whole brain was examined without performing any contrast. This allowed for an exploration of both qualitative similarities and differences among each condition, and a quantitative analysis of the absolute intensity values in each condition.

The most striking finding from this analysis is that while each condition shows very similar patterns of activity (i.e. the same areas are most active in each condition), the rest condition's intensity values are consistently higher in the areas of greatest activation than those of the other conditions (Figure 10). Because the intensity values of each image were normalized to that image's mean, all images in the final analyses have the same mean value (mean = 1). The average rest image, however, has a greater range of values than do the other conditions' averages. See Appendix, Figures A65, A66, and A67, for detailed results.

Figure 10: Whole brain averages.

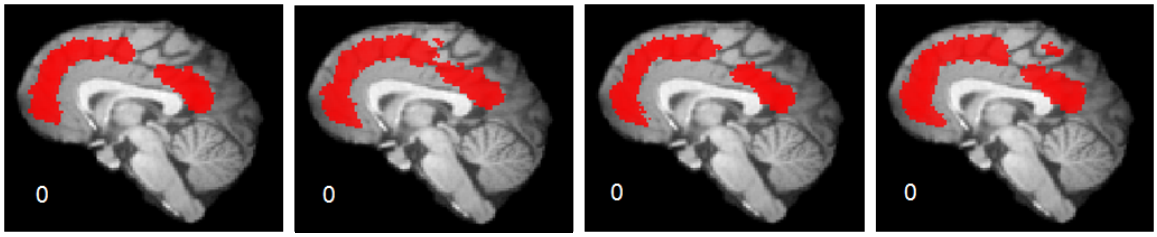


Left to right: non-social average, social average, rest average. Color bar represents intensity value. See Appendix for whole brain results. Z = 10 mm superior to anterior commissure.

Each condition's average image was thresholded to show the top 5% most active voxels, with the same method used to create the resting state ROI described above. A qualitative comparison of the most active areas in each condition shows a very high

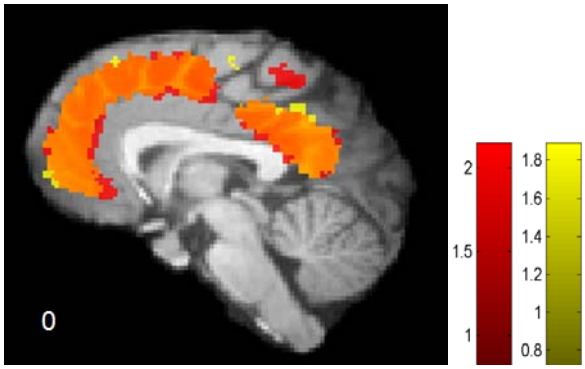
degree of similarity: in each condition, the most active voxels are in cortical midline areas (very similar to the medial portion of the default mode network described in humans) (Figure 11). Although the anatomical extent of activation was similar in each condition, the threshold value—the normalized intensity representing the minimum value in the top 5%—was higher at rest (Figure 12).

Figure 11: Top 5% most active voxels in each averaged condition.



Left to right: both high social, low social, non-social, rest.

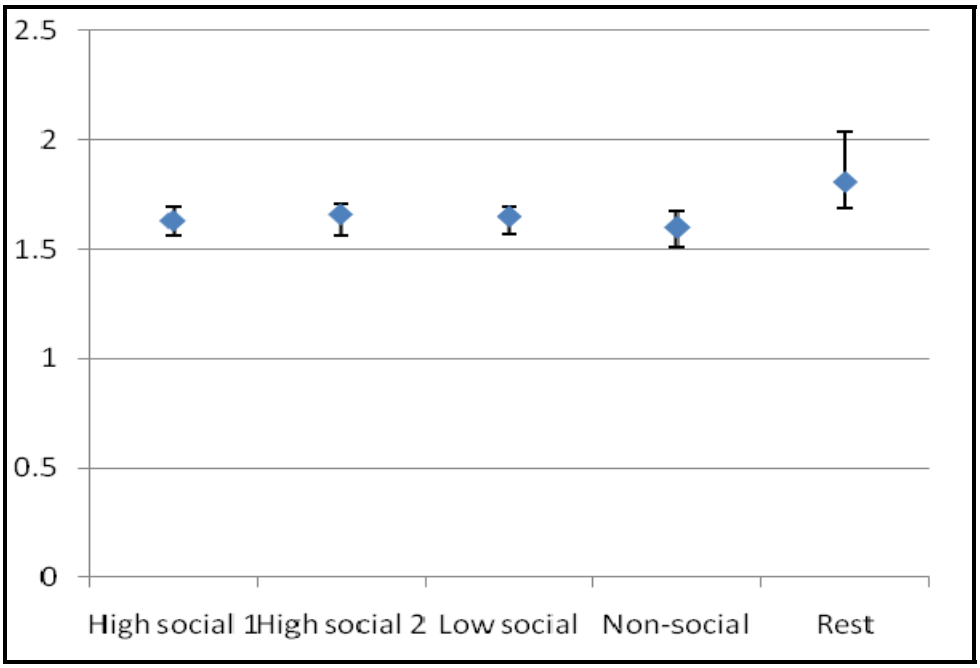
Figure 12: Overlap of top 5% most active voxels in all social conditions and rest.



Red = rest, yellow = all socials.
Orange indicates overlap.
Color bars indicate intensity values.

An ROI was created to represent the voxels common to each condition's top 5% most active areas, and both the condition average and individual scans' intensity values were compared within this region (Figure 13). The four task conditions' minimum, mean, and maximum intensity values were all similar, and all significantly lower than those values in the rest condition (Table 4). In addition, the standard deviation of intensity values in the rest condition was higher than those of the other conditions.

Figure 13: Condition average means within the top 5% common ROI.



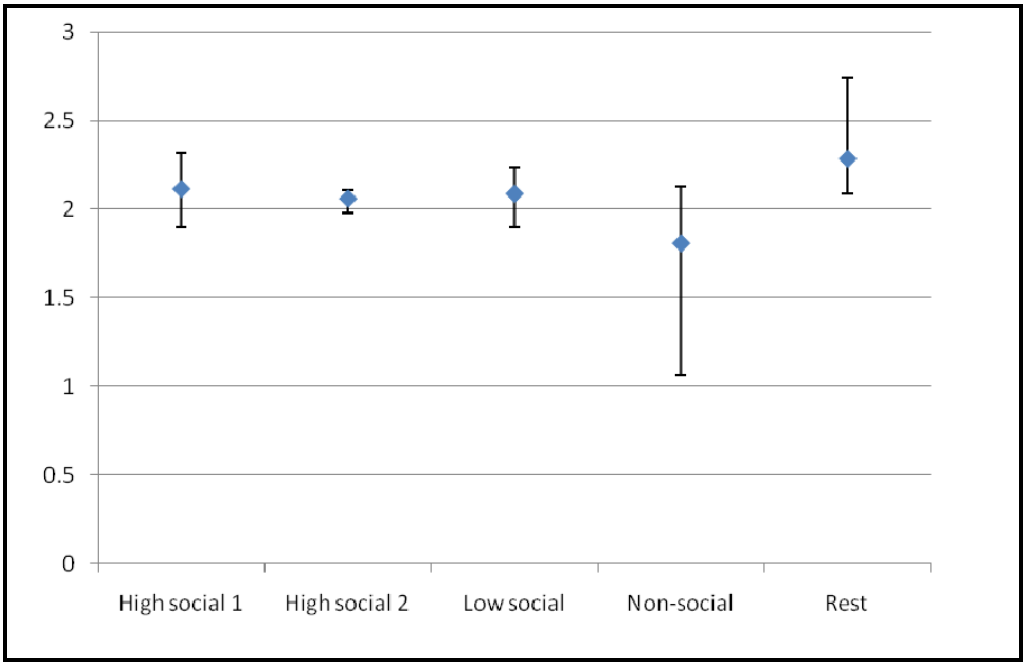
Error bars represent range of mean values across subjects.

Table 4: One-way ANOVA comparison of condition average means in the top 5% common ROI.

Conditions	Significance level
Rest/ high social #1	**p = 0.015**
Rest/ high social #2	**p = 0.035**
Rest/ low social	**p = 0.024**
Rest/ non-social	**p = 0.006**
High social #1/high social #2	p = 0.682
High social #1/ low social	p = 0.823
High social #1/non-social	p = 0.655
High social #2/ low social	p = 0.852
High social #2/non-social	p = 0.397
Low social/ non-social	p = 0.505

Maximum intensity values and standard deviations were also compared in the whole brain for each scan (Figure 14). (In the whole brain, the minimum value for each scan is zero, and the mean for each is one.) Again, the rest condition shows a higher maximum value, although this difference was not statistically significant (Table 5). However, it should be noted that there is an overall larger spread of variation in the whole brain averages, with larger standard deviations in each condition. Histograms of the intensity values in each condition's averaged image show a skew toward higher values in the task-related conditions, but a more even spread at rest (Figure 15).

Figure 14: Condition maxima within the whole brain.

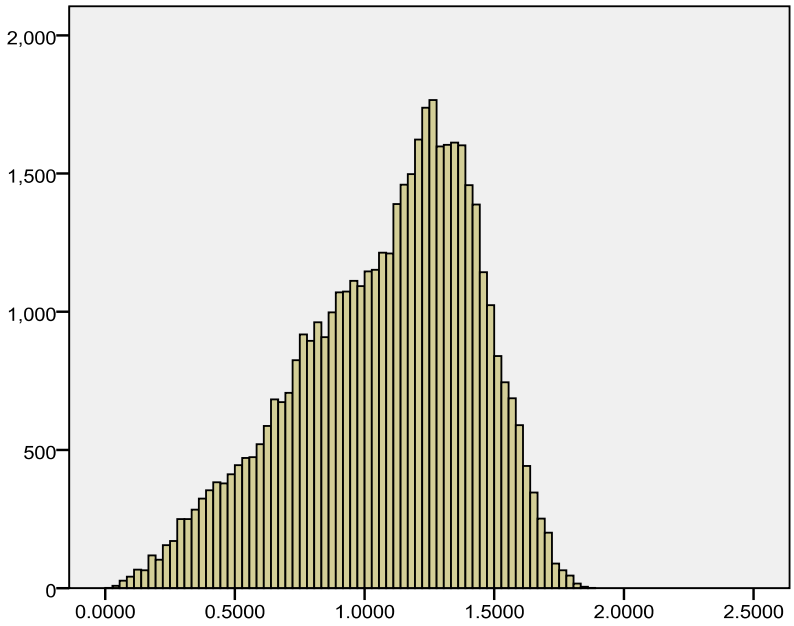


Error bars represent range of maximum values across subjects.

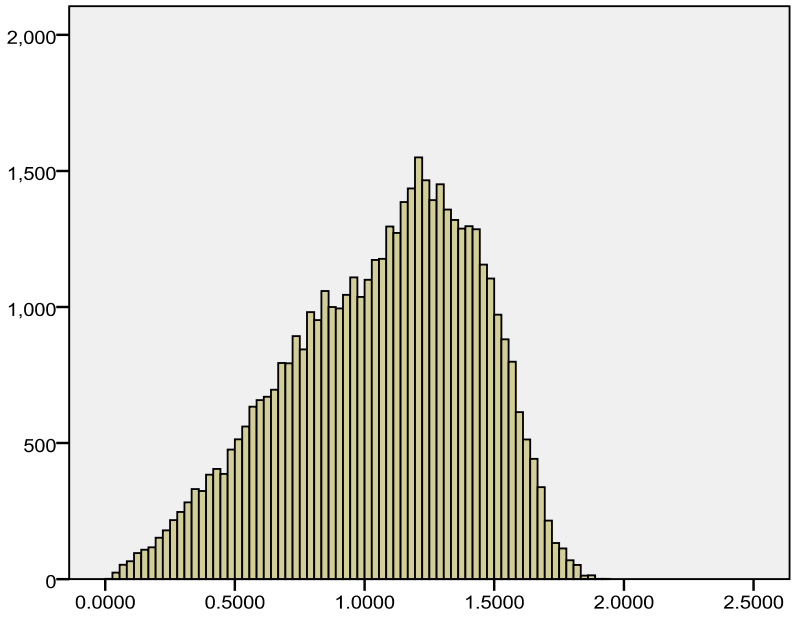
Table 5: One-way ANOVA comparison of condition maxima in the whole brain.

Conditions	Significance level
Rest/ high social #1	p = 0.549
Rest/ high social #2	p = 0.429
Rest/ low social	p = 0.487
Rest/ non-social	p = 0.377
High social #1/high social #2	p = 0.845
High social #1/ low social	p = 0.922
High social #1/non-social	p = 0.770
High social #2/ low social	p = 0.922
High social #2/non-social	p = 0.922
Low social/ non-social	p = 0.845

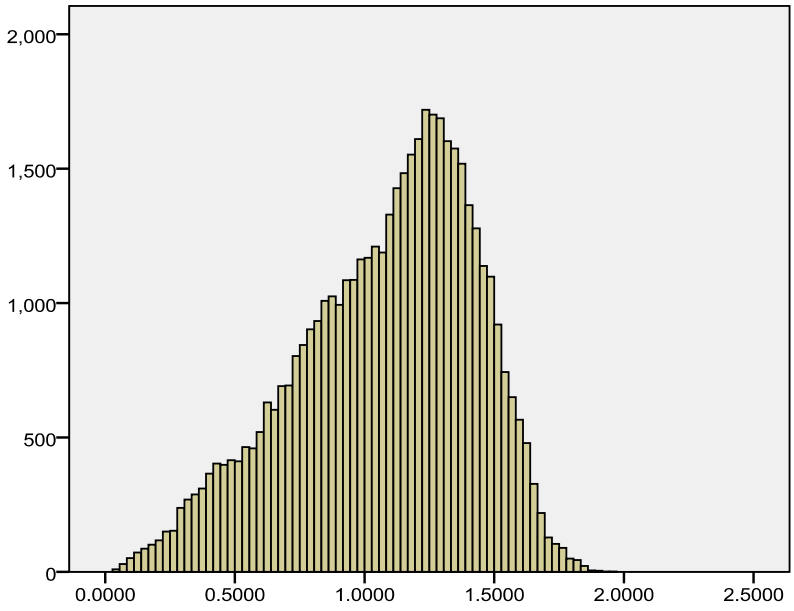
Figure 15: Spread of voxel values in each condition's whole-brain average.



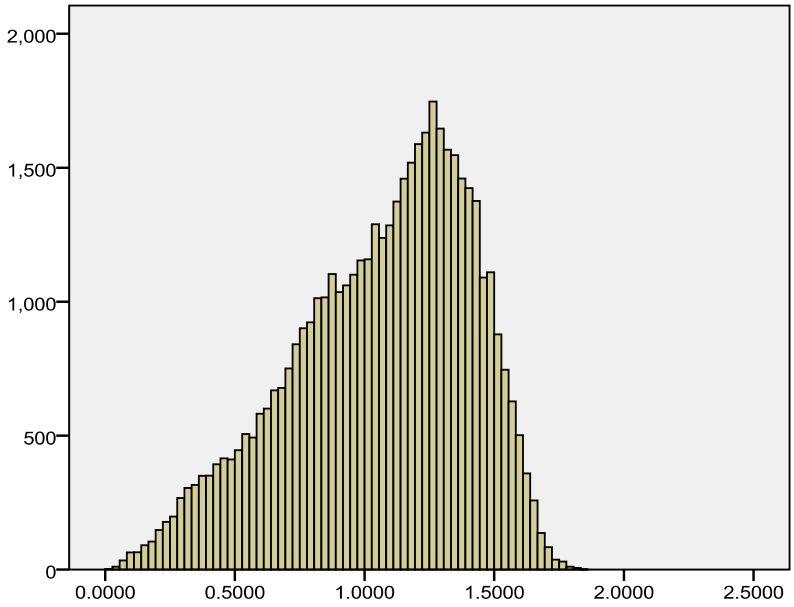
High social #1: maximum intensity = 1.87



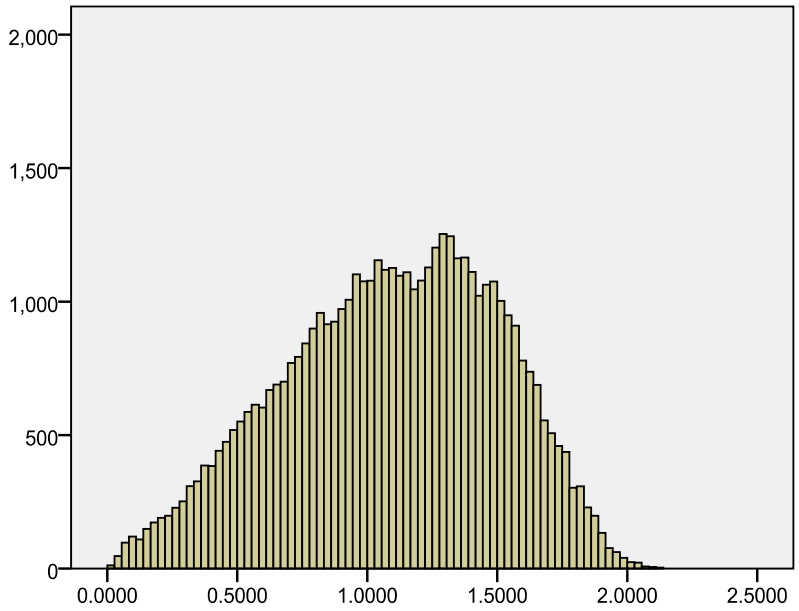
High social #2: maximum intensity = 1.92



Low social: maximum intensity = 1.95



Non-social: maximum intensity = 1.84



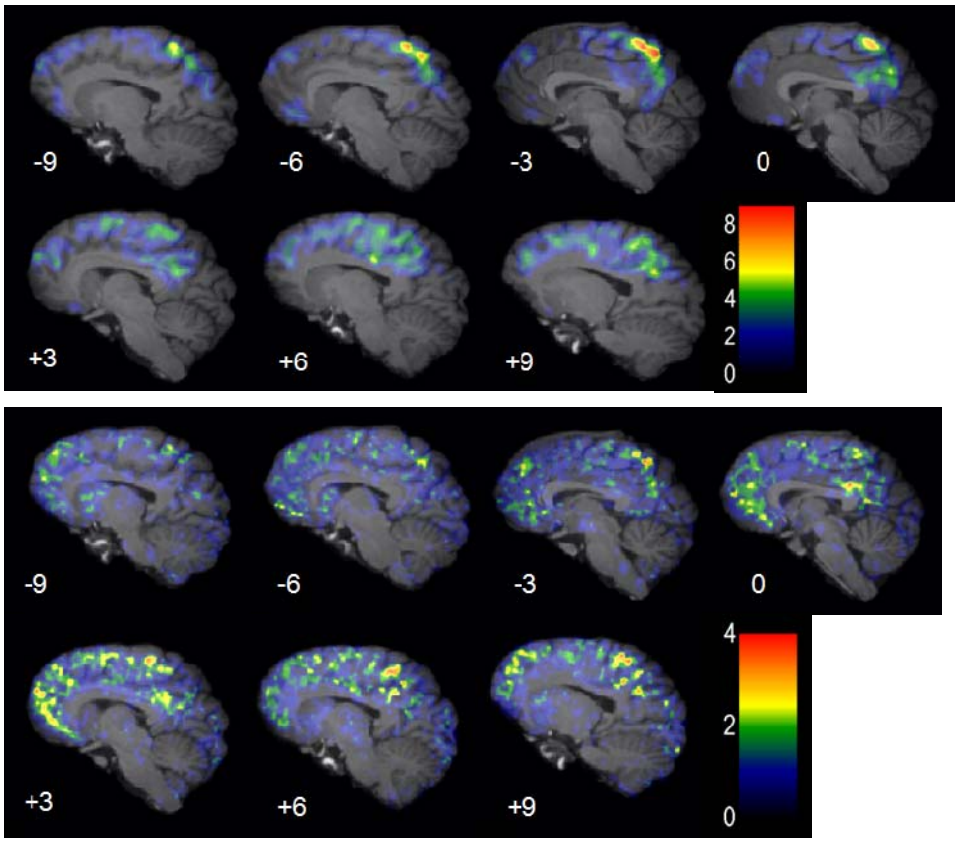
Rest: maximum intensity = 2.13

X-axis represents intensity value of voxels (mean = 1 for all conditions, n = 47,764 voxels). Y-axis represents number of voxels at each intensity value.

Subtraction contrasts

Simple subtraction contrasts (e.g. rest minus non-social) show very similar results to the t-test contrasts described above; as such, these analyses serve largely as a confirmation of the t-test model (Figure 16). One salient difference between these methods of analysis, however, is the greater spread of activity in the subtraction contrasts. As these contrasts show differences between conditions in each subject, they are more apt to show a larger degree of between-subject variation. In Figure 15, each colored voxel in the subtraction contrast represents an area where at least one subject has higher activity in the rest condition than in high social #1. The threshold in this figure, 0.3, is liberal; all voxels with a difference in intensity between the two conditions of at least 0.3 are shown. In a contrast rest minus high social #1, a value of zero represents a voxel with the same intensity value in each condition, and positive values represent voxels with higher activity at rest. Each subject's mean and maximum difference for this contrast are shown in Table 6.

Figure 16: T-test vs. subtraction contrast.



Rest > high social #1 as a t-test (top) ($p < 0.05$, uncorrected) and as a subtraction contrast (bottom) (thresholded at > 0.3).
Color bars indicate value of t-statistic (top) and number of individuals at that voxel (bottom).
X-coordinates in millimeters from midline.

Table 6: Subtraction contrast values, rest - high social #1.

Subject	**Mean difference**	**Max difference**
Jarred	0.35	1.72
Katrina	0.16	0.88
Patrick	0.18	1.17
Scott	0.19	1.23

Chapter 4: Discussion

Contrasts among conditions

T-tests comparing these study conditions—high social (both #1 and #2), low social, non-social, and rest—reveal consistent activations in a number of brain areas. The cortical midline structures identified as highly active at rest in chimpanzees (Rilling et al. 2007) are also active here during rest and during social cognition. The most salient of these midline areas is the precuneus; posterior cingulate cortex (PCC) and medial prefrontal cortex (MPFC) are active as well. Social cognitive tasks (relative to non-social) show activity in the insula and amygdala (both largely left-lateralized); relative to rest, these tasks activate the fusiform gyrus. Finally, the left ventral striatum activates preferentially in the high social conditions, relative to low social.

Activity in precuneus and posterior cingulate cortex

Medial parietal cortical areas, including the precuneus and PCC, are highly active both at rest (when contrasted with any task) and during social cognitive tasks (when contrasted with the non-social task). These areas are consistently identified with the default mode network in humans, and also with both other- and self-related mental activity (particularly autobiographical episodic memory recall). These results suggest that chimpanzees may engage in thinking related to their own past experiences or to experiences with other individuals (or both) both at rest and during a social cognitive task.

Iacoboni et al. (2004) demonstrated increased activity in the precuneus (as well as DMPFC) when subjects viewed videos of actors engaged in dyadic social interactions, similar to the high social conditions in this study. This precuneus activity appeared in this conditions relative to rest, and also relative to a condition in which videos were shown of actors behaving alone (similar to the low social condition in this study). The authors suggest that this medial parietal activity is a response to social relationships and interactions in particular, more so than simply to observing other individuals.

The precuneus activation seen in the present study is similar to that of Iacoboni et al. (2004) in many ways, with some critical differences. The most obvious of these differences is that this area is *not* more active during the social cognitive tasks than it is at rest (although an examination of the social conditions' whole-brain activity does show highest levels of activation in cortical midline structures, including medial parietal cortex). Rest activity remains highest in medial parietal cortex relative to task conditions in chimpanzees, regardless of those tasks' degree of social content. (Note, however, that Iacoboni et al. (2004) did not employ a similar task; instead, subjects passively viewed videos, creating a condition similar to the resting state in many ways.) Second, there is not a distinct precuneus activation in the high social conditions when compared to the low social condition (i.e. both high socials > low social). The precuneus *is* active in high social #2 > low social; recall, however, that this second high social condition appears similar to rest across all its contrasts. There is no precuneus activation present in high social #1 > low social at $p < 0.05$. Third, there is some precuneus activity in the low social condition compared to non-social, suggesting that—as predicted—this condition

does elicit some level of social response by virtue of the fact that it shows conspecifics, regardless of their behavior.

The overall greatest levels of precuneus activation are seen at rest (compared with any task) and during the social cognitive tasks (compared with the non-social tasks, but *not* compared with rest). This result suggests, first, that ongoing mental processes at rest are also present during social cognition—that the resting state shares features with social cognition in chimpanzees. Second, based on human functional neuroimaging literature, this mental activity may be related to autobiographical memory recall and thoughts about the self and others. Several studies associate reflection on the self—one's own mental states, memories, and characteristics—with activity in midline parietal areas (Lou et al. 2004, Northoff et al. 2006, Seger et al. 2004, Uddin et al. 2007), collectively suggesting that these areas are a critical component of the neural instantiation of the self. Retrieval of episodic memories about the self is particularly emphasized in much of this research (Northoff et al. 2006). Seger et al. (2004) additionally demonstrate that making judgments about the self and judgments about another person both activate the precuneus, albeit in different portions: the authors distinguish superior and posterior segments of the precuneus, related to judgments about the self and about others, respectively.

In chimpanzees, the activation seen in social cognition relative to non-social (i.e., each social condition compared to non-social individually, as well as all social > non-social) largely conforms to Seger et al.'s (2004) superior activation, related to the self. This same superior activation is present at rest; however, activation at rest (relative to each condition except high social #2, as well as to all social conditions together) also extends into the inferior segment of the precuneus and PCC, related to judgments about

others (Seger et al. 2004). This inferior activation is most extensive in rest > non-social. This difference in extent of activation suggests that the social cognitive tasks presented here spark some self-reflection in chimpanzees. Considering the precuneus's proposed role in autobiographical memory recall (Cabeza and Nyberg 2000), perhaps viewing these social interactions prompts recollection of the subjects' own past interactions with others. Meanwhile, at rest, chimpanzees may be engaged in ongoing thoughts about the self *and* thoughts about others. It is possible that the absence of a task frees up attentional resources for more diverse consideration of such social content.

Activity in medial prefrontal cortex

The MPFC is notable in that it underlies mental processes related to representing one's own and others' mental states, the foundation of theory of mind (Frith and Frith 1999, Gallagher and Frith 2003); unlike other cortical areas, it appears to be exclusively dedicated to this area of mental activity. Much like medial parietal areas, the MPFC represents both the self and others (den Ouden et al. 2005, Vogeley et al. 2001). Its role in the human default mode network, then, supports the description of the default mode as fundamentally social. Like humans, chimpanzees show considerable MPFC activation at rest (Rilling et al. 2007). Here, that MPFC activity is present (when examined via t-tests in the whole brain, exclusive of the cerebellum and brain stem) at rest relative to task conditions and in social task conditions relative to non-social, but to a much lesser degree than the precuneus and posterior cingulate. Much like the precuneus activity, this suggests a role of reflection on the subjects' own mental states, thought about others' putative mental states, or both, while at rest and during these social cognitive tasks.

When brain activity across conditions is explored within the resting state ROI, the MPFC activation at rest and in social cognition becomes more salient. In fact, in the contrast rest > all socials, the MPFC activation is more extensive than that of the precuneus (although the peak voxel value is highest in precuneus). These activations are largely found in dorsomedial prefrontal cortex (DMPFC); one exception, however, is rest > high social #2. In this contrast, medial prefrontal activity is strongly centered in ventromedial prefrontal cortex (VMPFC). Within the resting state ROI, this contrast shows overall less activity than any other contrast between rest and a task.

Activity in insula

In addition to medial cortical activations, the social conditions relative to non-social (both high socials > non-social and all social > non-social) also produce activity in the left insula. Self-related and other-related activity have also been described in the insula (Seger et al. 2004); these authors report activation in the insula both when subjects make a judgment about their own preferences, and a judgment about an acquaintance's preferences. Fink et al. (2006) describe insula activation when retrieving autobiographical memories (relative to rest and to retrieving memories about another person) (note, however, that their results are right-lateralized while those of the present study are largely left-lateralized). Similarly, the experience of disgust and the observation of disgust have both been shown to activate the insula (Wicker et al. 2003). The experience of the emotion is replicated when we observe it in someone else, providing a mechanism by which we understand others' experiences and mental states. In this way, the insula (the right anterior segment specifically) is thought to play a role in empathy and the

relationship between one's own experiences and the experiences of others. Together, these results further suggest a role of self-reflection in chimpanzees while observing social interactions, possibly with a representation of others as well.

Activity in amygdala

Many contrasts show activation primarily in limbic structures, both midline and left-lateralized. Activity in the amygdala is prominent in these contrasts, particularly when social cognitive tasks are contrasted with rest (e.g. high social #1 > rest, low social > rest, all socials > rest). In the high social #1 > high social #2 contrast, amygdala activation is present bilaterally. In social vs. rest contrasts, the amygdala activation is primarily seen on the left. The amygdala is most commonly associated with responses to emotionally salient stimuli, specifically interpreting others' emotions (Adolphs et al. 2001) (a critical process for interpreting social cues). Brothers and Ring (1992) specifically highlight the importance of limbic structures for processing social information in both humans and other primates, and limbic areas with strong connections to frontal cortex—particularly the amygdala—are thought to be important in theory of mind functions (Seger et al. 2004).

The consistent activation in the amygdala in the social tasks here, relative to rest, suggests that these stimuli may carry some emotional valence for the chimpanzees. The social interactions presented are positive and affiliative in nature (grooming and playing), and the subjects may have a positive emotional reaction to these stimuli (see below, *High social vs. low social*, for a discussion of reward-related activity). It is also possible that the interaction with an experimenter that is inherent in the task conditions produces a

state of greater emotional arousal than is seen at rest. However, that explanation would not account for the decreased amygdala activity seen in the non-social condition.

Activity in fusiform gyrus

Relative to rest, each social condition shows activity in the fusiform gyrus (bilateral, but more extensive on the right). This area has been implicated in recognition of faces in both humans (Allison et al. 1994, Grill-Spector et al. 2004, Kanwisher et al. 1997) and chimpanzees (Parr et al. 2009). The degree to which the area of the fusiform gyrus that is most active when viewing faces (the fusiform face area, FFA) is specialized for that function is debated in the human neuroimaging literature (Gauthier et al. 1999, 2000; Kanwisher 2000). The overall function of this area is processing of higher-order visual information (not limited to faces), and it is likely that the video nature of these tasks, rather than the conspecifics' faces seen in the videos, accounts for this fusiform activation. One of the most commonly cited functions of the FFA is recognizing individuals, which chimpanzees are able to do (Parr et al. 2000). However, the design of this study's tasks specifically and intentionally did not require matching of individual identity, as the individuals featured in each video differed from those pictured in the match and foil images. It should be noted as well that the non-social condition, when compared to rest, also shows activation in the fusiform gyrus; it is less extensive in this contrast than in the social conditions. The clip art stimuli used in the non-social task are visually distinct and brightly colored, possibly accounting for some complex visual processing.

Activity in ventral striatum

The most striking result when the two high social conditions are compared to the low social condition (i.e. high social #1 > low social, high social #2 > low social, and both high socials > low social) is the strong activation in the left ventral striatum. This is an area typically associated with reward in the human neuroimaging literature, suggesting that in this study, the presentation of social stimuli may have been positively valenced for chimpanzees. Both high and low social conditions presented the chimpanzees with videos of conspecifics, which would be reasonably assumed to be of great interest. It is possible that the high social videos were simply more salient in that regard as a result of featuring more animals. However, a critical difference between these conditions is not just the number of behaving animals, but also the nature of that behavior: direct interactions among individuals that carry social information. These stimuli are meaningful; they are informative about conspecifics' relationships. Further, the categories of social behavior in these conditions (grooming and playing) are positive interactions. Perhaps the subjects' observation of these affiliative behaviors triggers their own positive feeling in response. (Parr (2001) demonstrated that video stimuli with emotional content can produce an emotional response in chimpanzees. (In light of these results, only positively valenced interactions were used in this study so as to avoid an agonistic or stressful response to the high social conditions.)

Whole-brain averages

Each experimental condition—rest, high social, low social, and non-social—shows a similar pattern of activity when their averaged images are viewed without contrasts; the areas with the highest absolute level of activity are consistent across conditions. This pattern suggests that while there may be significant differences among conditions when they are directly compared, those differences are small relative to the brain's overall activity. Raichle and Mintun (2006) argue that the majority of the brain's activity reflects ongoing basal metabolism, rather than task-related function. That is, the contrasts between conditions that are revealed by functional neuroimaging methods and appear as active areas actually represent a very small change in the brain's overall activity.

Although each condition shows highly similar anatomical activity, the maximum intensity value is highest at rest. Additionally, the spread of values across that whole-brain average is wider at rest than in the task conditions, with a greater standard deviation. (The task conditions generally show most voxels clustered just above the mean.) The nature of the resting state condition may account for this difference—as cognitive and attentional resources are left unconstrained, the brain's activity is more likely to vary.

The similarity of activity patterns across conditions, combined with the higher intensity levels of activation at rest, suggest that in the chimpanzee brain there are ongoing cognitive processes at rest that continue during focused tasks, but are lessened in their activity. That is, processes that are salient at rest become background activity when there are other attentional demands. In this regard, contrasts between conditions may not

be the most effective way to analyze data such as these—or at least should not be used as the only means of analysis—as that approach masks informative similarities among conditions.

The patterns of activity seen here differ from what has been demonstrated in the human literature, particularly by Iacoboni et al. (2004) in which social stimuli activated cortical midline default mode structures to an even higher degree than seen at rest. It is likely that even the high social conditions in this study still featured a high enough level of focused attentional demand to deactivate the default mode, and that these attentional demands were sufficient to effectively cancel out a social cognitive effect in this respect. The logistics of study design with these subjects also require an experimenter to be present for testing during the uptake period of task condition, representing a significant difference between those conditions and the resting state.

Replicability

The high-social condition in this study was repeated in each subject for two reasons: one, to increase statistical power, and two, to assess replicability—the degree to which a study condition can produce similar results in separate scanning sessions in each subject. Thus, two high social conditions (high social #1 and high social #2) were analyzed, both in comparison with every other condition and with each other. In addition, the two high social conditions were lumped together (creating a "both high social" condition) for comparison with the low social, non-social, and rest conditions.

The results of these analyses demonstrate striking differences between the two high social conditions. If the study condition was well-replicated in the second scan, a

direct comparison of the two high social conditions would be expected to show minimal differences (i.e., there would be few active voxels in either high social #1 > high social #2 or vice versa). However, these comparisons do yield significant differences. High social #1, compared with #2, is active primarily in limbic areas, with virtually no activity in the midline cortical structures associated with rest or with social vs. non-social cognition (i.e. the all social > non-social contrast). The opposite contrast, however, shows extensive activation in the precuneus and surrounding cortex in high social #2, relative to high social #1. Overall, high social #1 appears to be most similar to the two other task conditions, while high social #2 appears to be most similar to rest.

Although the second high social condition's task featured novel stimuli, these were of the same categorical type as those in the first high social condition. Therefore, the second condition should not be expected to tap into social cognition to a greater or lesser degree than the first. A close look at the subjects' testing behavior in each scanning session may inform the differences between the two. In Table 3, Results section, note that three of the four subjects completed fewer trials in the high social #2 scanning session than in high social #1. It is reasonable to assume, then, that these subjects may have been less focused on the task, possibly representing a similarity with the resting state. Brain activity at rest and brain activity during a focused task have been described in the human literature as a continuum, such that activity in putative default mode regions gradually decreases as greater attentional resources are devoted to the task (Fox et al. 2005). The activity patterns that appear in high social #2 when contrasted with other task conditions—similar to rest in those same contrasts, but not as extensive—would support a similar conclusion in this study. It is not clear, however, why the high social #2

condition in particular would result in lessened attention compared to the other task conditions.

Note, however, that the difference between these two conditions is not reflected in a non-contrasted examination of each condition's areas of greatest activity, averaged across all four subjects. There, the most active areas fall along the cortical midline, just as in the other conditions. Again, an analysis of this type appears to be a critical complement to contrasting conditions via t-tests.

Task-positive and task-negative areas of activation

Fox et al. (2005) describe two networks in the brain (identified in humans with fMRI) that are anticorrelated—as activity in one increases, activity in the other decreases. These dichotomous networks are described as task-positive and task-negative, including areas that are consistently active during attention-demanding tasks, and consistently active at rest, respectively. The task-negative network includes the structures typically described in the default mode network: PCC, MPFC, and lateral parietal cortex. The task-positive network comprises middle temporal cortex, intraparietal sulcus, and the precentral sulcus (particularly the frontal eye field).

A primary finding of the present study from comparisons of the resting state to each task condition is that default mode activity is quite robust in chimpanzees. Each of these contrasts (i.e., rest > high social #1, rest > high social #2, rest > low social, and rest > non-social) shows areas of greatest activation in midline cortex, including MPFC and precuneus in particular. These results provide strong support for a task-negative network with considerable overlap with the one described in humans: chimpanzees at rest show

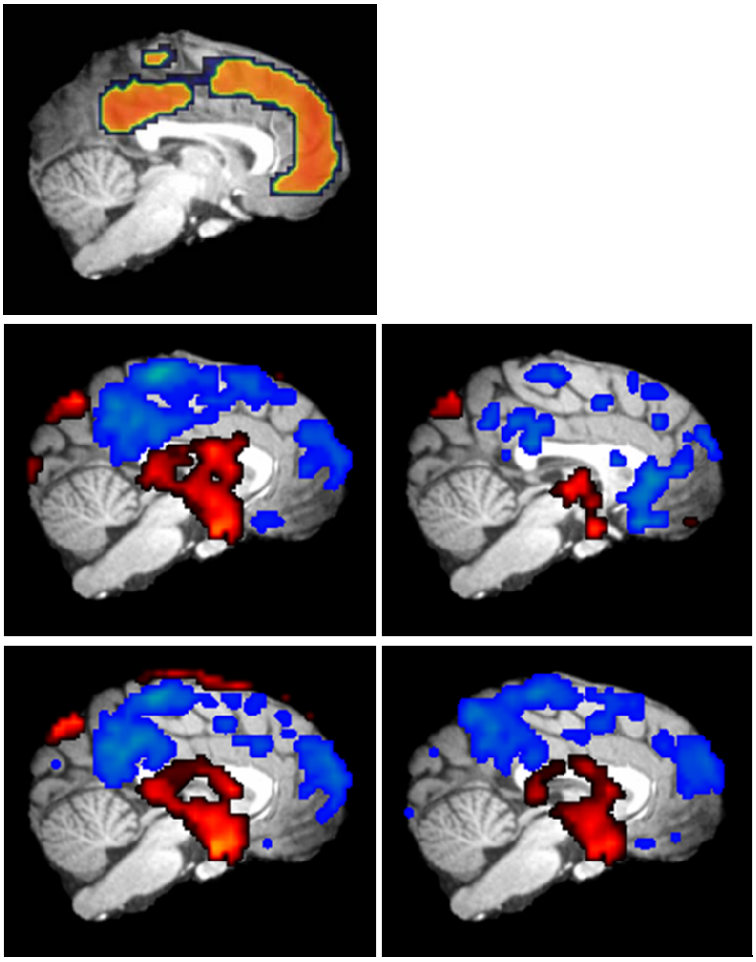
very high levels of activation in PCC and precuneus, and MPFC. (Activity in lateral parietal cortex is present, but to a lesser degree.) These activations persist when rest is contrasted with any of the task conditions studied here. The difference between rest and task activity is less pronounced in the high social #2 condition; this condition may represent an attentional state that is less focused on the task than were the other task conditions.

There is also evidence in this study of a task-positive network in chimpanzees, although for the most part it does not overlap with that described in humans. Instead, the task-related areas of activation (when compared with rest) are clustered in midline limbic structures, including medial temporal cortex (mostly amygdala) in particular. These results suggest that the chimpanzee brain is functionally organized in a similar way—with a dichotomy between task-positive and task-negative activity—but that the anatomical location and extent of the task-positive network varies significantly from that of humans. However, see below, *Variables between rest and tasks*, for a discussion of confounds that may account for some of these differences.

The default mode in humans was originally described (Gusnard et al. 2001, Gusnard and Raichle 2001, Raichle et al. 2001) in terms of *deactivations* of those areas during focused and attention-demanding tasks. While the chimpanzee resting state as described by Rilling et al. (2007) shows considerable similarity to the human default mode network, it was defined by looking at the areas with the overall highest levels of activity at rest irrespective of other conditions. This study takes that result a step further, demonstrating task-induced deactivations to those areas most active at rest during a variety of tasks (Figure 17) much as is seen in the human functional neuroimaging

literature. In this way, the present study further supports the presence of a default mode of function in chimpanzees, similar to that of humans.

Figure 17: Deactivations in the chimpanzee default mode network.



Top to bottom:
Top 5% most active voxels at rest
High social #1 > rest, high social #2 > rest
Low social > rest, non-social > rest
Activations shown in red, deactivations in blue; $p < 0.05$.

Variables between rest and tasks

While a primary aim of this study is to compare chimpanzees' brain activity at rest and during a variety of cognitive tasks, several differences between the rest condition and the task conditions should be noted as potential confounds. Chief among these is the presence of an experimenter during task conditions. During the uptake period, while the subject performs the task of interest, the experimenter monitors behavior and administers reinforcements (in this case, juice) as the subject works. In this way, the experimenter can monitor the testing conditions, the subject's attentional state, any disruptions in the testing area, and so on, and (to some degree) keep the subject on-task. In the rest condition it was critical to maintain an environment as free of distractions as possible, including any interactions that the chimpanzees might have engaged in during the uptake period. It was therefore very important to not have an experimenter present in that condition. A remote video feed allowed the subjects to be monitored during the uptake period to ensure that there were no significant disruptions or interactions between the subject and the cage mate. Interacting with an experimenter under conditions very similar to that of scanning sessions is not unusual for these subjects; they are extensively trained using these methods. However, the interactive element inherent in the testing environment is a key difference between task conditions and the rest condition.

Second, each of these subjects is pair-housed with a cage mate, and cage mates were left together during the rest condition but separated during task conditions. The logistics of testing during scan periods necessitate this separation of subjects from their cage mates. This is primarily done to prevent the cage mate from interfering with testing. (Individuals vary in this regard, but during training some subjects' cage mates disrupted

testing, or tried to displace the subject in order to perform the task themselves. Training sessions are sometimes performed with the cage mates separated, so this condition is not unfamiliar to the subjects.) Scanning sessions of task conditions also entail strictly-controlled timing of the end of the testing session and the vets' administration of a sedative to the subject, which cannot be accomplished with a cage mate present. At rest, as a major goal was to create a non-stressful condition, subjects were left with their cage mates for the bulk of the uptake period. Before scans were collected in this condition, attempts were made to habituate the subjects to separation from the cage mate without a testing session (i.e. alone without either the cage mate or an experimenter). Despite multiple habituation sessions, subjects did not become accustomed to this situation, but instead displayed many behaviors indicative of anxiety and heightened external attention (e.g. piloerection, pacing, etc.). By contrast, when left with their cage mates, subjects appeared to be relaxed; interactions between cage mates were minimal or even non-existent during rest scanning sessions. (In one session the subject and cage mate interacted extensively, and this scan was canceled and repeated later.) Subjects were separated at the end of the uptake period at rest, before vets administered the sedative.

Together, these two major differences between scanning sessions at rest and during task conditions may contribute to differences in brain activity that are not attributable to the content of the tasks themselves, but rather to a possibly heightened state of emotional arousal (from interaction with the experimenter) or a heightened state of anxiety (from separation from the cage mate and/or anticipation of anesthesia, as the rest condition's lack of a testing component is unlike any other scanning condition), or both.

Conclusion

Clear relationships are seen in this study between brain function during social cognitive tasks and at rest in the chimpanzee brain. The cortical midline structures—medial prefrontal cortex, precuneus, and posterior cingulate—that are highly active in chimpanzees at rest (and are also consistently identified as part of the human default mode network) are also significantly active during social cognition. This activity is especially apparent when compared to activity during a non-social cognitive task. A striking difference, however, between these areas' activity at rest and in social cognition is their degree of activation: the resting state consistently produces higher absolute levels of brain activity in these areas. It seems, therefore, that the mental processes engaged by social cognitive tasks are ongoing at rest, but perhaps less constrained; or, stated another way, that the chimpanzee brain's default activity continues but to a lesser degree during attention-demanding tasks.

The nature of these activations, and their location in brain areas that in the human neuroimaging literature are ascribed self- and other-reflective roles, suggests that processes related to self-reflection and autobiographical memory may be at work both when chimpanzees rest and when they focus on social stimuli.

The existence of a default mode in chimpanzees is supported by this study in two ways. First, as described by Rilling and colleagues (2007), the absolute highest levels of activity in the resting brain are found in the same areas (particularly midline cortical areas) that are assigned to the default mode network in humans. Second, multiple tasks are shown here to deactivate those midline cortical areas, just as attention-demanding tasks produce deactivations in default mode network structures in humans. These results

further suggest the presence of a task-negative network and possibly a task-positive network in the chimpanzee brain. Given the variation seen between the two high social cognitive tasks presented here, it is possible that there exists a continuum between resting brain activity and fully-engaged attention on a task.

Caveats and limitations

Functional neuroimaging data in non-human primates are inherently noisy. When using FDG PET with great apes, there are many factors that are likely to influence the outcome of an experiment but cannot be controlled. First, all testing in this study was performed by necessity in the housing area among several conspecifics. As such, the usual background stimuli from other individuals were always present, particularly vocalizations. While every effort was made to limit such distractions, it is not possible to achieve complete quiet in that environment. It is likely however that this literal background noise was consistent and therefore canceled out across scanning sessions.

Second, the relatively long uptake period of FDG (45 – 60 minutes) means that all brain activity within that timeframe is represented in the final image. External stimuli in the housing area certainly contribute to that brain activity. As most of the uptake of FDG occurs within the first 15 minutes after dosing, subjects in this study were required to begin testing quickly and work steadily for that time in order for the scan to be completed. (Scans were canceled when subjects did not work sufficiently in that critical window of the uptake period.) The method of anesthesia and the elapsed time between the end of testing and sedation may also influence brain activity seen in the final PET image. While the majority of the chimpanzees took a hand injection of Telazol at the end

of each scan's testing period, a few scan sessions required darting of the subject—certainly a stressful event. Generally, subjects were transported quickly to the scanning facility after sedation. Unexpected delays were occasionally encountered, however, introducing another variable into the end results.

Almost all cognitive testing with non-human primates is hindered by the nature of experimental design for non-verbal species. While human research participants can report directly on their thoughts and experiences, studies with non-human primates must make inferences based strictly on behavior. The match-to-sample paradigm has been used extensively with chimpanzees to yield robust conclusions about their cognitive abilities; it can be reasonably assumed to be a valuable instrument in assessing chimpanzees' interpretation of conspecifics' behavior. However, the possibility always remains that a given task is not actually tapping into the facet of cognition for which it is intended. Many factors are involved, and non-verbal subjects may in fact attend to an aspect of the task that the experimenters had not intended (or indeed considered). See Discussion, *Variables between rest and tasks,* for an exploration of the non-task-related factors that may have influenced the subjects' brain activity in this study.

Directions for future research

With regard to the default mode in apes and the relationship between rest and cognition, further manipulations of the resting state would be illuminating. While many similarities are seen in this study between chimpanzees' brain activity at rest and during a social cognitive task, these data do not provide evidence that the default mode network in chimpanzees is *more* active during social cognition than it is at rest, as is suggested in

recent human functional neuroimaging literature (e.g. Iacoboni et al. 2004). However, a study condition that presents social stimuli without invoking the same degree of focused attention as these tasks might better assess the potential social nature of the chimpanzee default mode. The effect of social stimuli on the human default mode was initially demonstrated using passive presentation of video stimuli rather than a task (Iacoboni et al. 2004), and a similar experiment with chimpanzees would be an ideal follow-up to this study.

It is likely that the neuroimaging results from the task conditions in this study are related in part to the testing procedures themselves, rather than following entirely from the cognitive content of the tasks. In order to tease apart these factors, several manipulations of the test conditions would be informative. For instance, to evaluate the influence of the experimenter, these tasks could be automated so that no human presence is necessary. Conversely, to evaluate the degree of arousal generated simply by interacting with the computer, a human experimenter could interact with the chimpanzee and give intermittent rewards without an accompanying task.

Finally, expanding this research to other primate species is critical. Any evolutionary approach to the study of human characteristics benefits from a wide view of primate phylogeny. As we are most closely related to chimpanzees and bonobos, studies of these species are especially informative about our own evolutionary origins. However, looking beyond these apes would enrich this line of research. Research with other great apes (gorillas and orangutans) could determine if characteristics shared by humans and chimpanzees are specializations of the *Homo – Pan* clade. Likewise, research with other catarrhine primates would help identify hominoid specializations. Therefore, a clear next

step for this research paradigm is to perform these and similar studies with other primate species. Of course, this research is limited both by the availability of captive primate species and—with regard to functional neuroimaging specifically—the presence of neuroimaging facilities in conjunction with primate research facilities. While it is unlikely that functional neuroimaging studies with great apes other than chimpanzees can be performed, studies with Old World monkey species (particularly rhesus macaques) are readily feasible.

Appendix

Table A1: Maximum t-statistic value in each contrast

Contrast	In whole brain exclusive of cerebellum and brain stem	In resting state ROI
High social #1 > high social #2	5.9	4.3
High social #1 > low social	5.3	4.6
High social #1 > non-social	6.5	4.6
High social #1 > rest	5.7	2.4
High social #2 > high social #1	6.4	4.9
High social #2 > low social	5.3	4.3
High social #2 > non-social	8.1	6.2
High social #2 > rest	4.1	4.4
Both high social > low social	5.3	5.0
Both high social > non-social	6.0	5.3
Both high social > rest	4.6	3.7
Low social > high social #1	4.8	3.6
Low social > high social #2	5.6	2.7
Low social > non-social	6.4	4.4
Low social > rest	6.1	2.6

All social > non-social	6.8	5.2
All social > rest	5.3	3.4
Non-social > high social #1	4.5	2.8
Non-social > high social #2	6.5	3.3
Non-social > both high social	6.3	3.3
Non-social > low social	5.1	3.9
Non-social > all social	6.0	3.3
Non-social > rest	5.1	4.1
Rest > high social #1	9.2	6.8
Rest > high social #2	6.2	4.5
Rest > both high social	7.6	5.9
Rest > low social	8.6	7.0
Rest > all social	8.6	6.8
Rest > non-social	10.6	8.5
Rest > all tasks	9.6	7.6
All tasks > rest	5.3	3.74

Results for each contrast ($p < 0.05$), whole brain exclusive of cerebellum and brain stem. Color bar indicates value of t-statistic. Anterior commissure at Z = 6.

Figure A1: High social #1 > high social #2

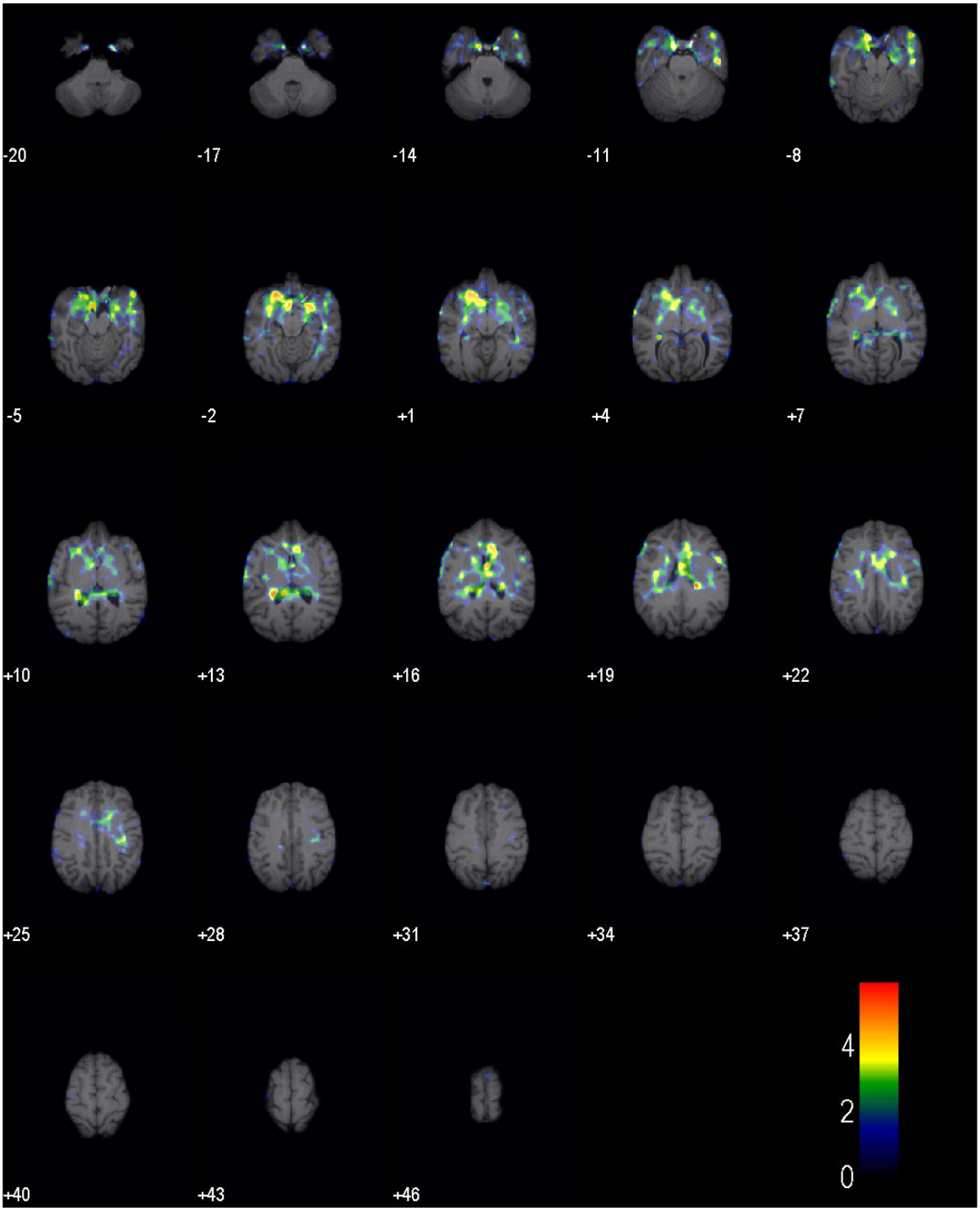


Figure A2: High social #1 > low social

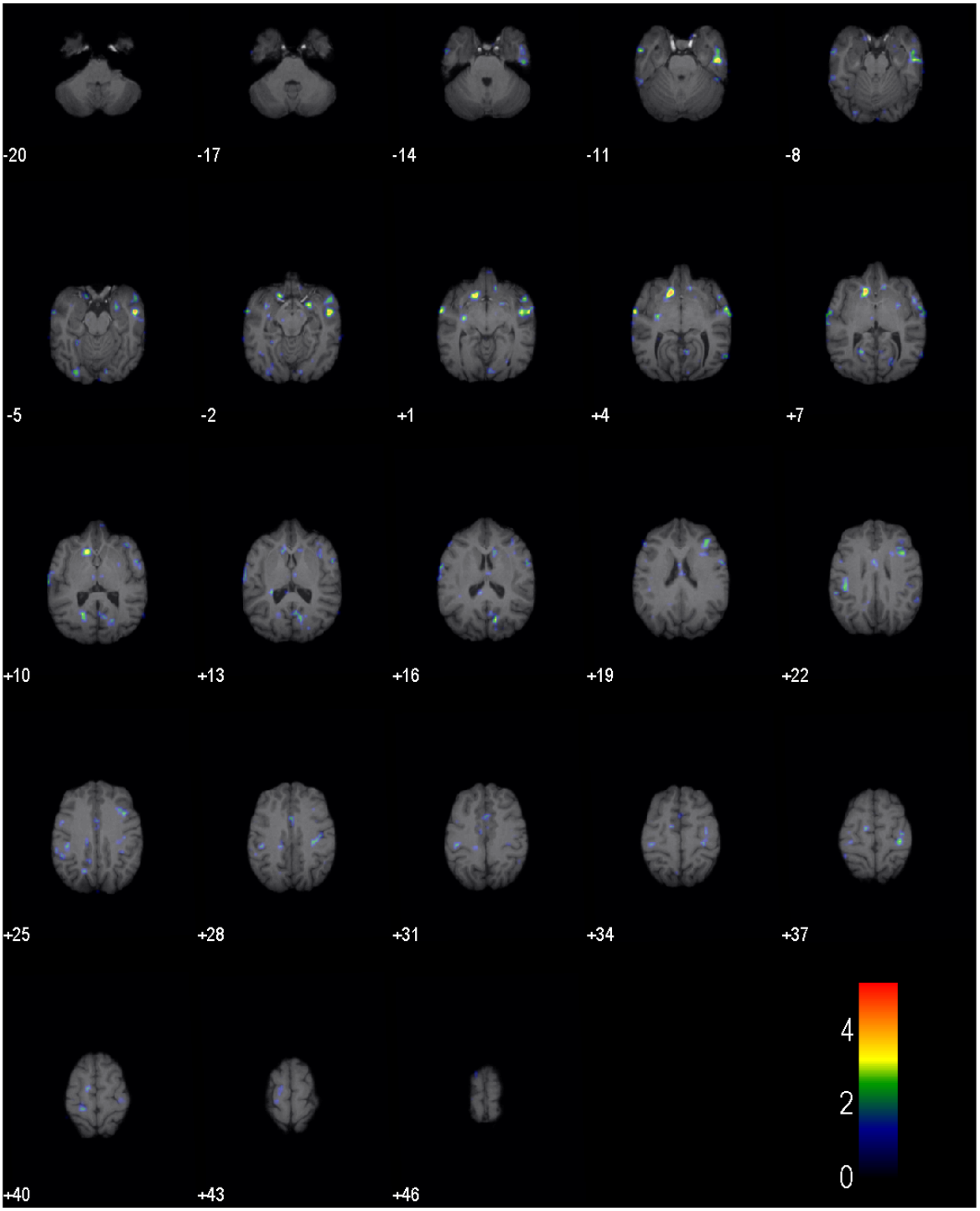


Figure A3: High social #1 > non-social

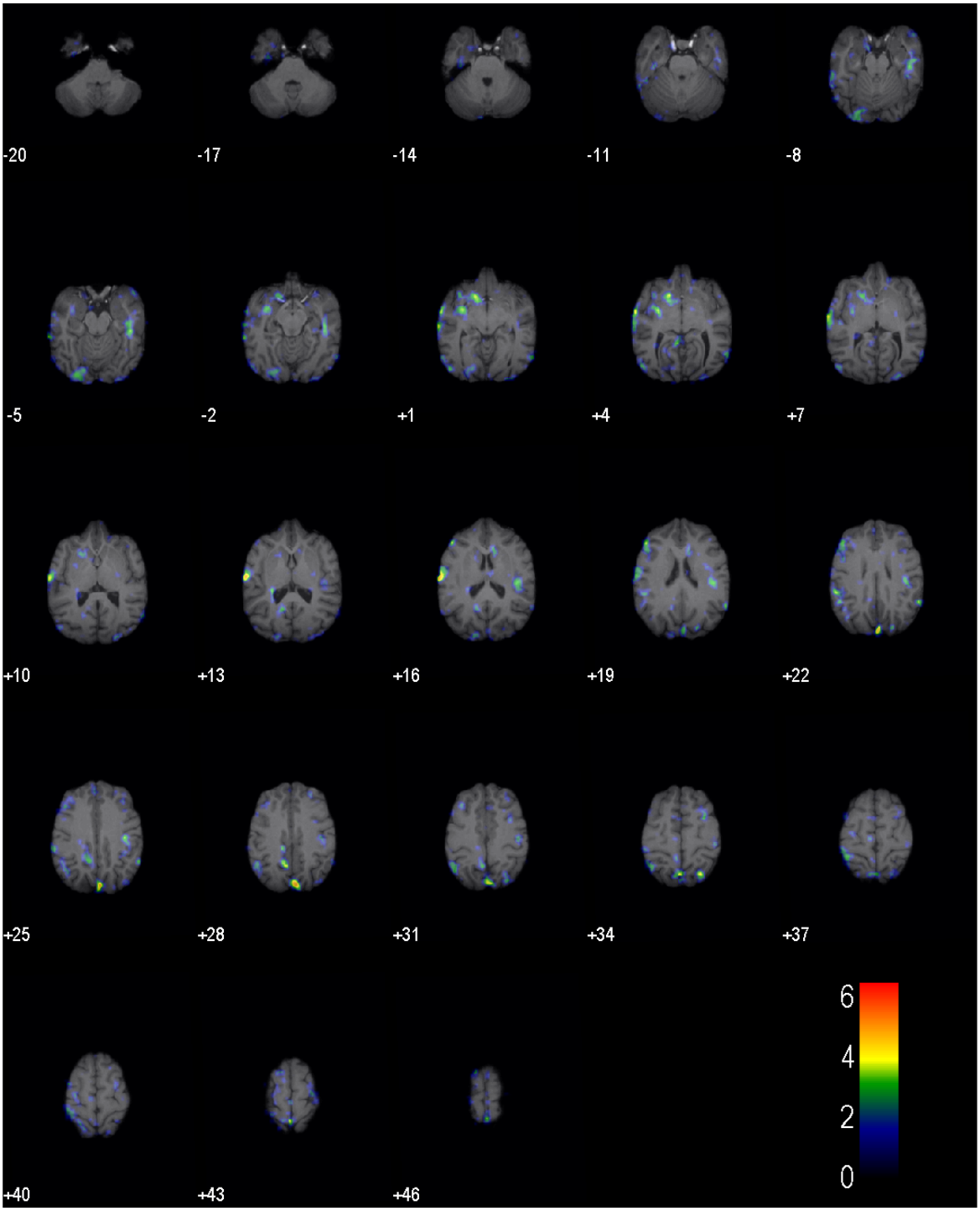


Figure A4: High social #1 > rest

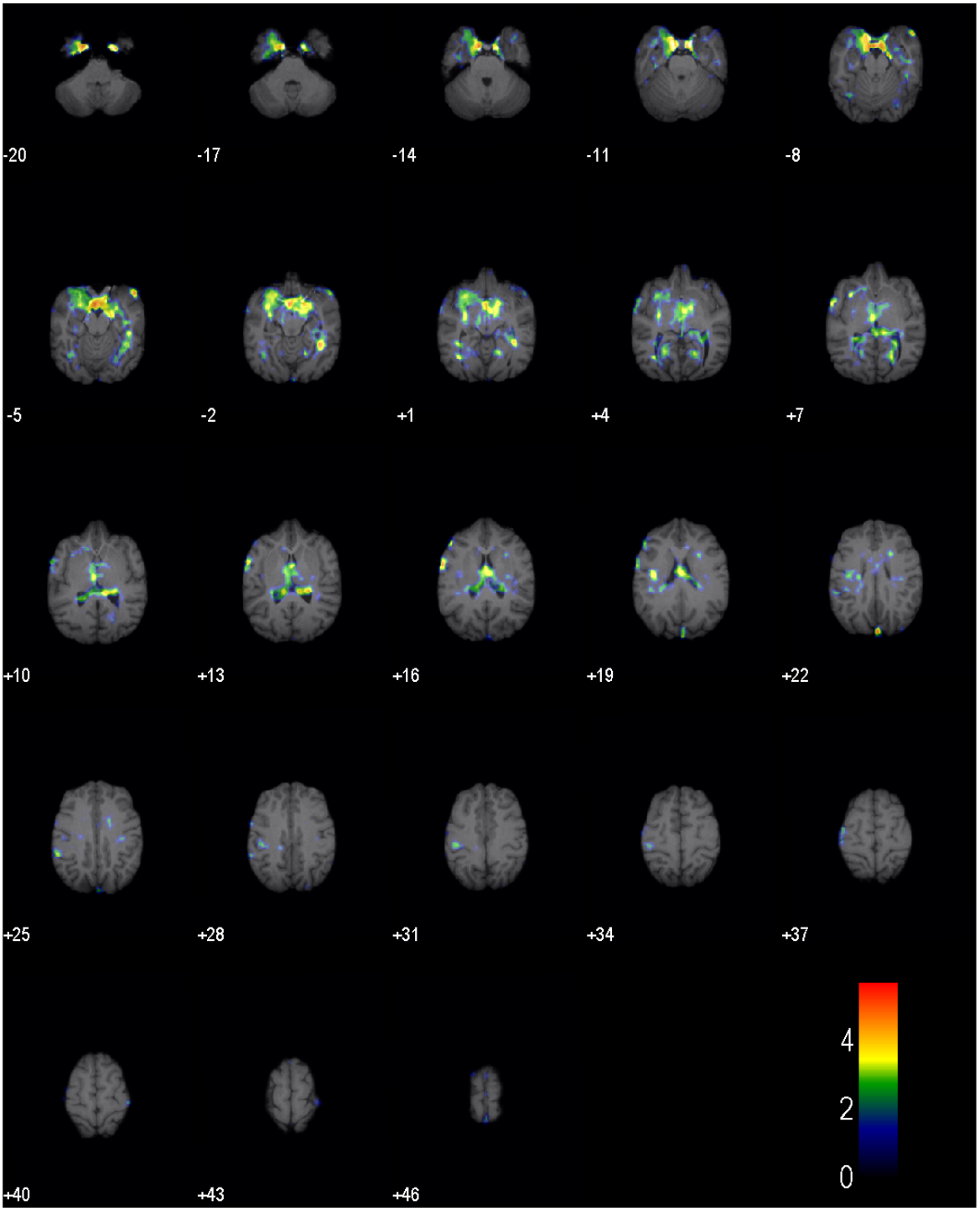


Figure A5: High social #2 > high social #1

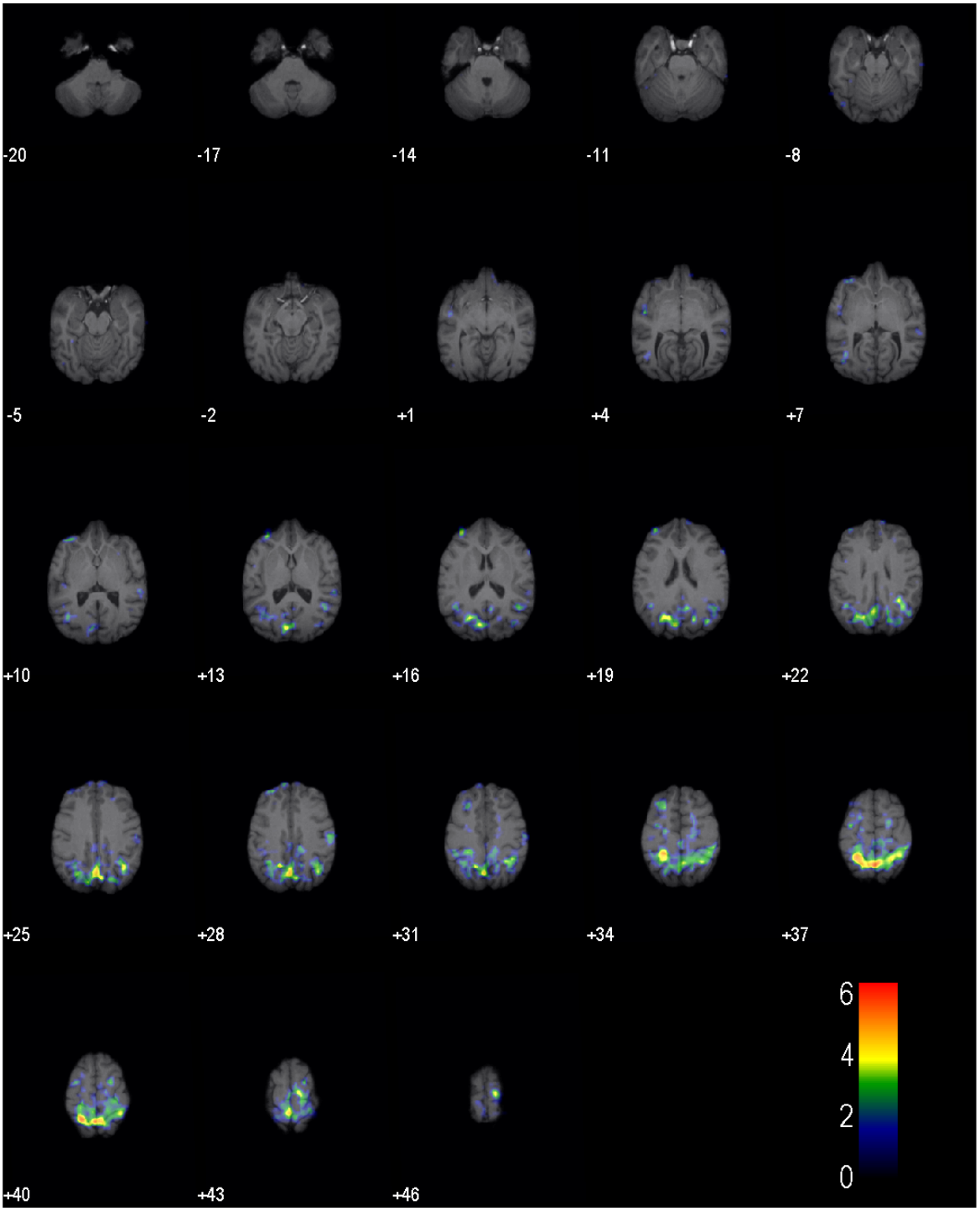


Figure A6: High social #2 > low social

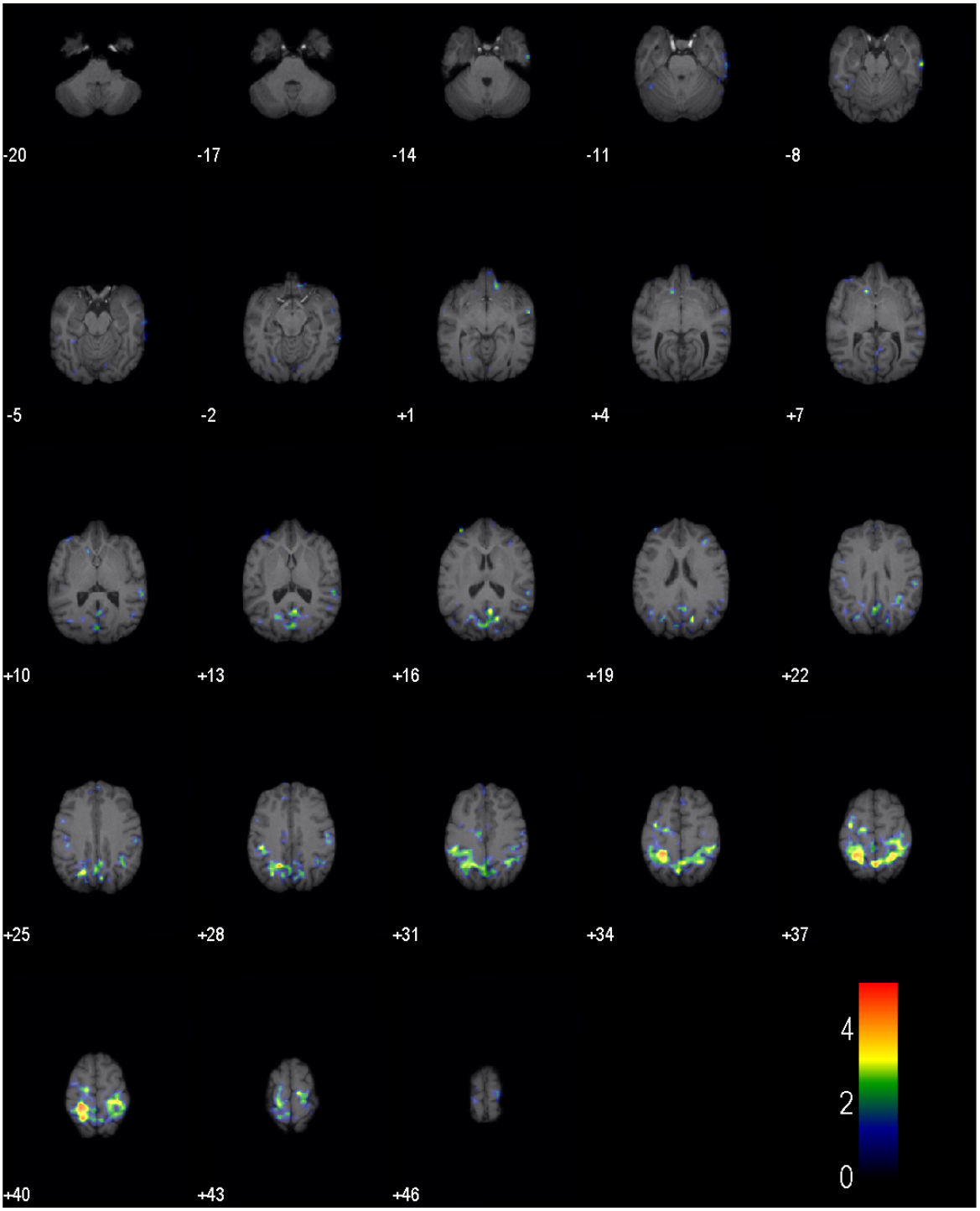


Figure A7: High social #2 > non-social

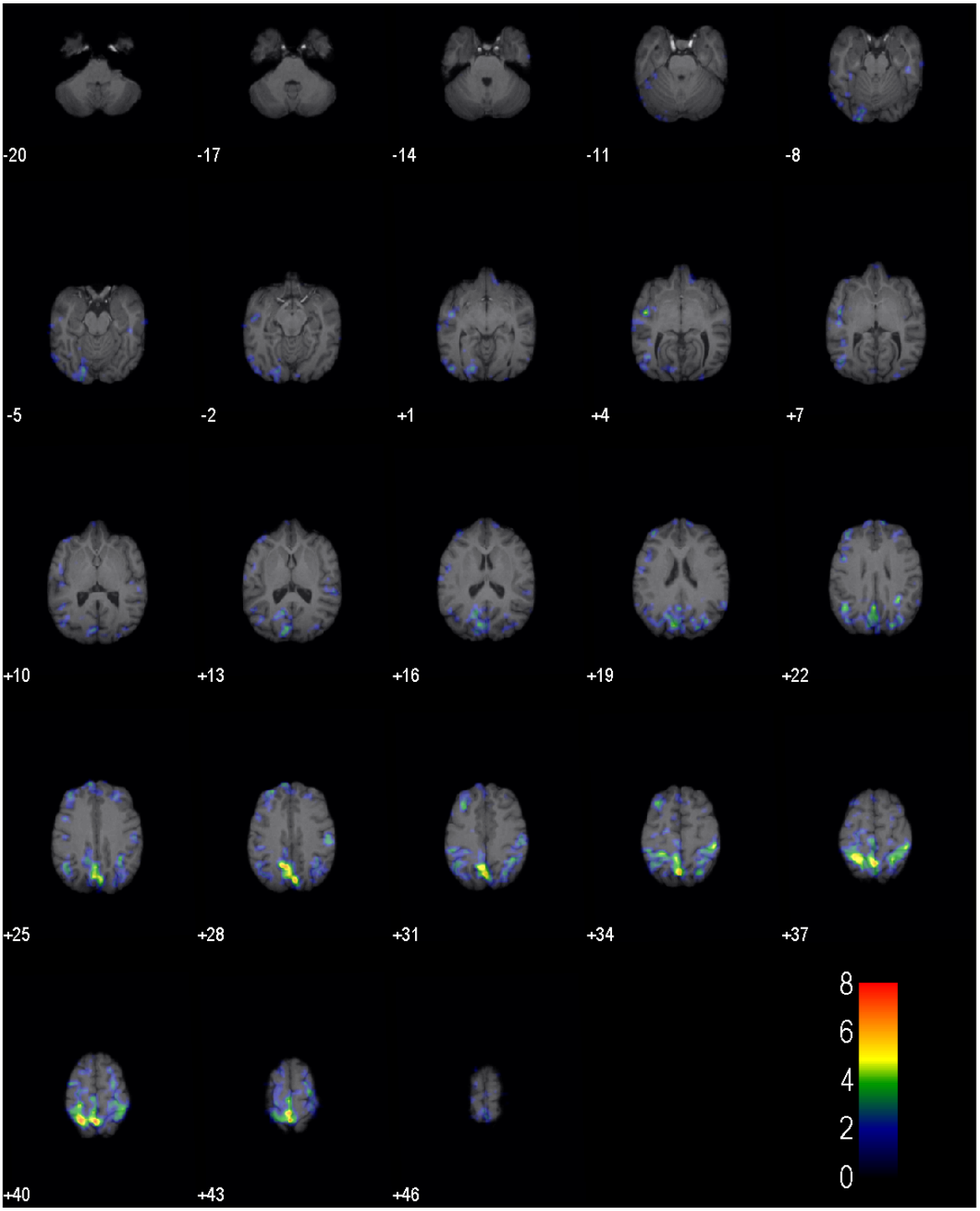


Figure A8: High social #2 > rest

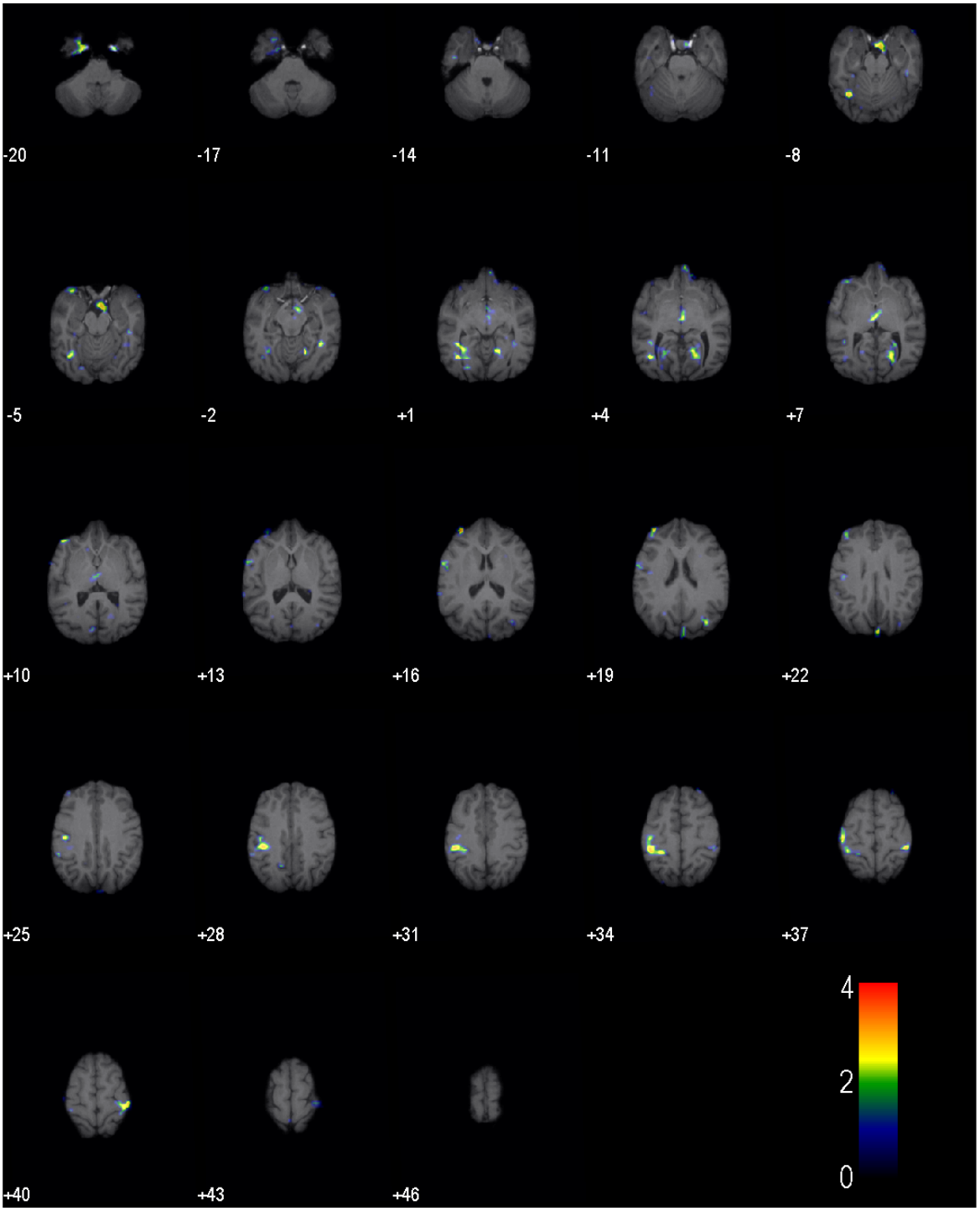


Figure A9: Low social > high social #1

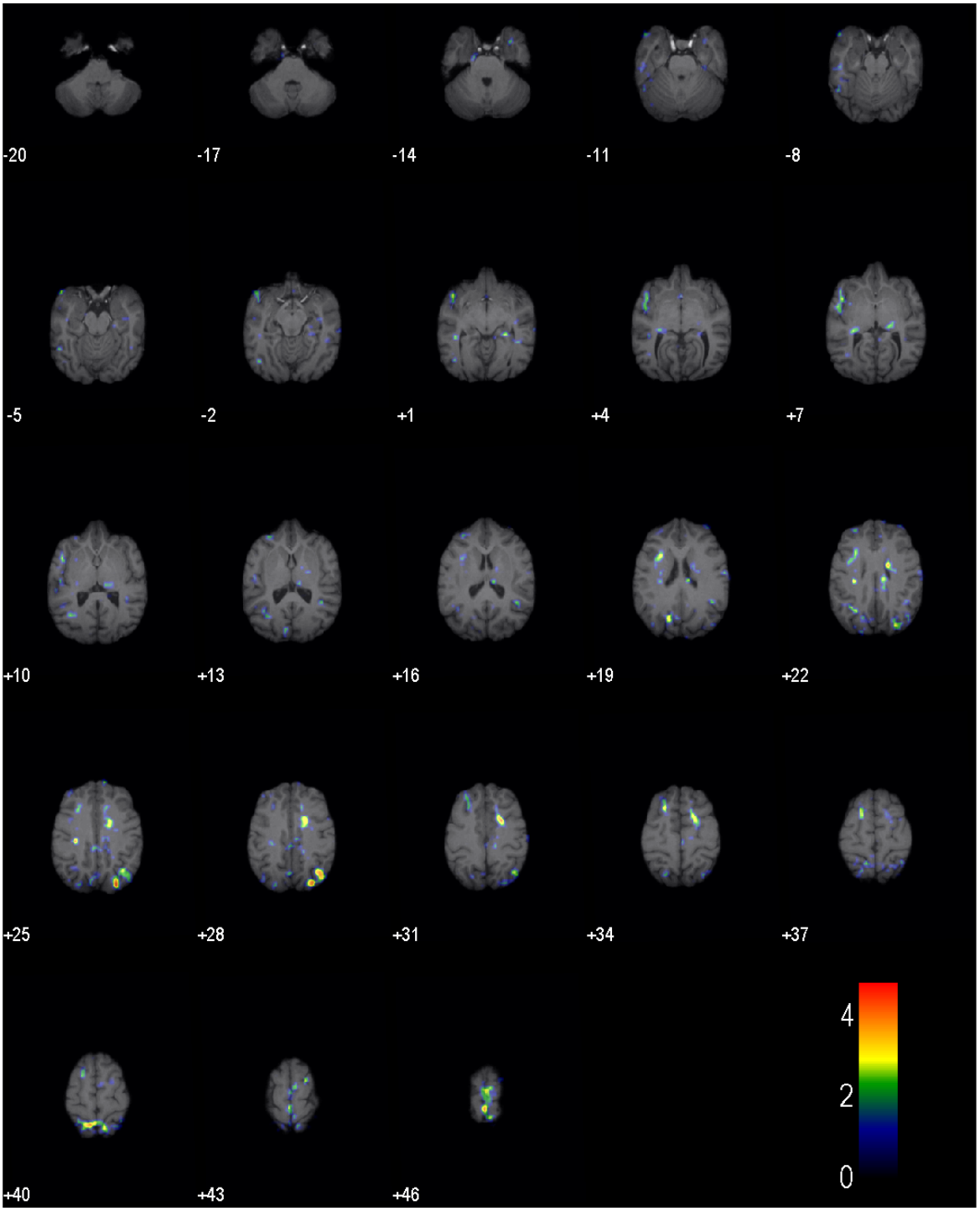


Figure A10: Low social > high social #2

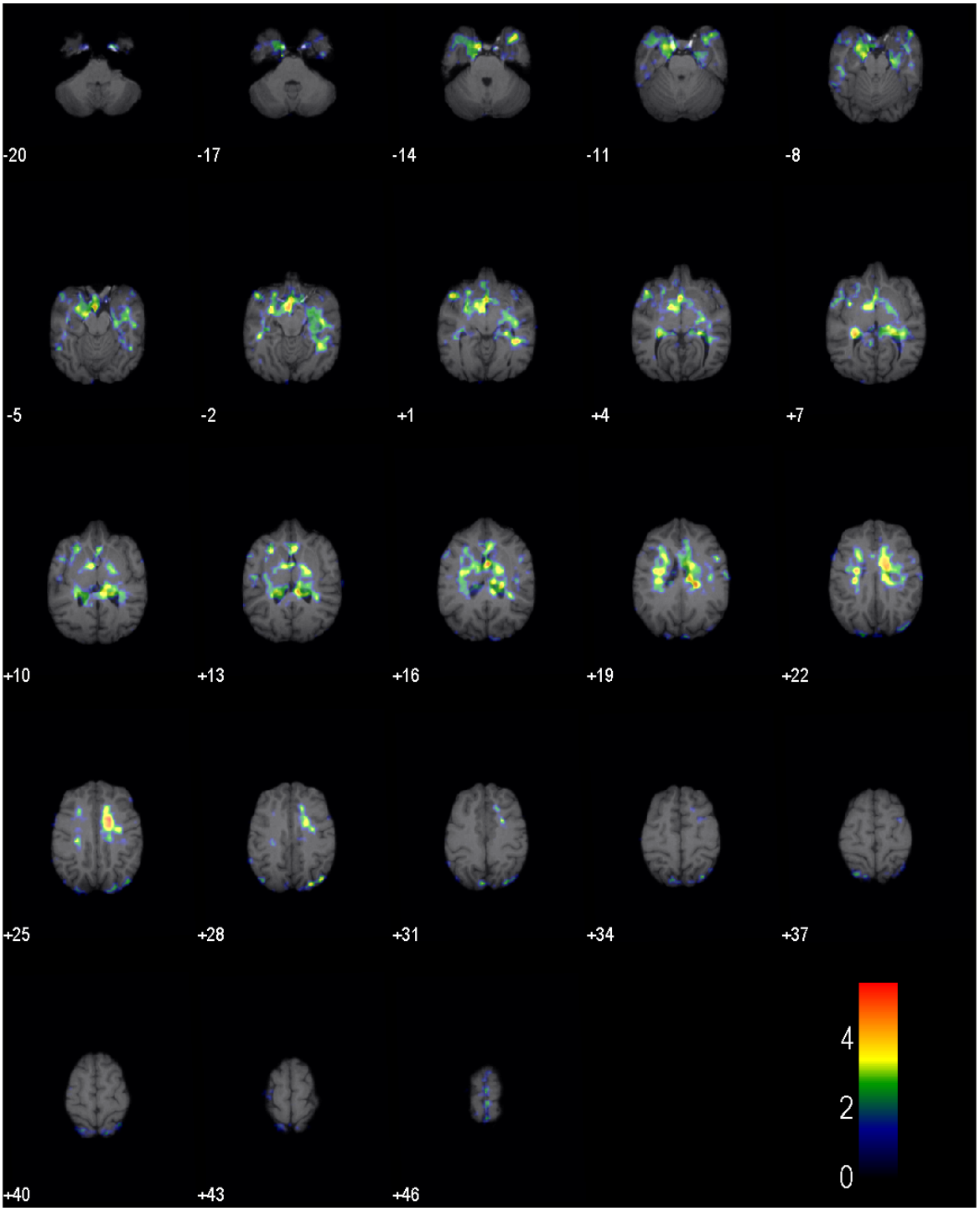


Figure A11: Low social > non-social

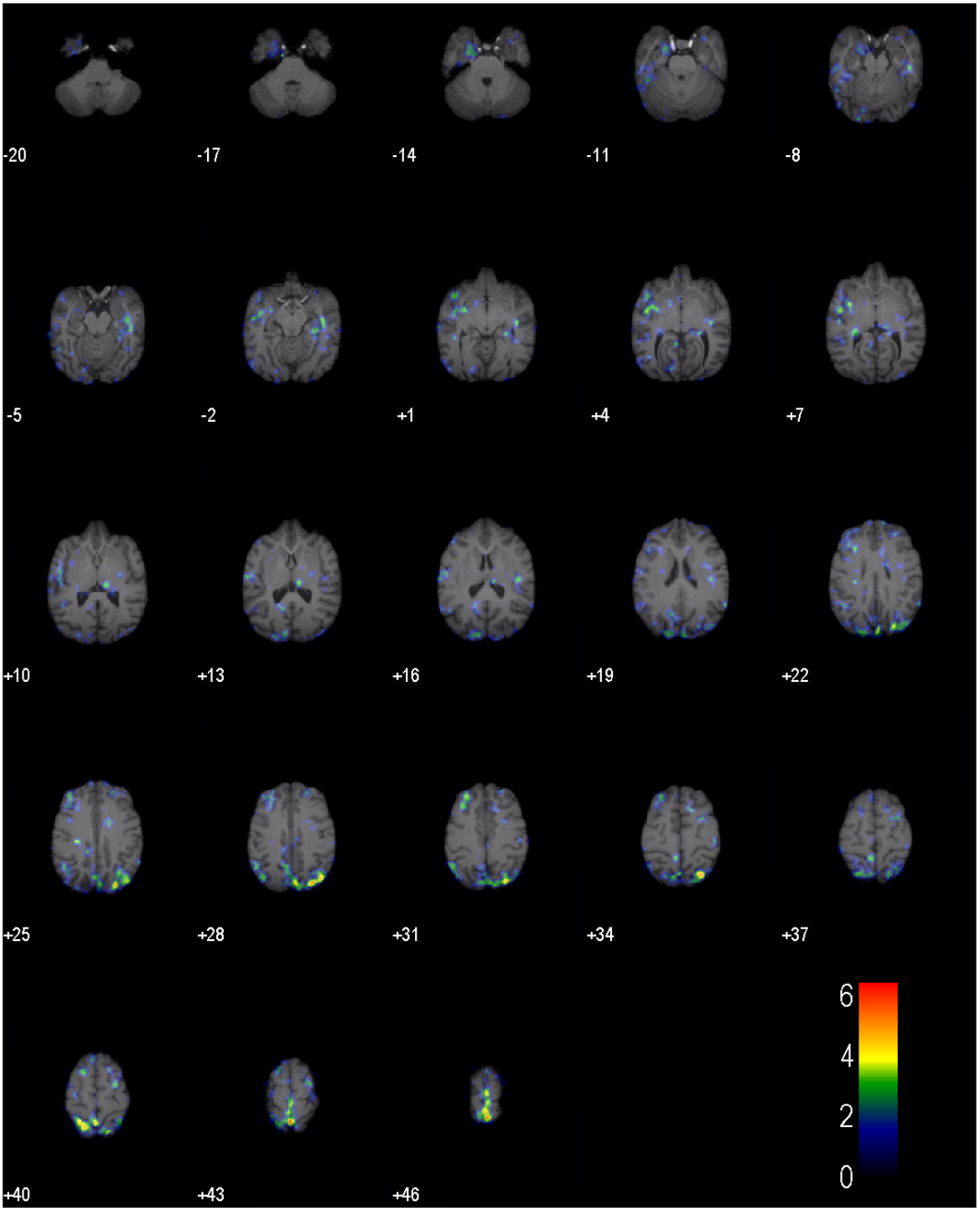


Figure A12: Low social > rest

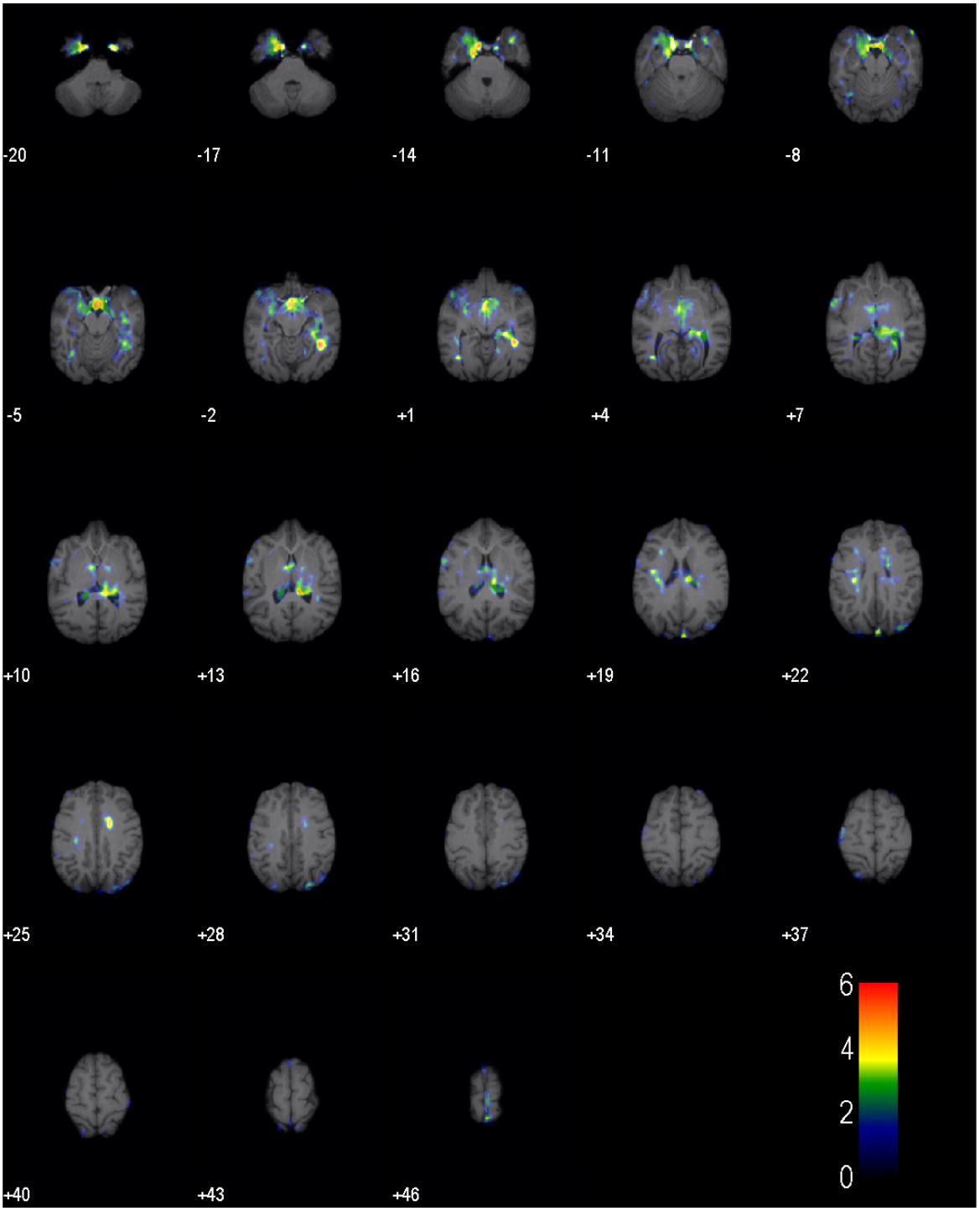


Figure A13: Non-social > high social #1

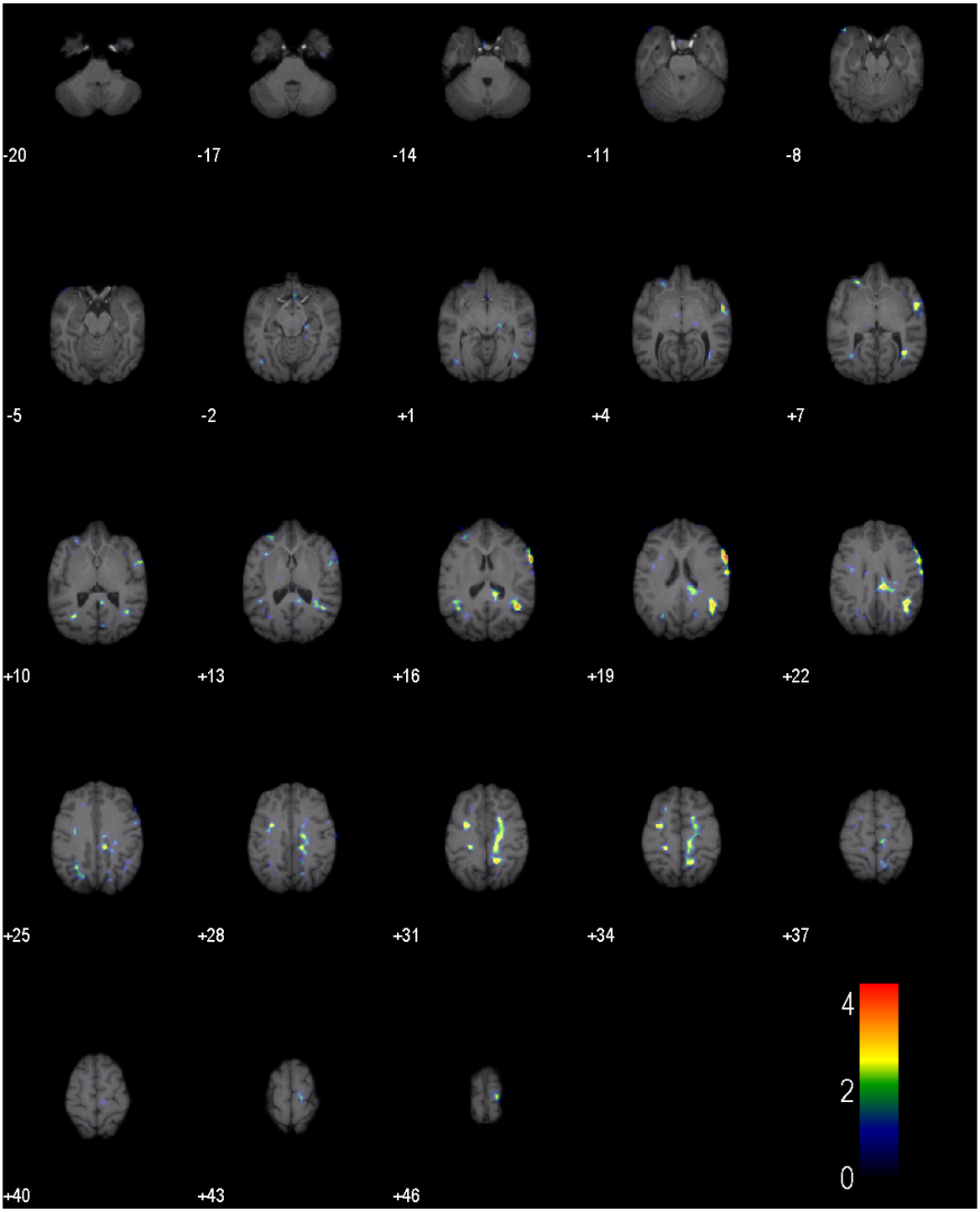


Figure A14: Non-social > high social #2

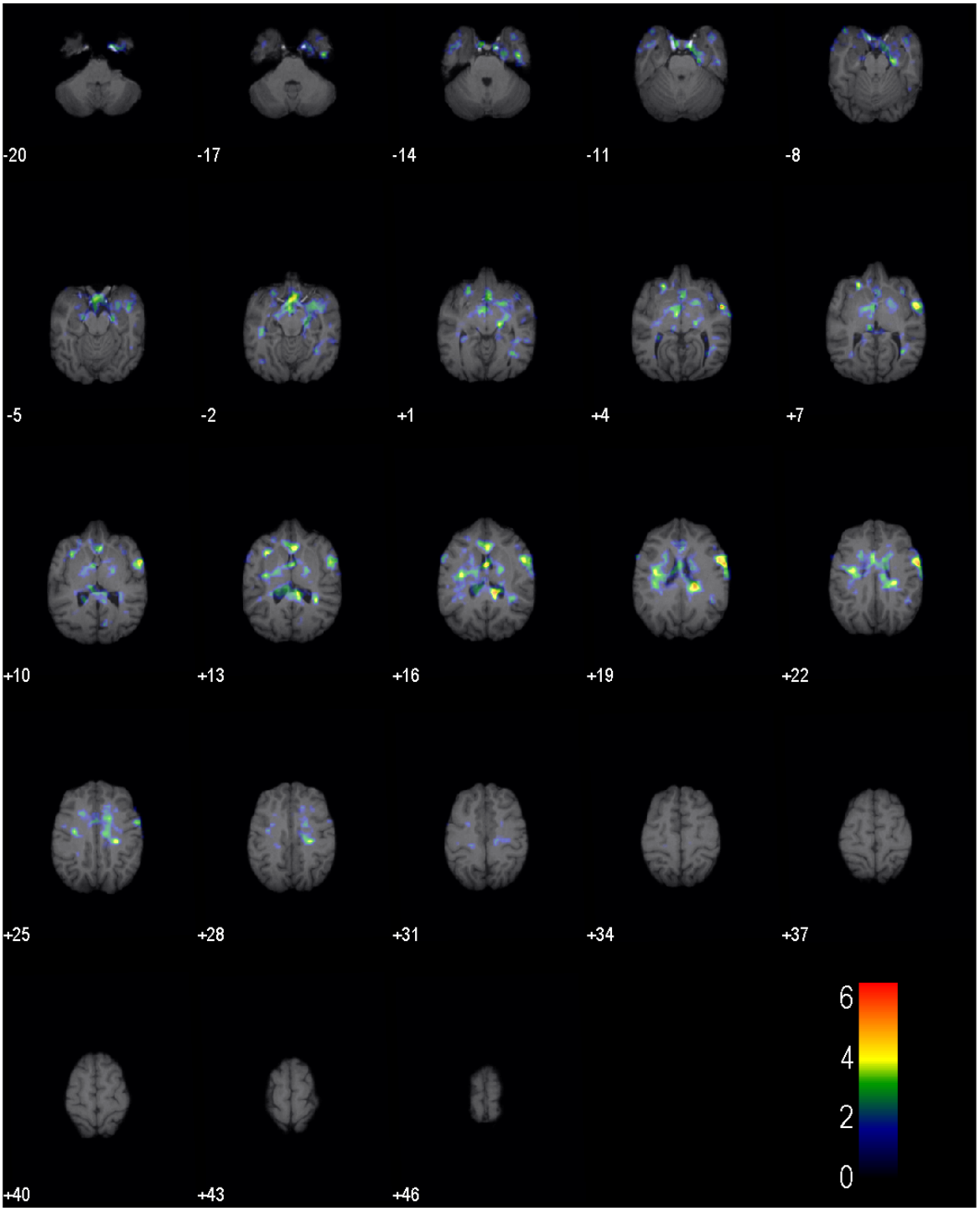


Figure A15: Non social > low social

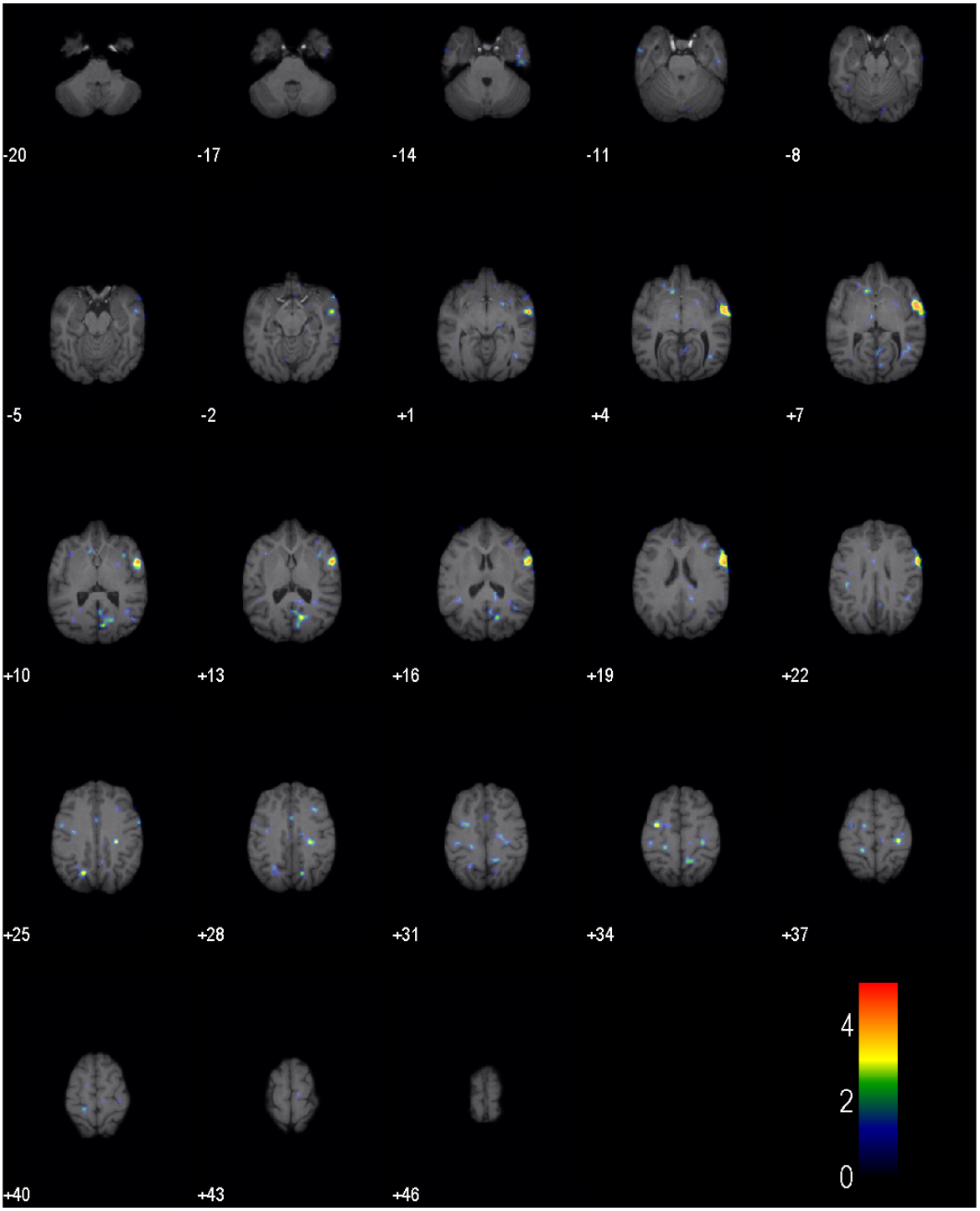


Figure A16: Non-social > rest

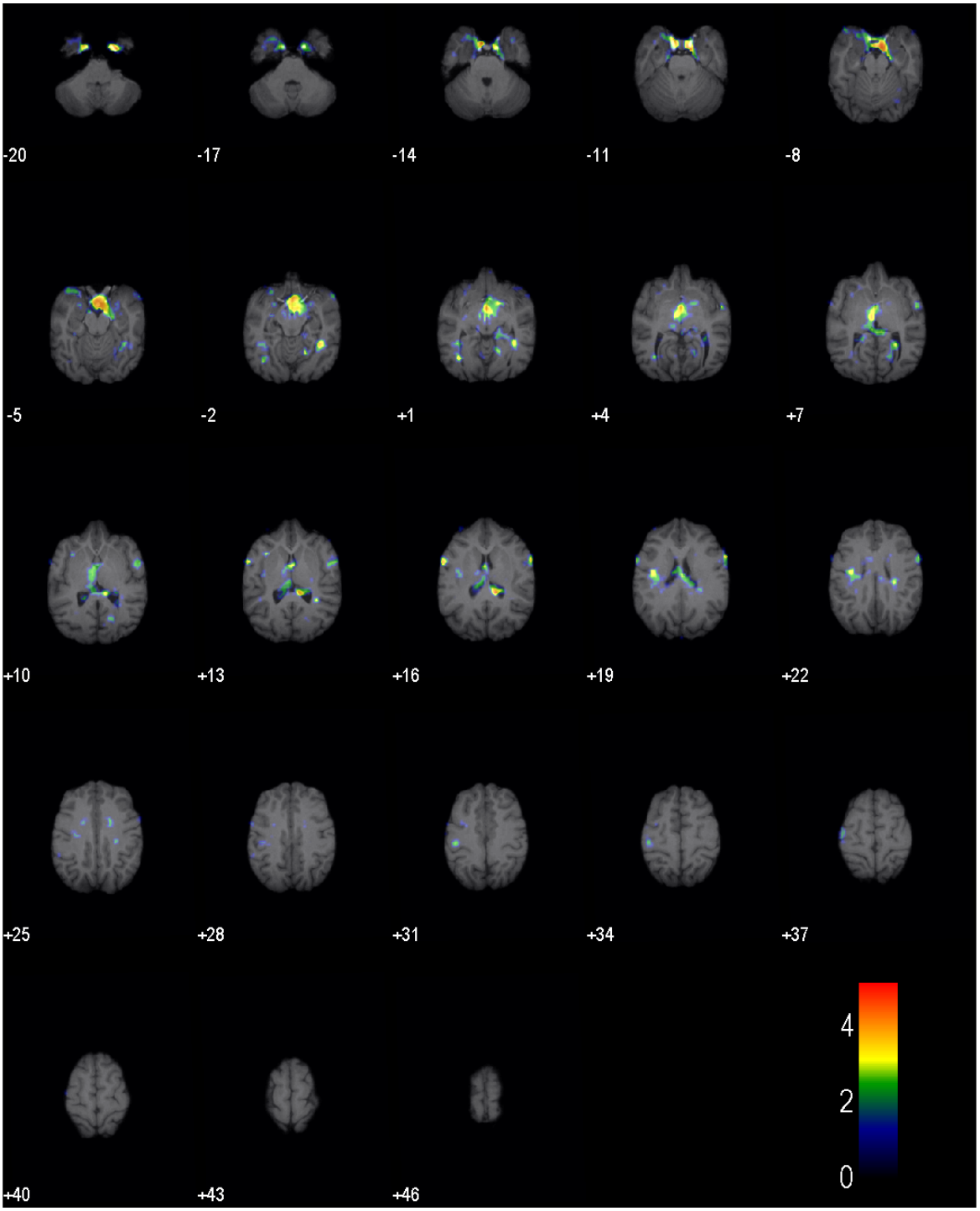


Figure A17: Rest > high social #1

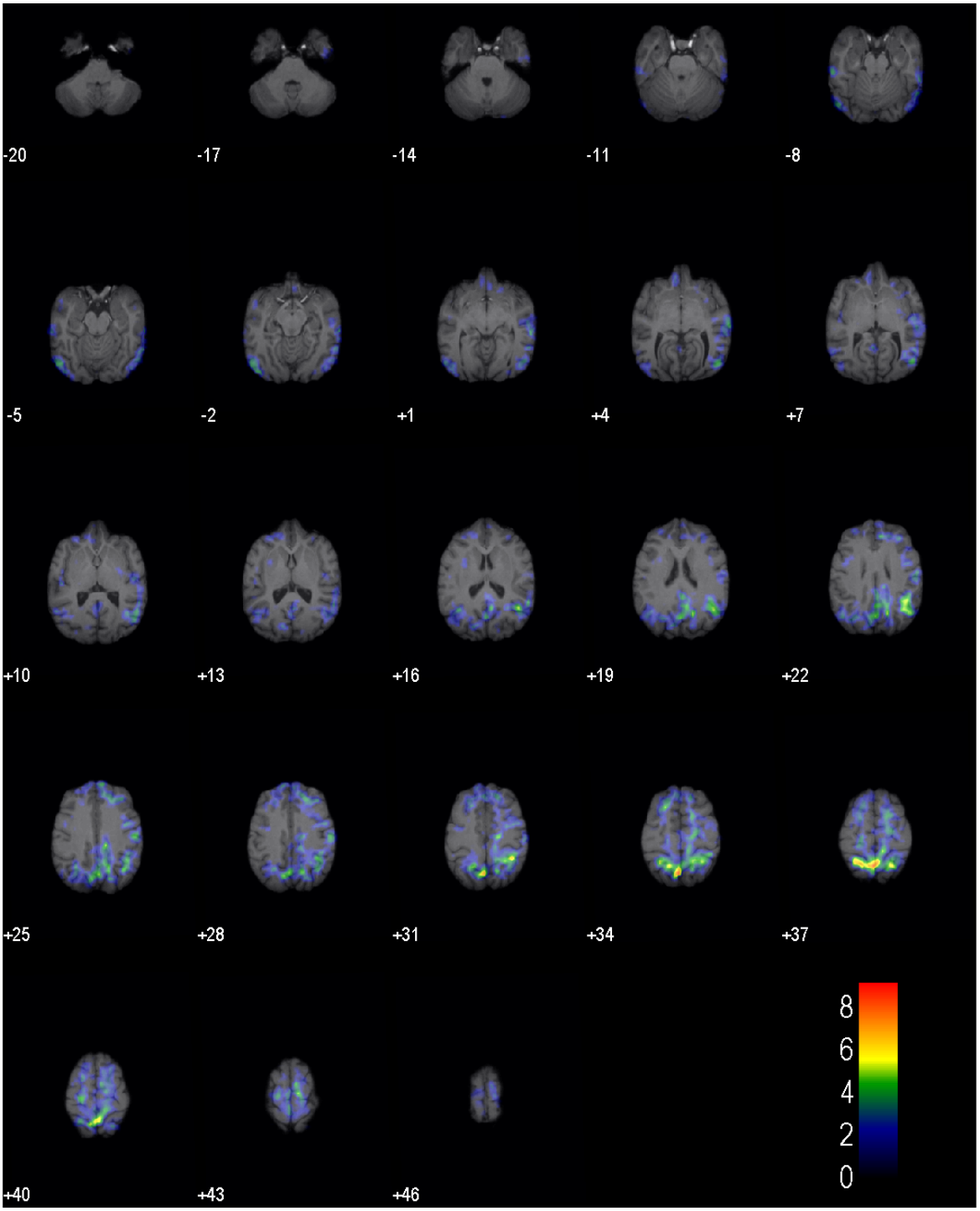


Figure A18: Rest > high social #2

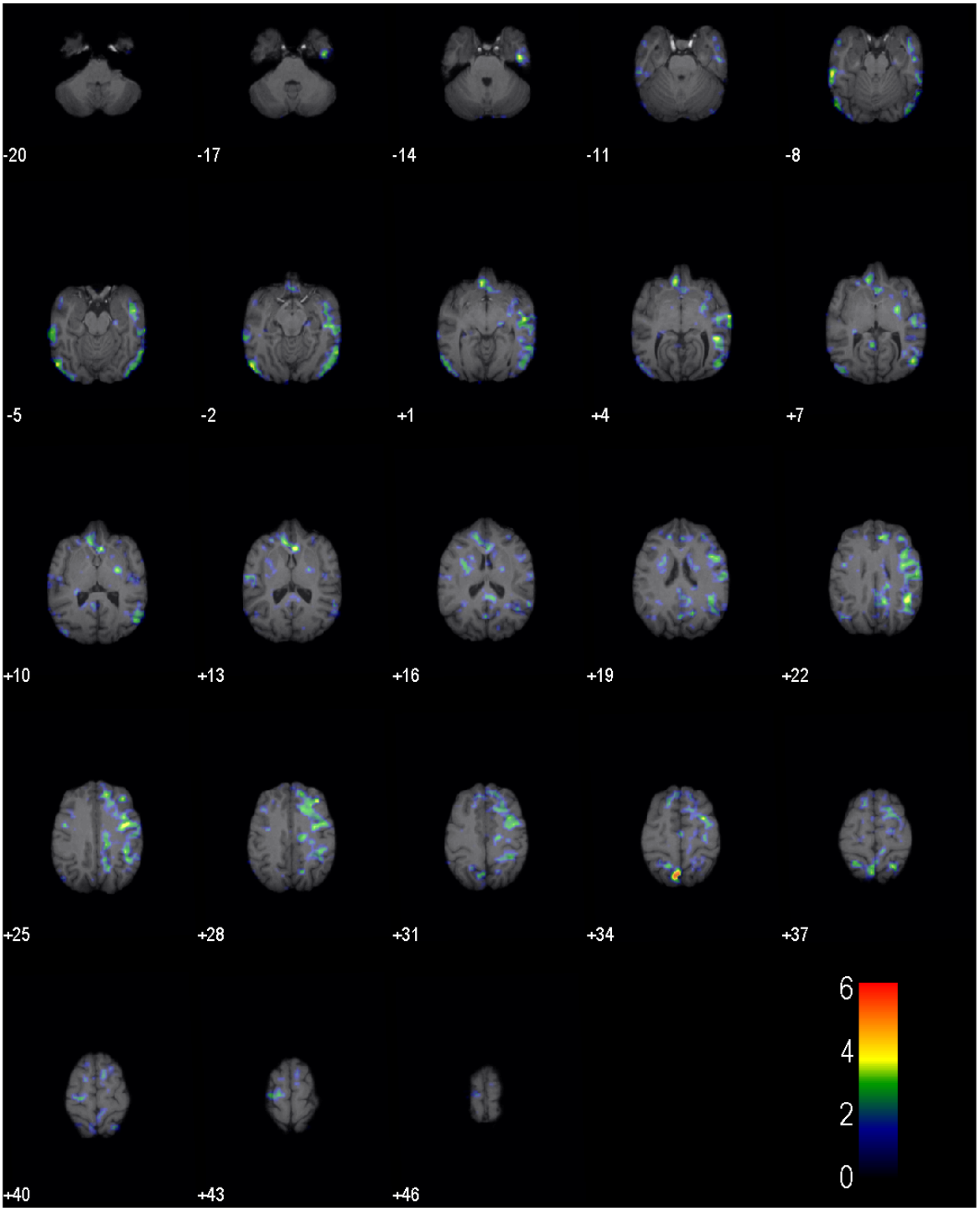


Figure A19: Rest > low social

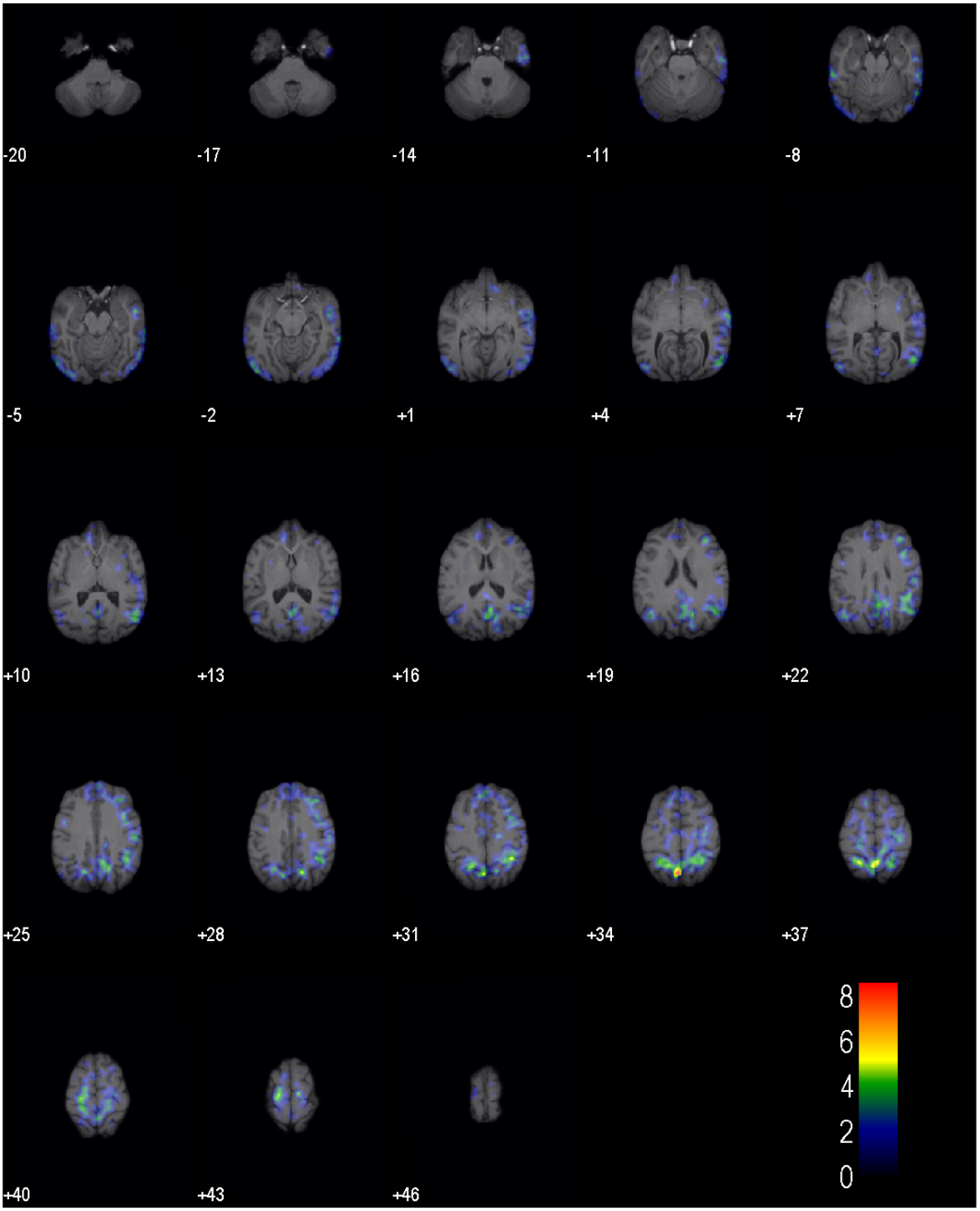


Figure A20: Rest > non-social

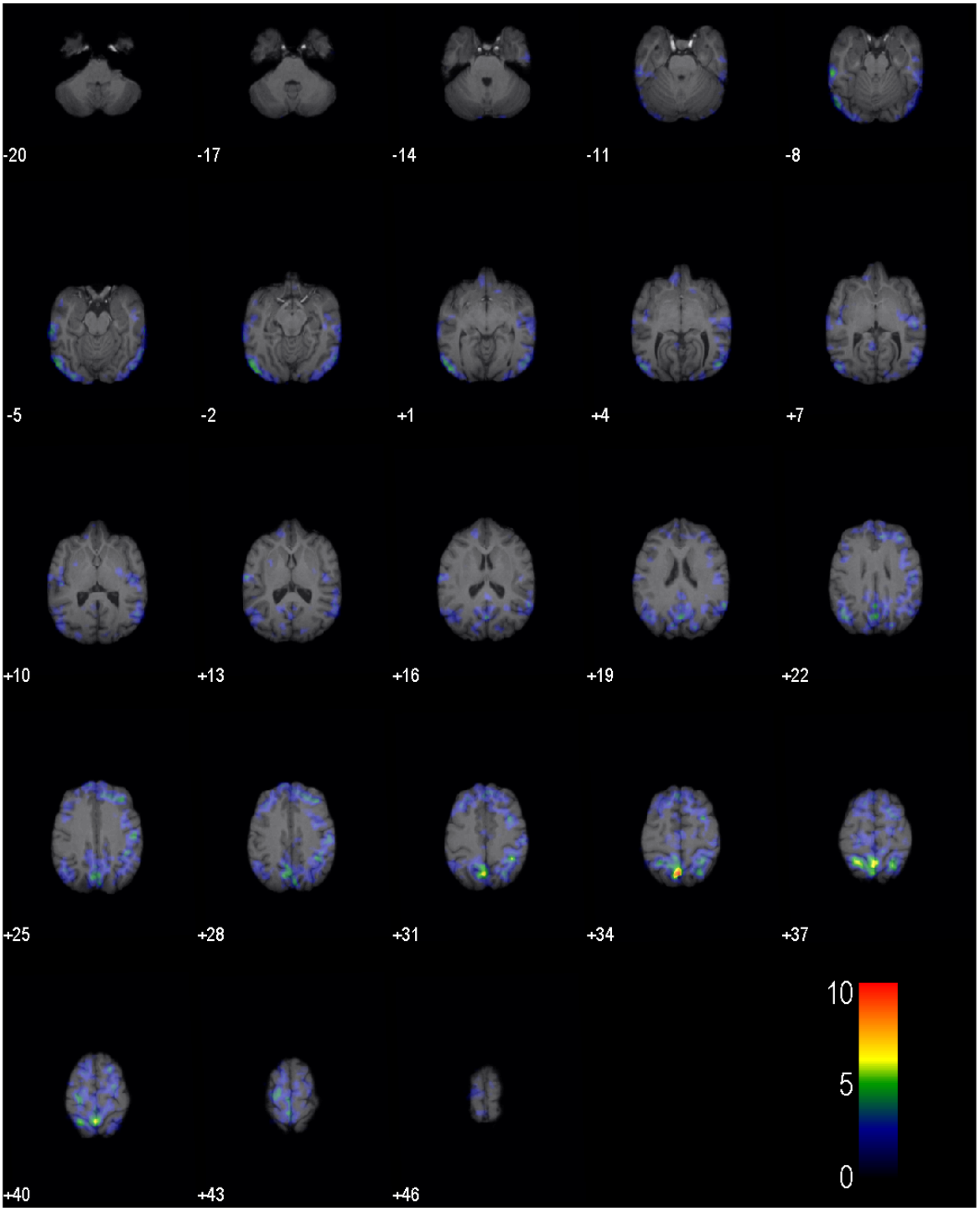


Figure A21: Both high socials > low social

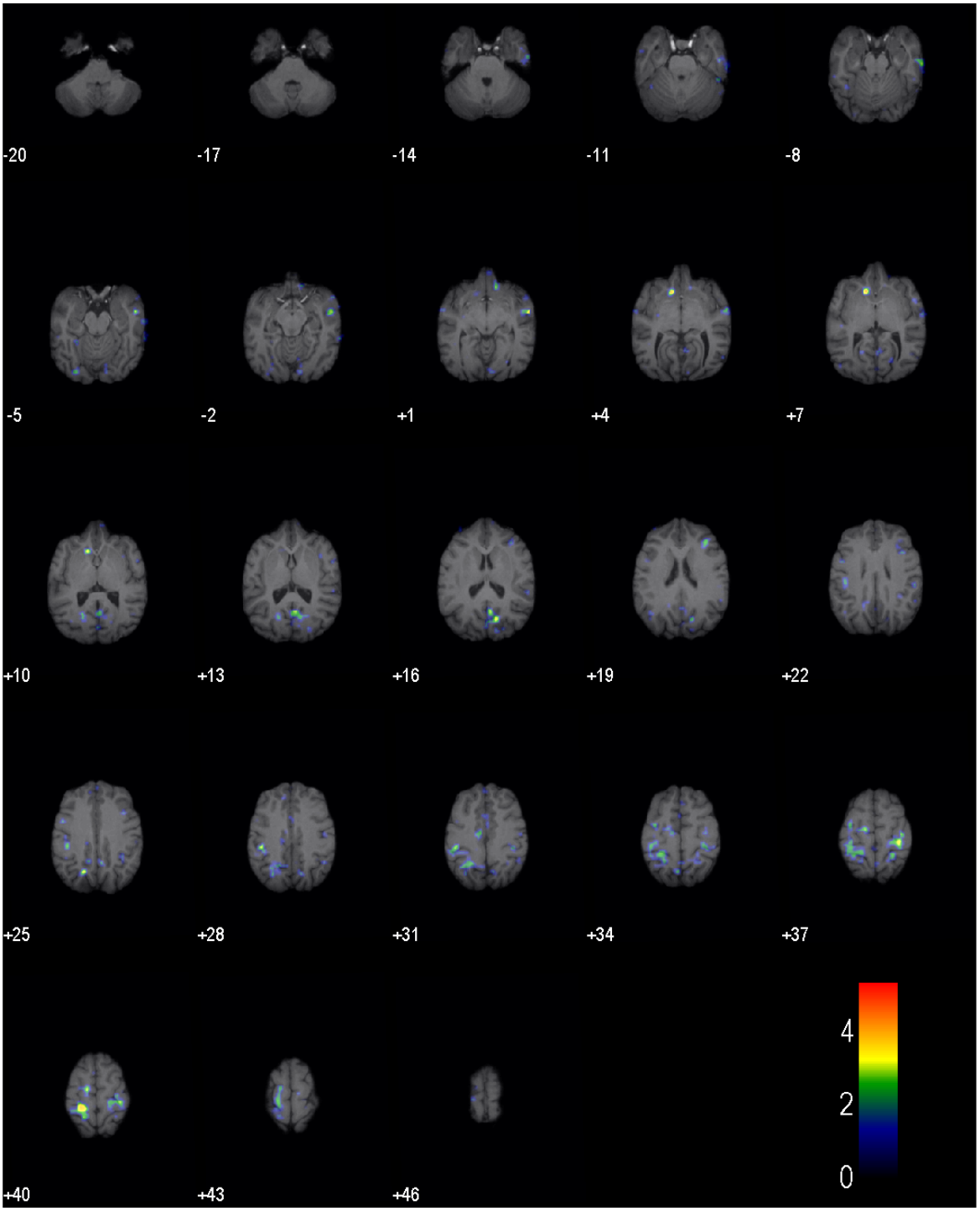


Figure A22: Low social > both high socials

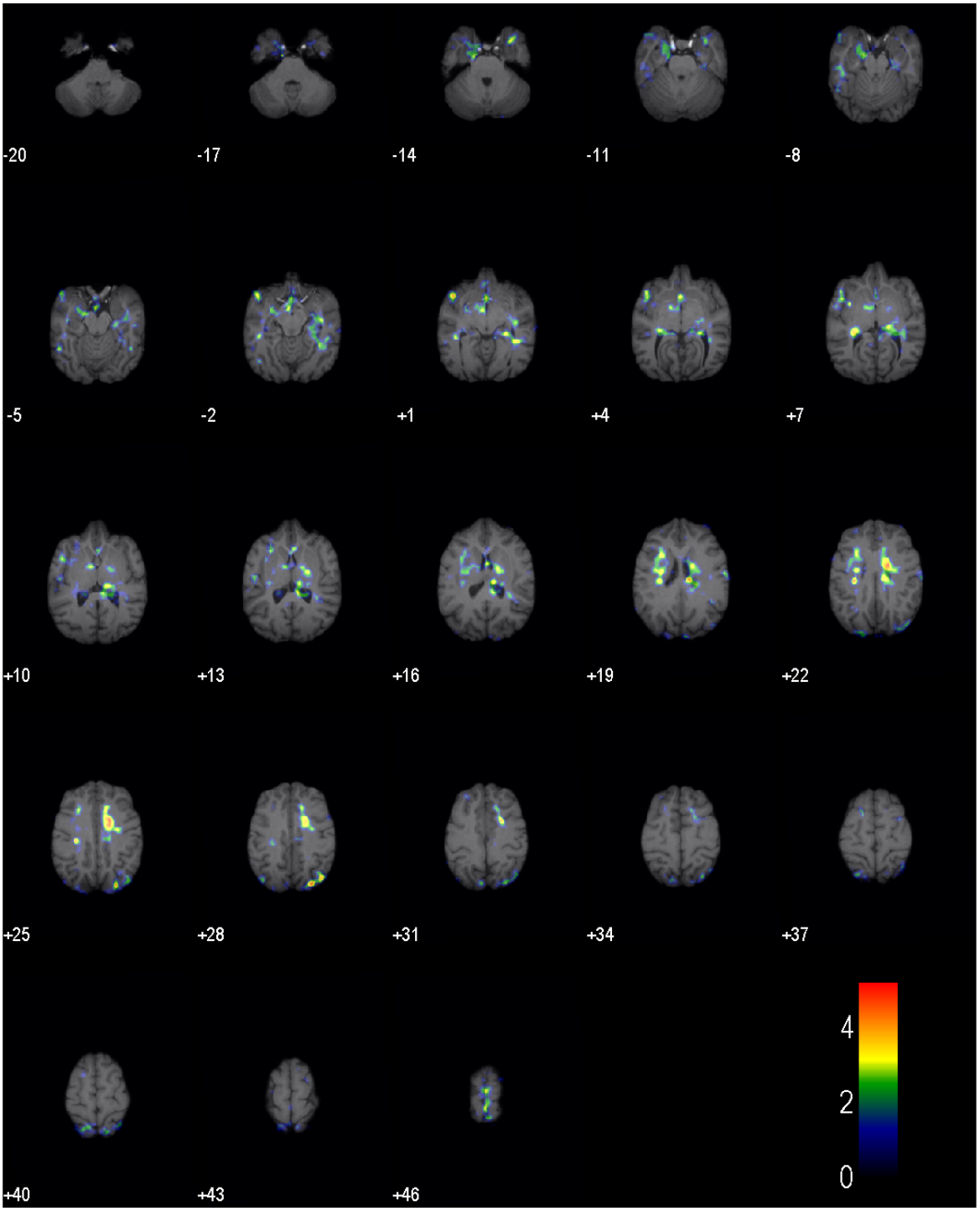


Figure A23: Both high socials > non-social

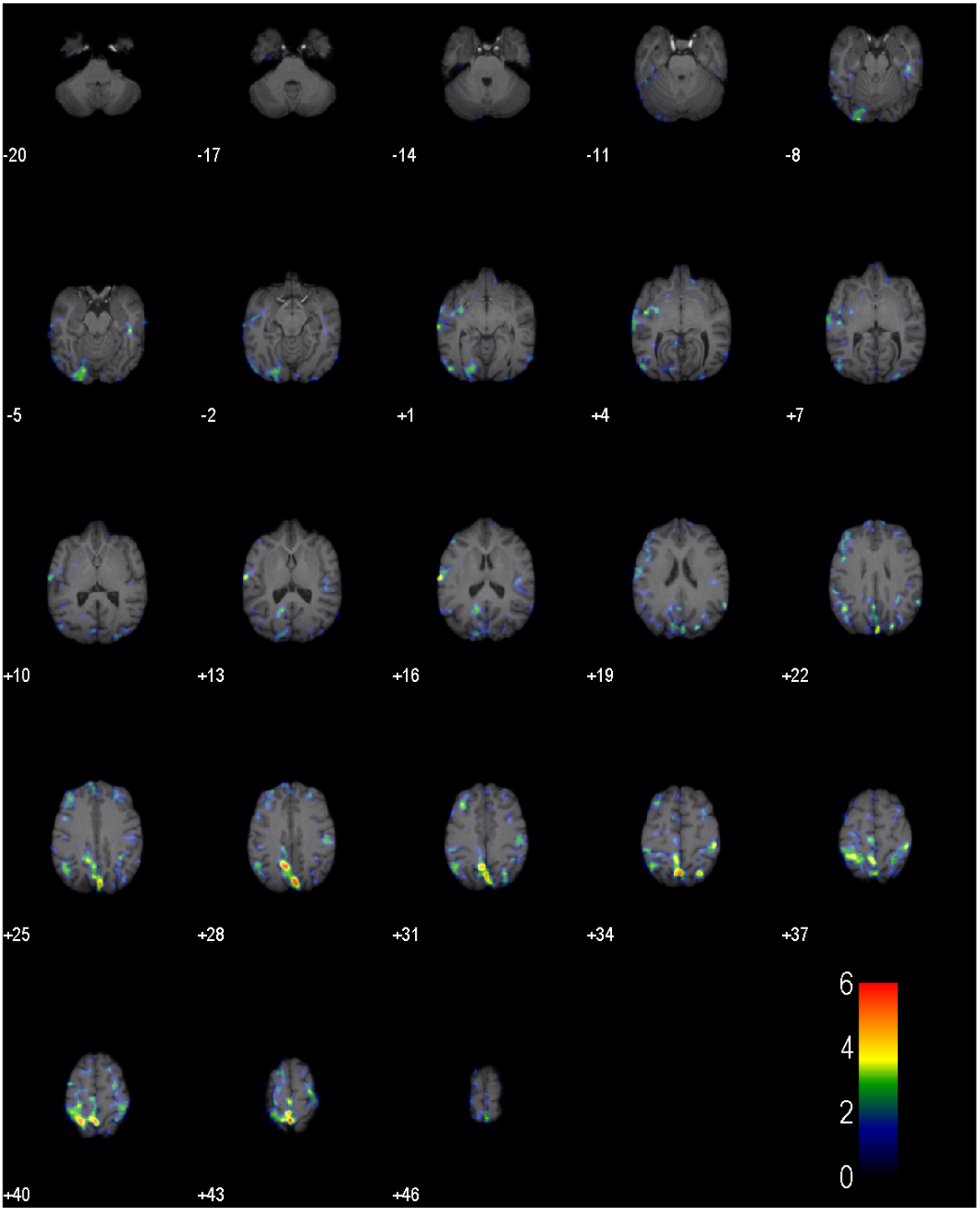


Figure A24: Non-social > both high socials

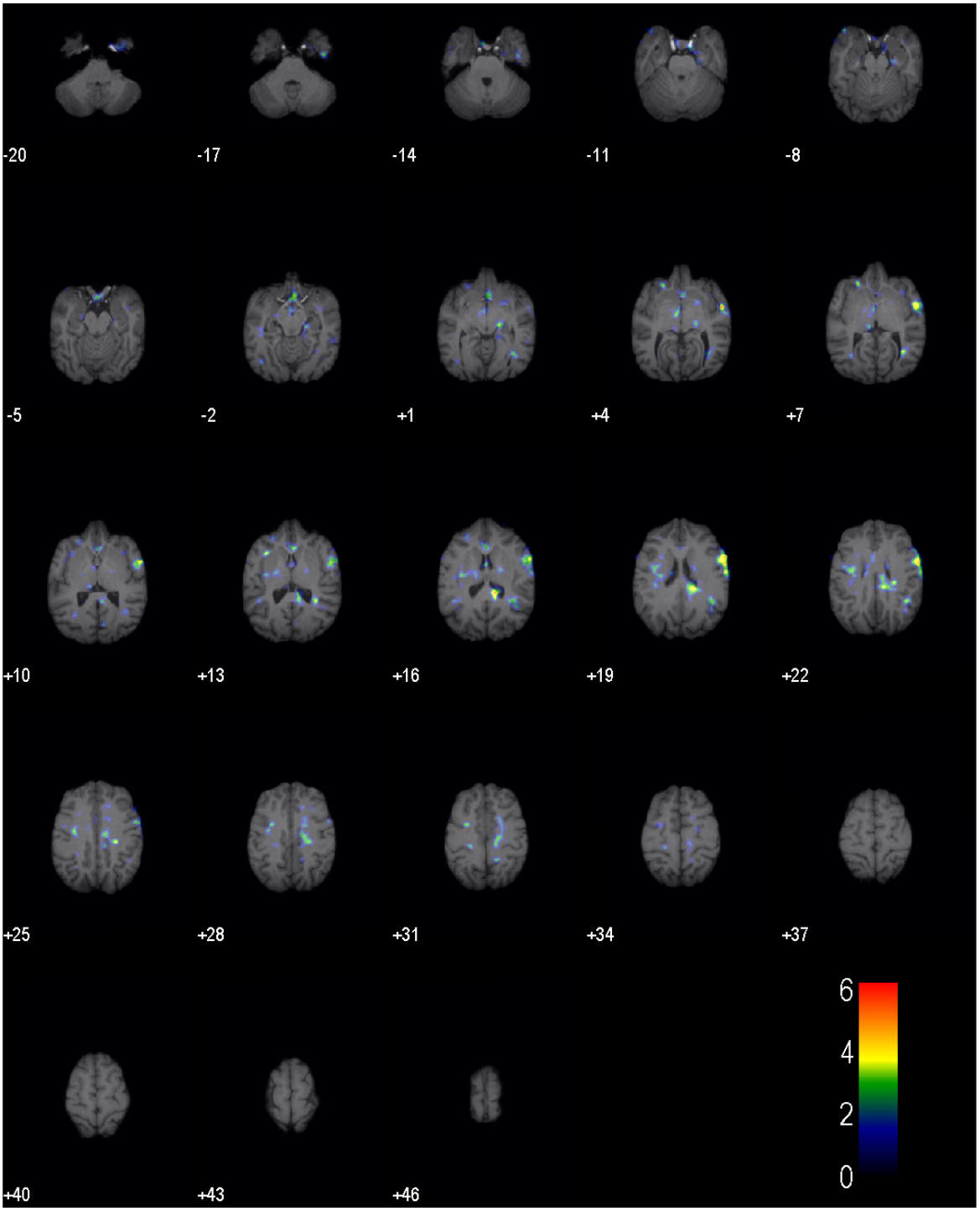


Figure A25: Both high socials > rest

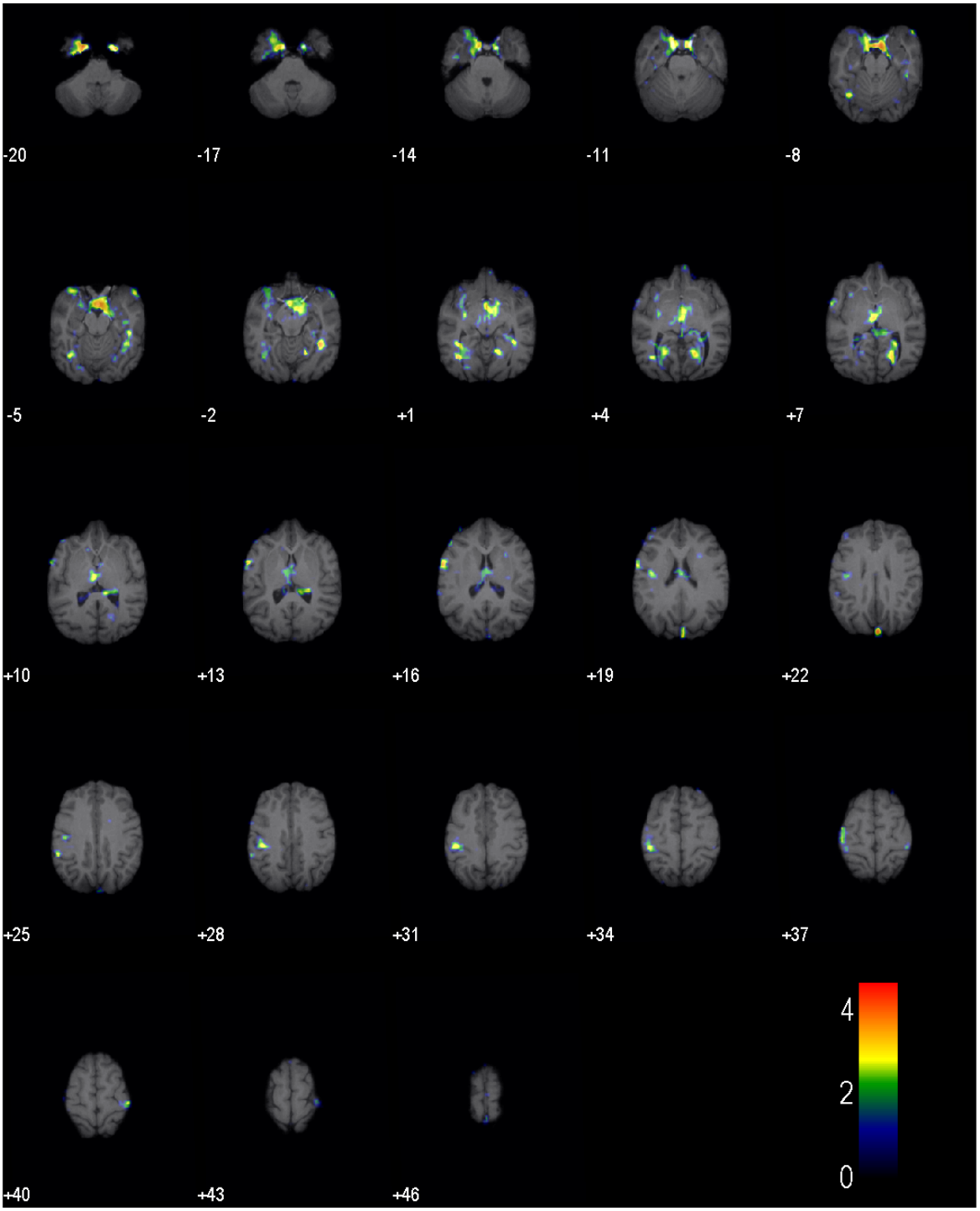


Figure A26: Rest > both high socials

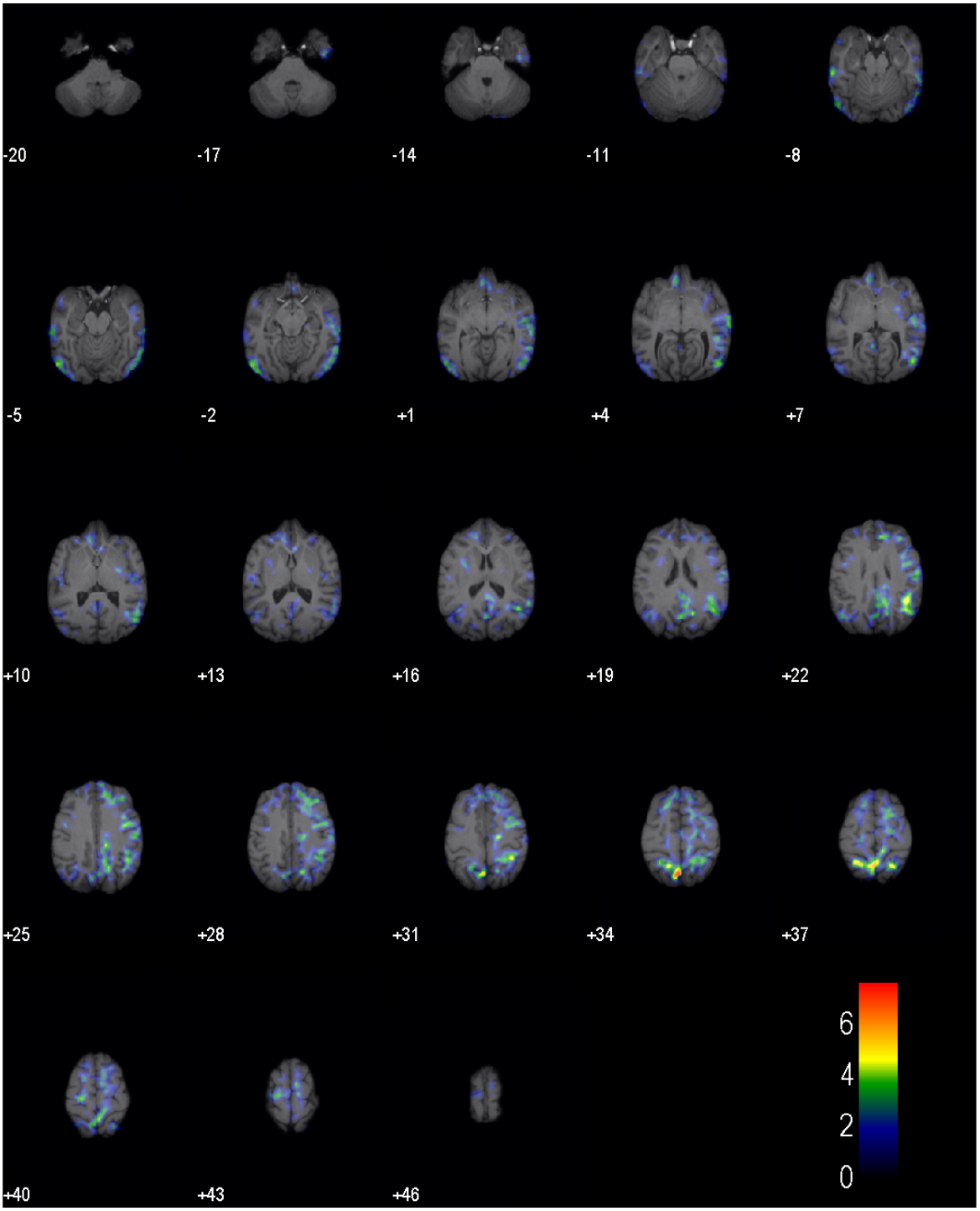


Figure A27: All socials > non-social

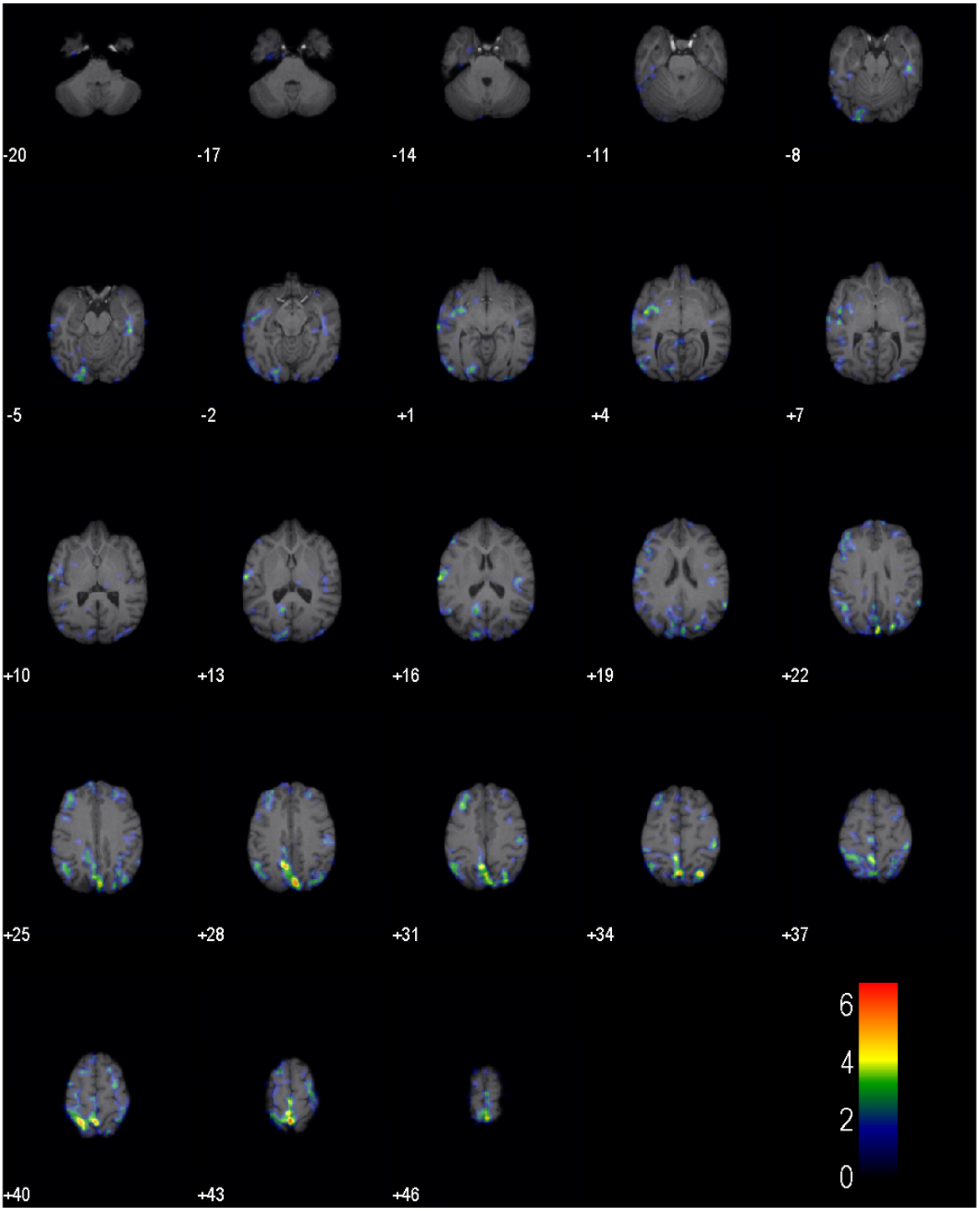


Figure A28: Non-social > all socials

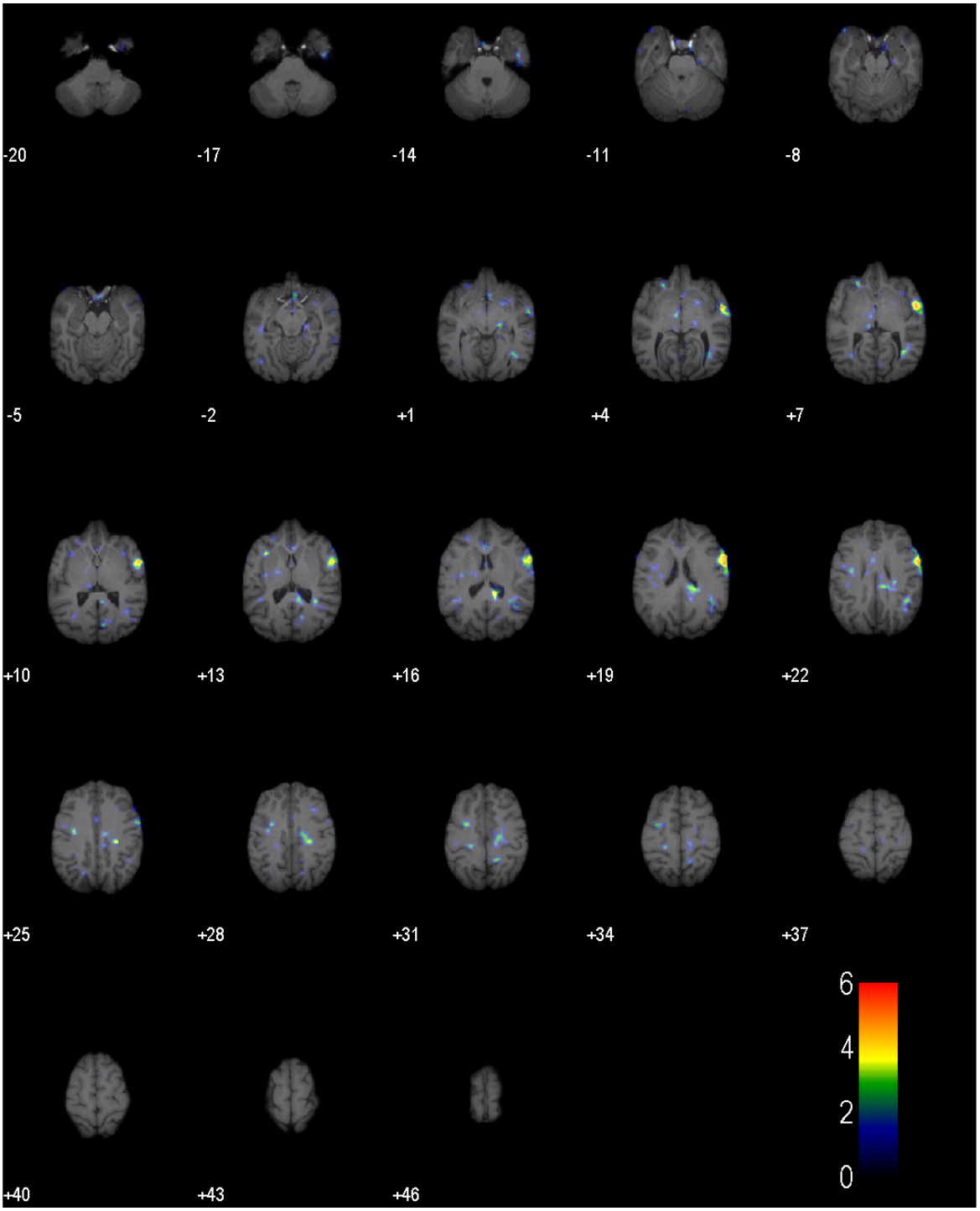


Figure A29: All socials > rest

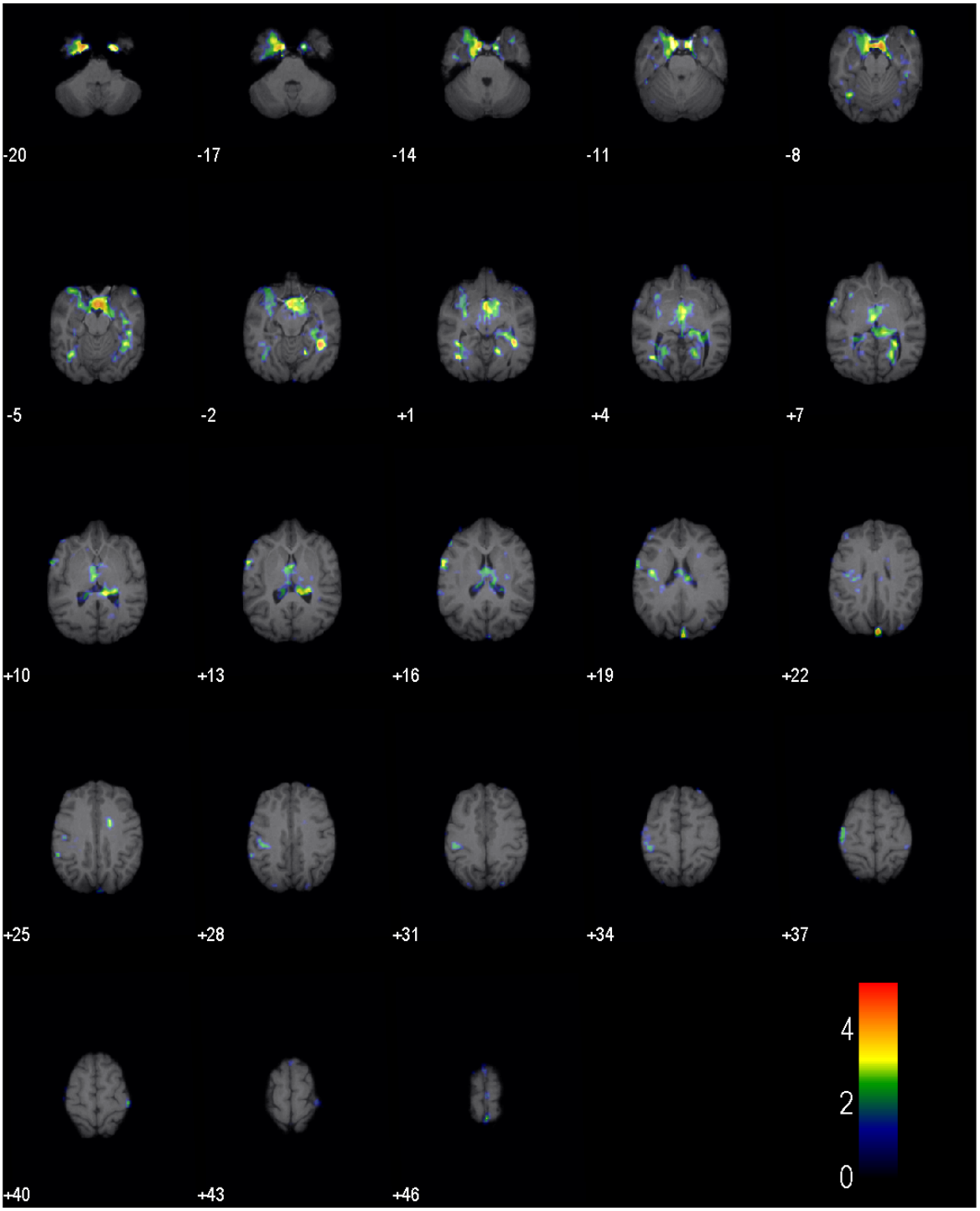


Figure A30: Rest > all socials

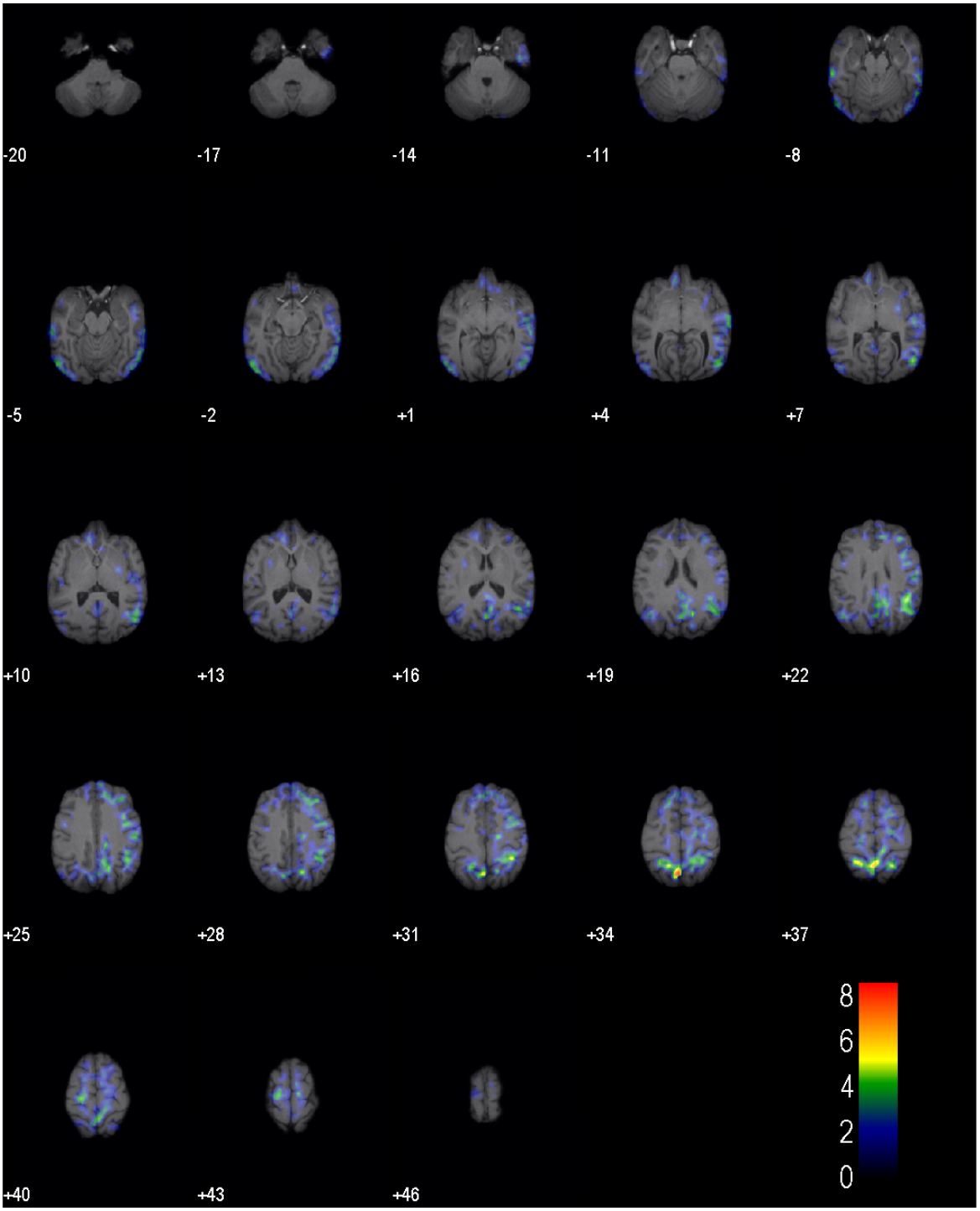


Figure A31: Rest > all tasks

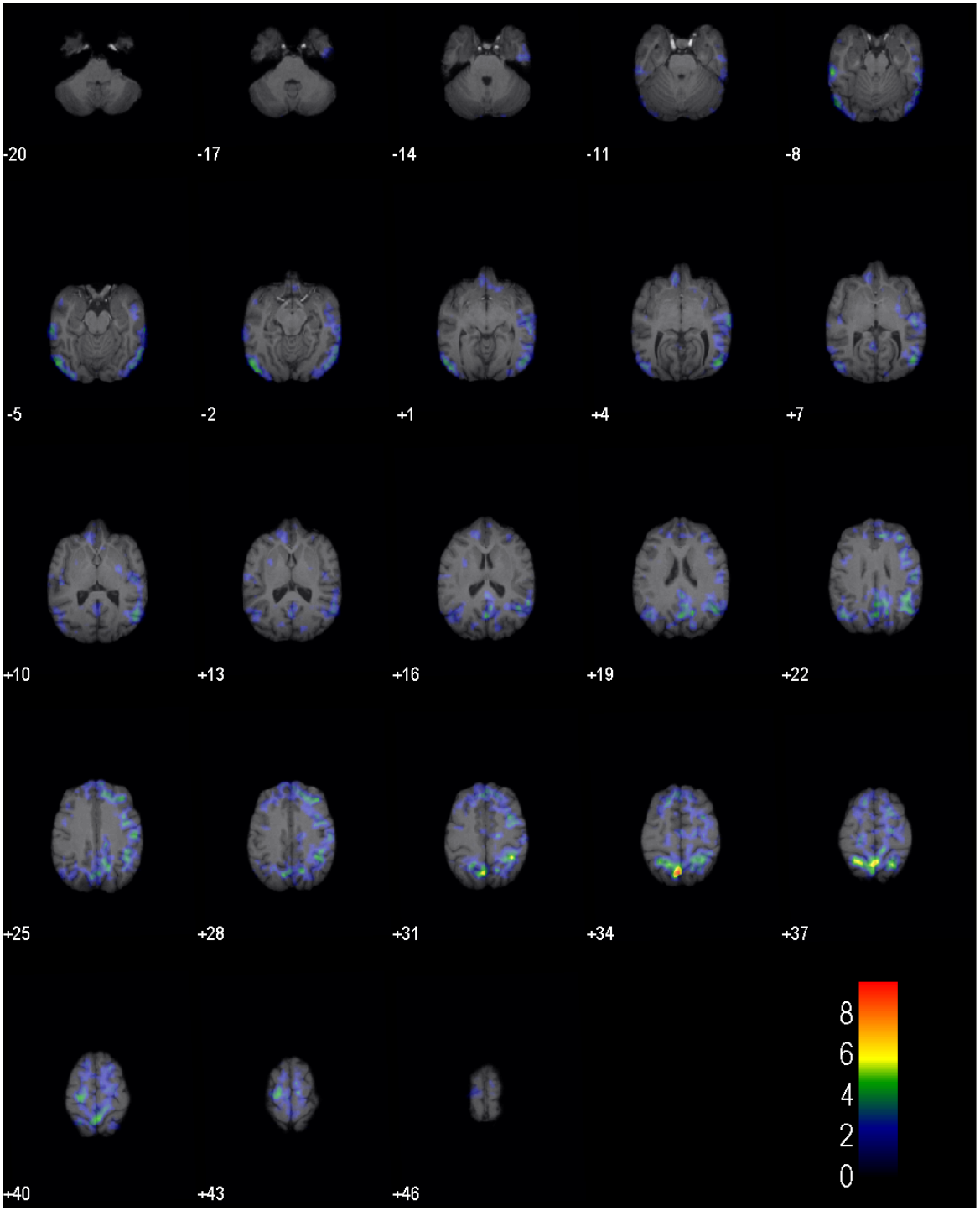
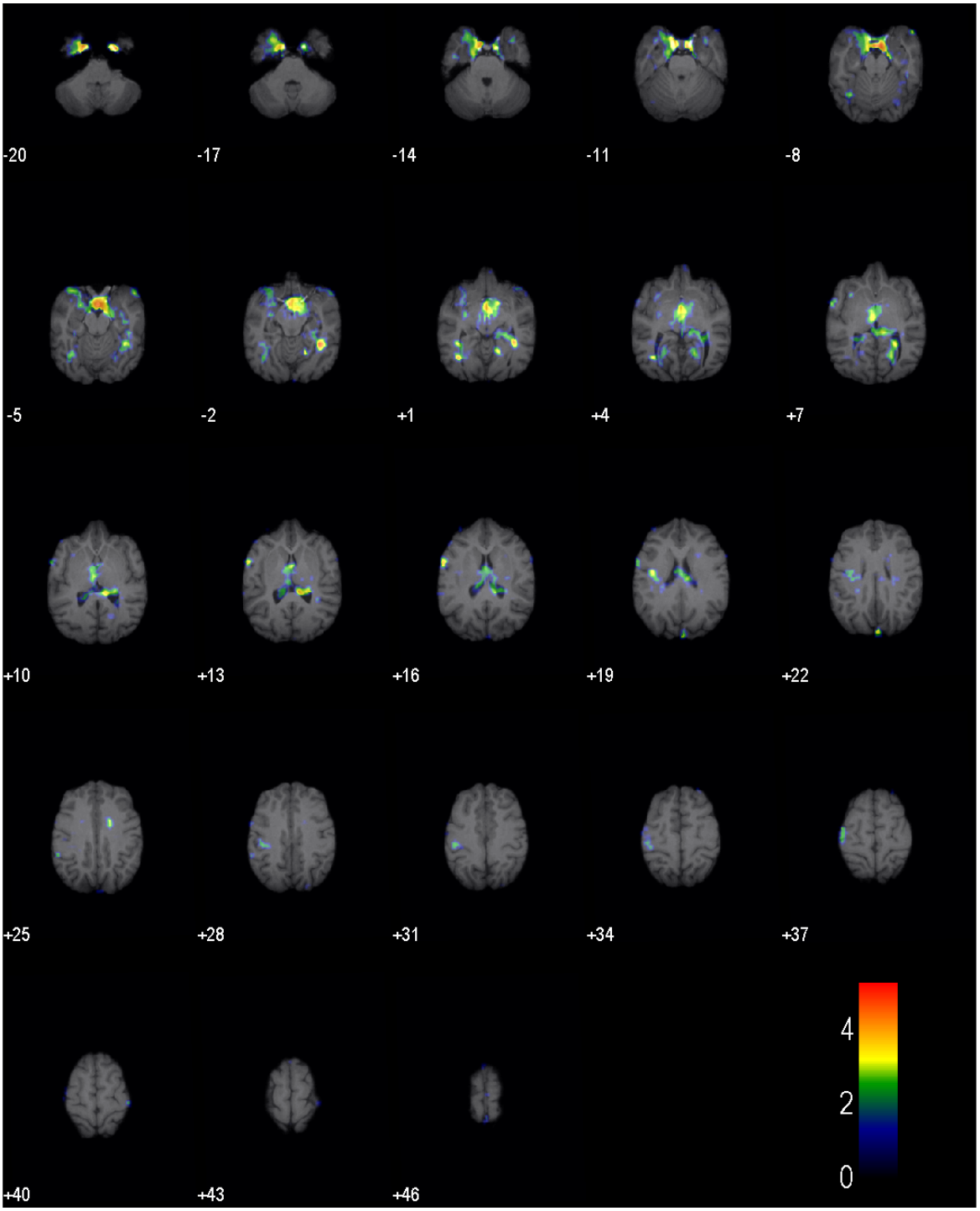


Figure A32: All tasks > rest



Results for each contrast ($p < 0.05$), resting state ROI. Color bar indicates value of t-statistic. Anterior commissure at Z = 6.

Figure A33: High social #1 > high social #2, resting state ROI

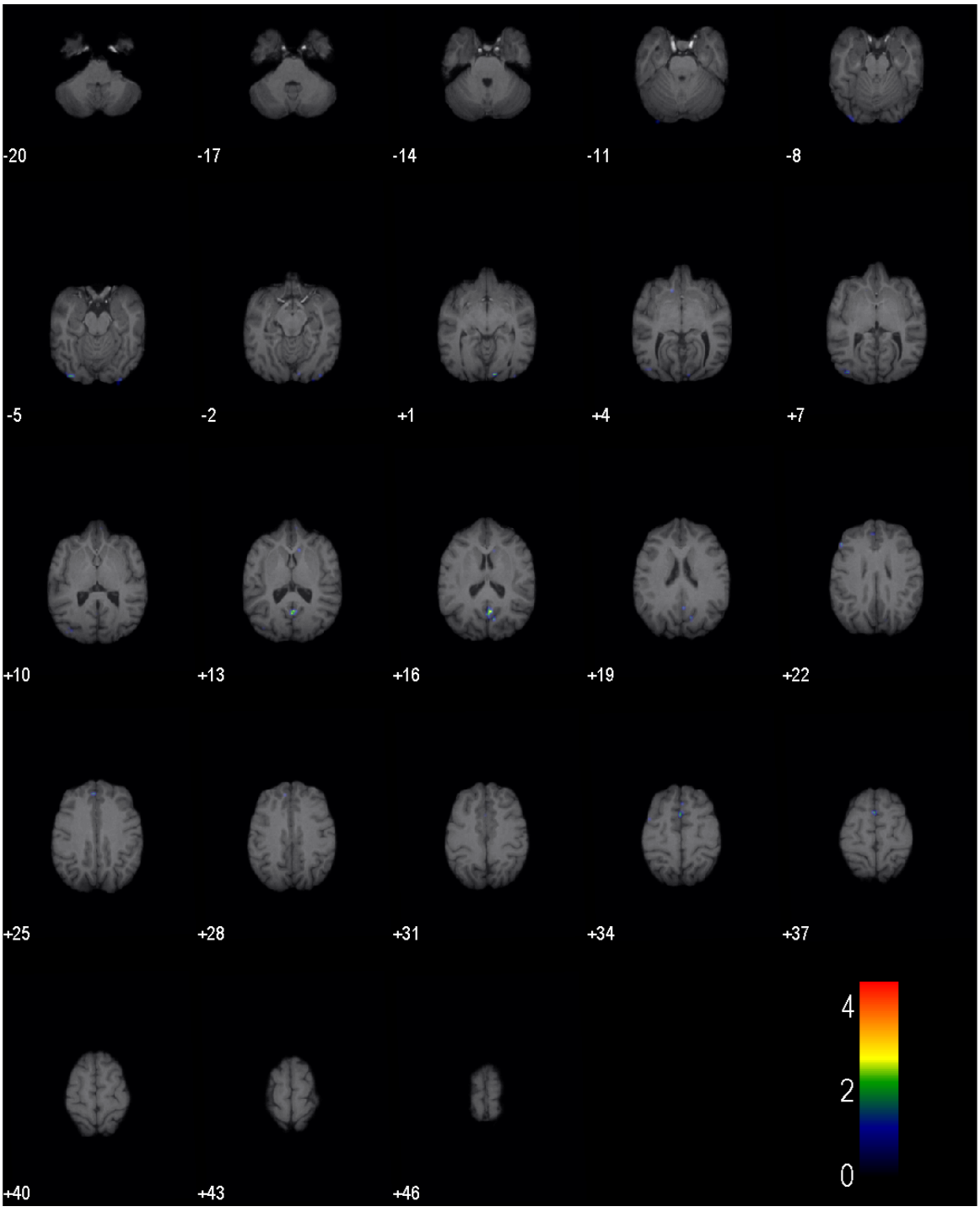


Figure A34: High social #1 > low social, resting state ROI

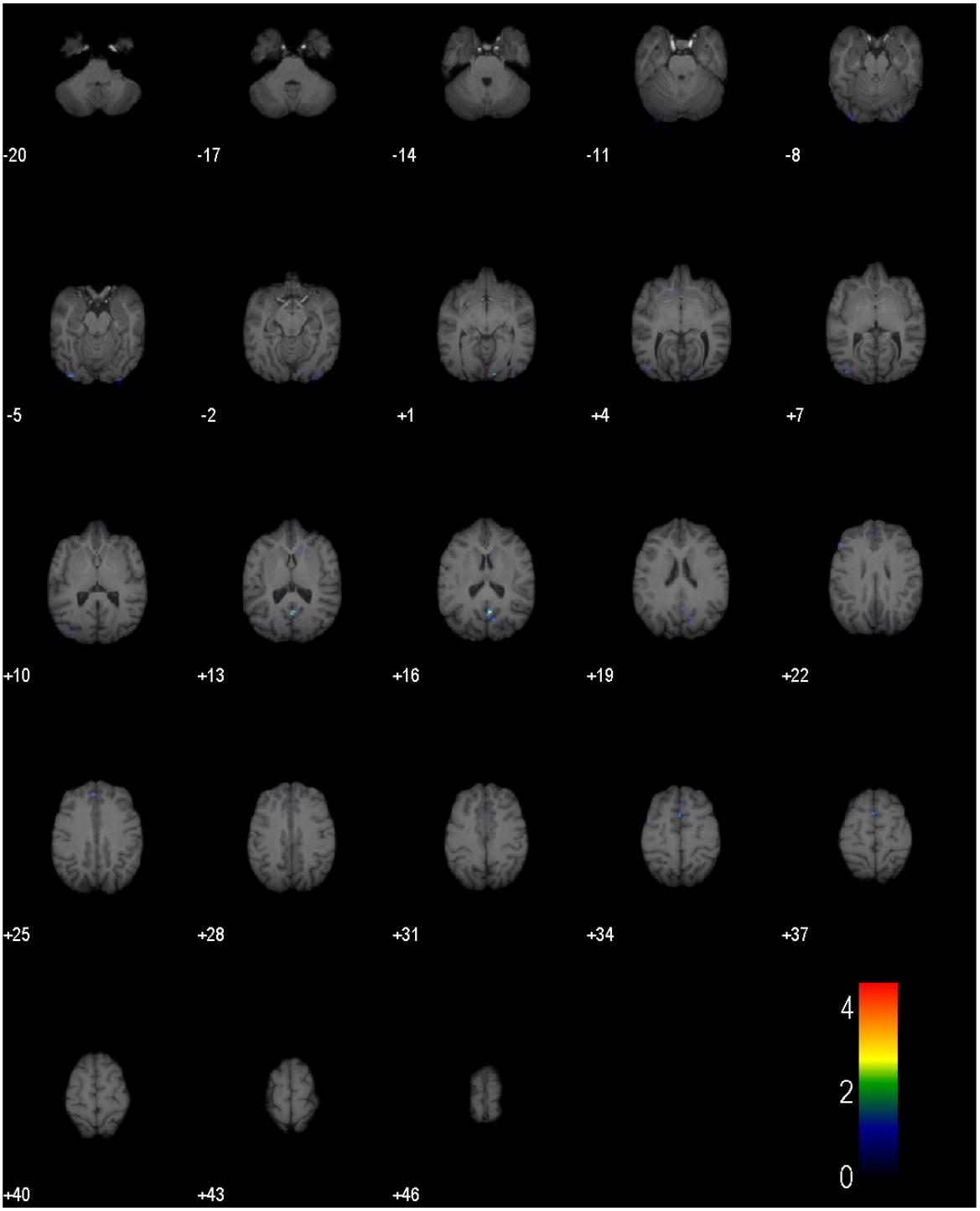


Figure A35: High social #1 > non-social, resting state ROI

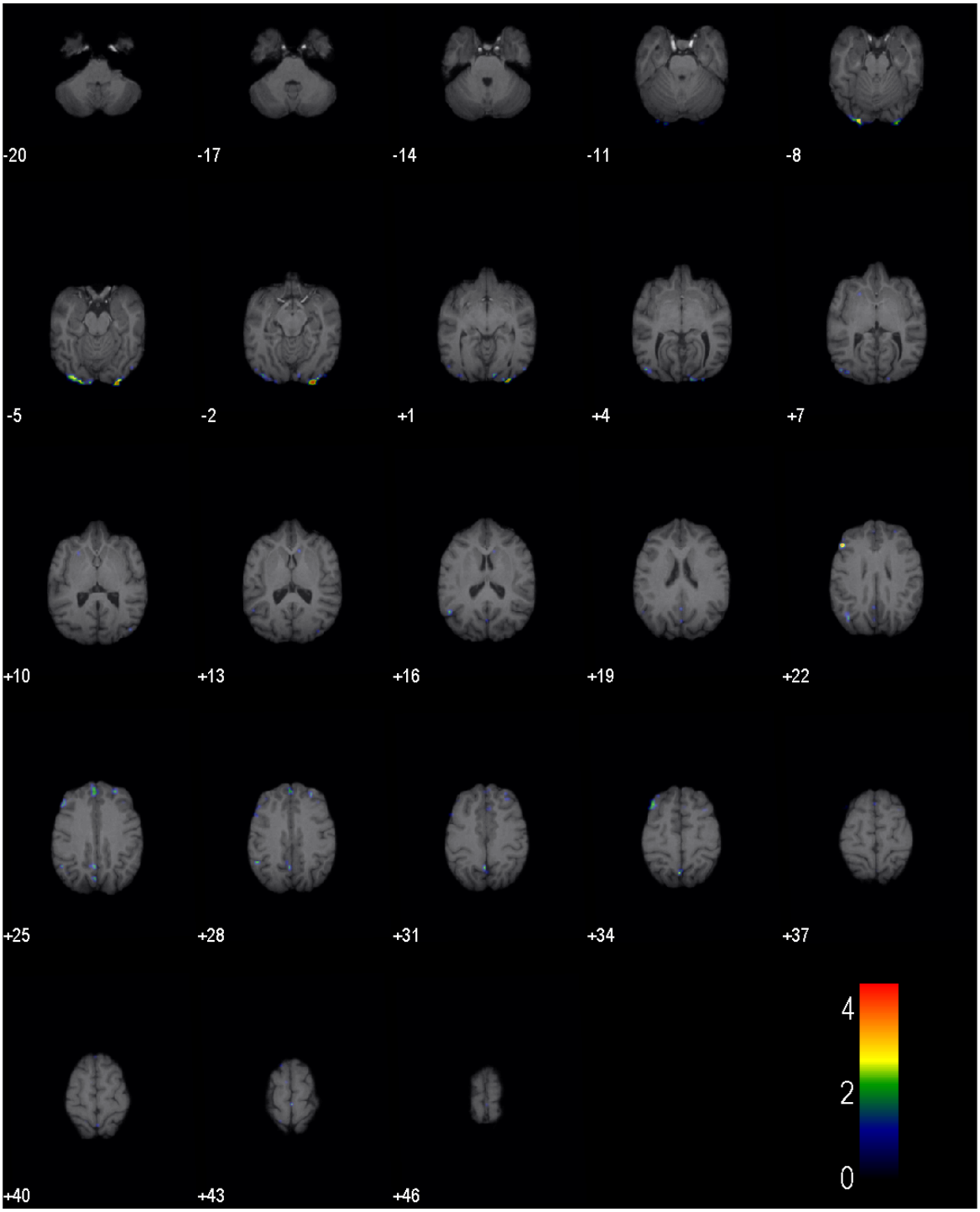


Figure A36: High social #1 > rest, resting state ROI

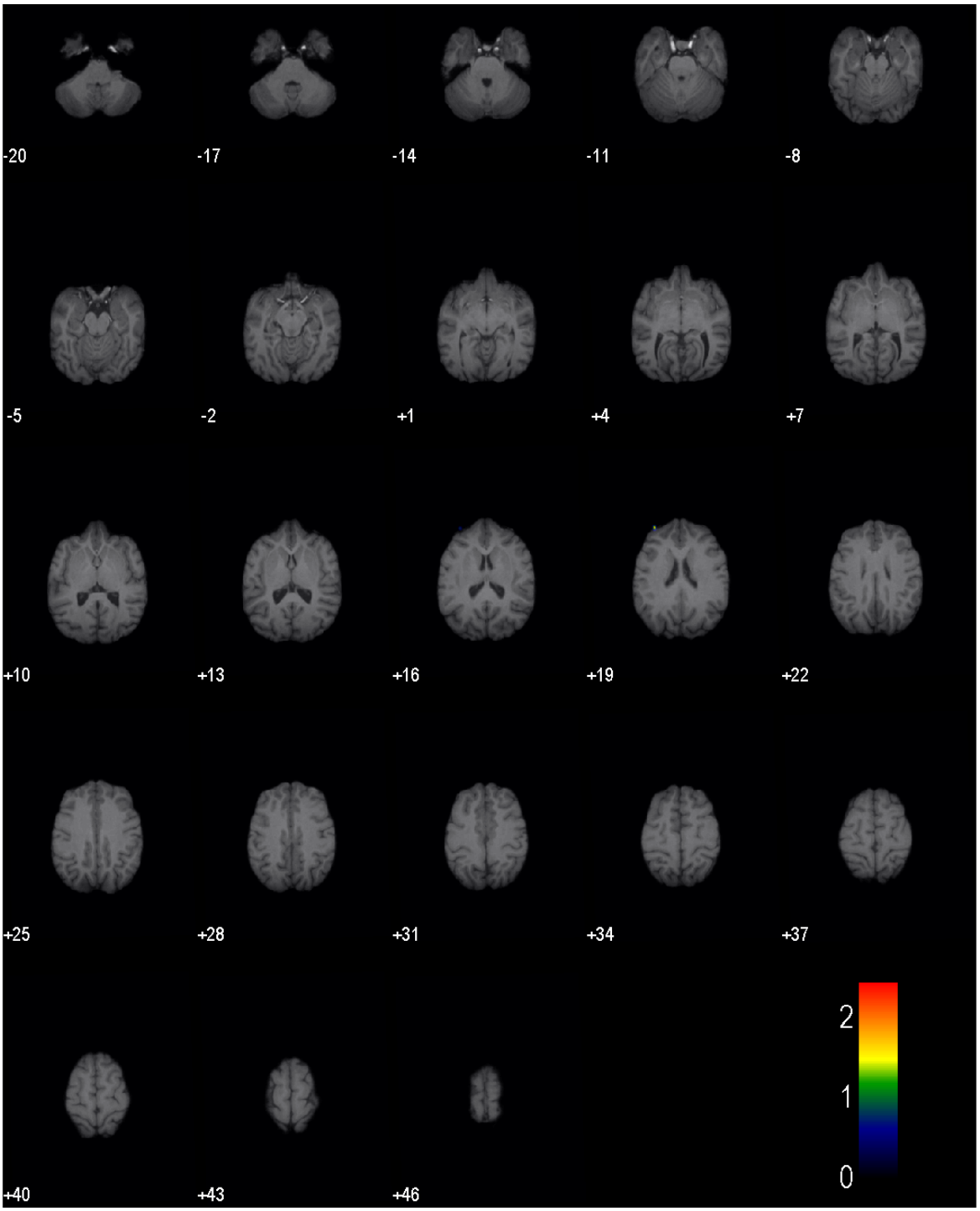


Figure A37: High social #2 > high social #1, resting state ROI

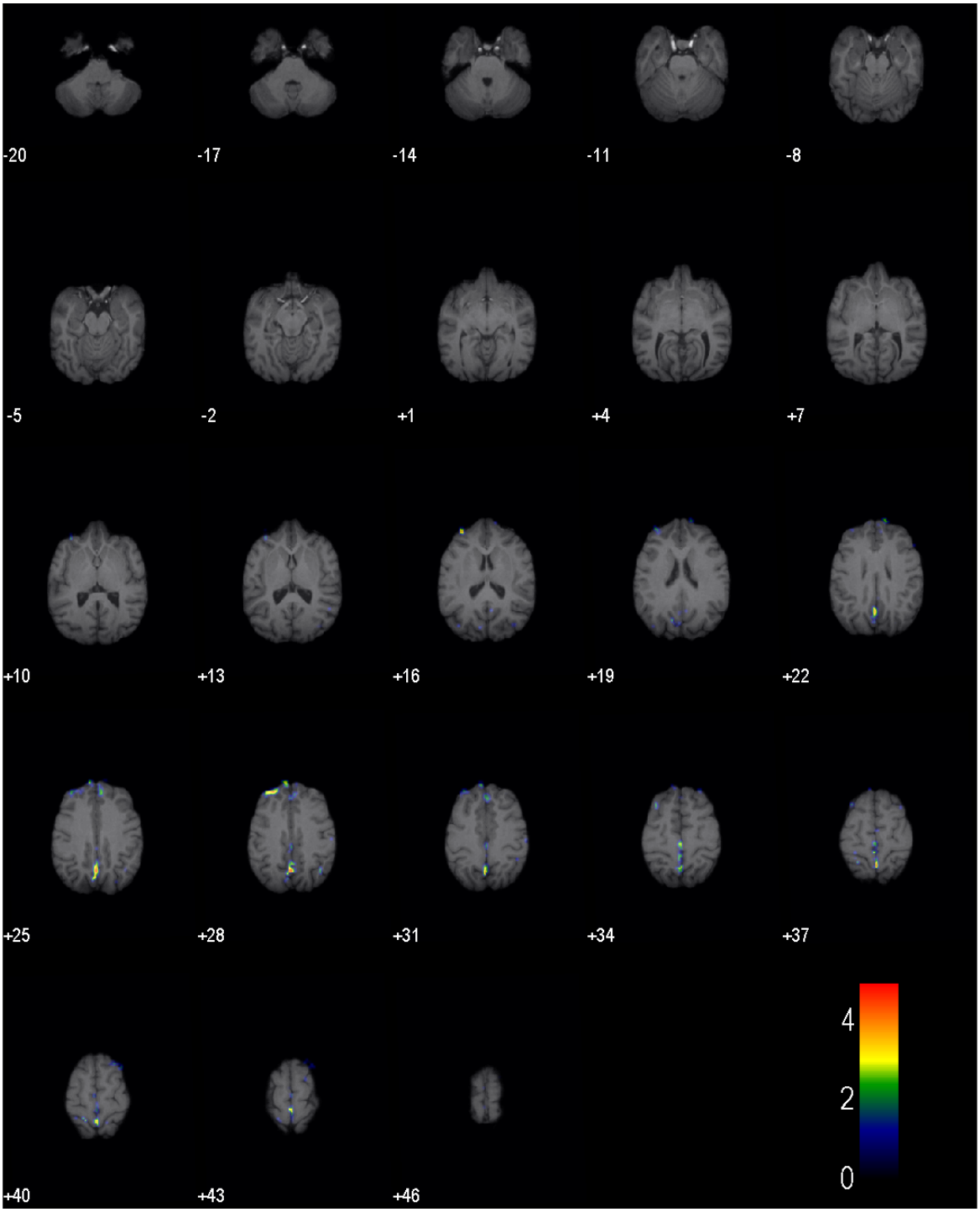


Figure A38: High social #2 > low social, resting state ROI

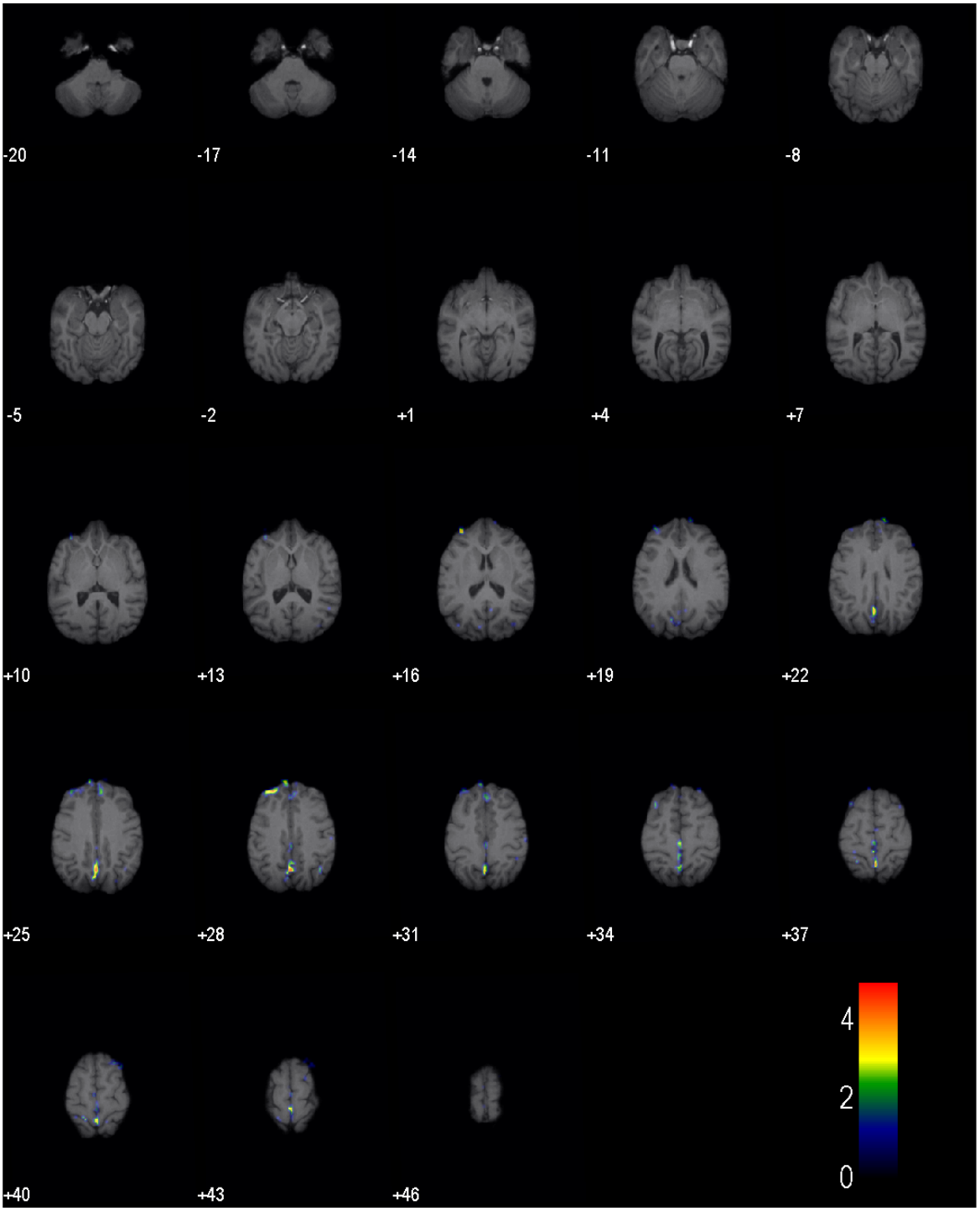


Figure A39: High social #2 > non-social, resting state ROI

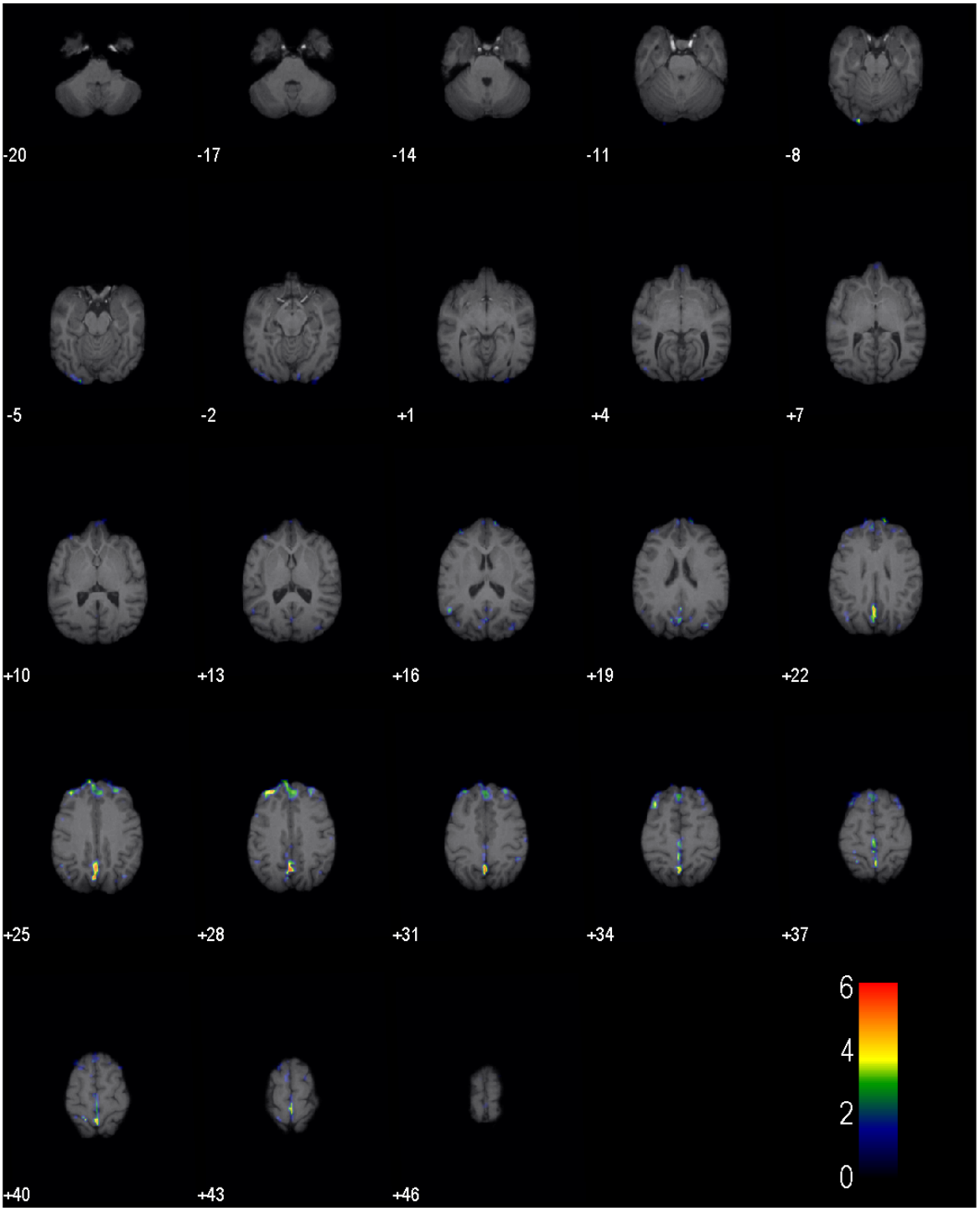


Figure A40: High social #2 > rest, resting state ROI

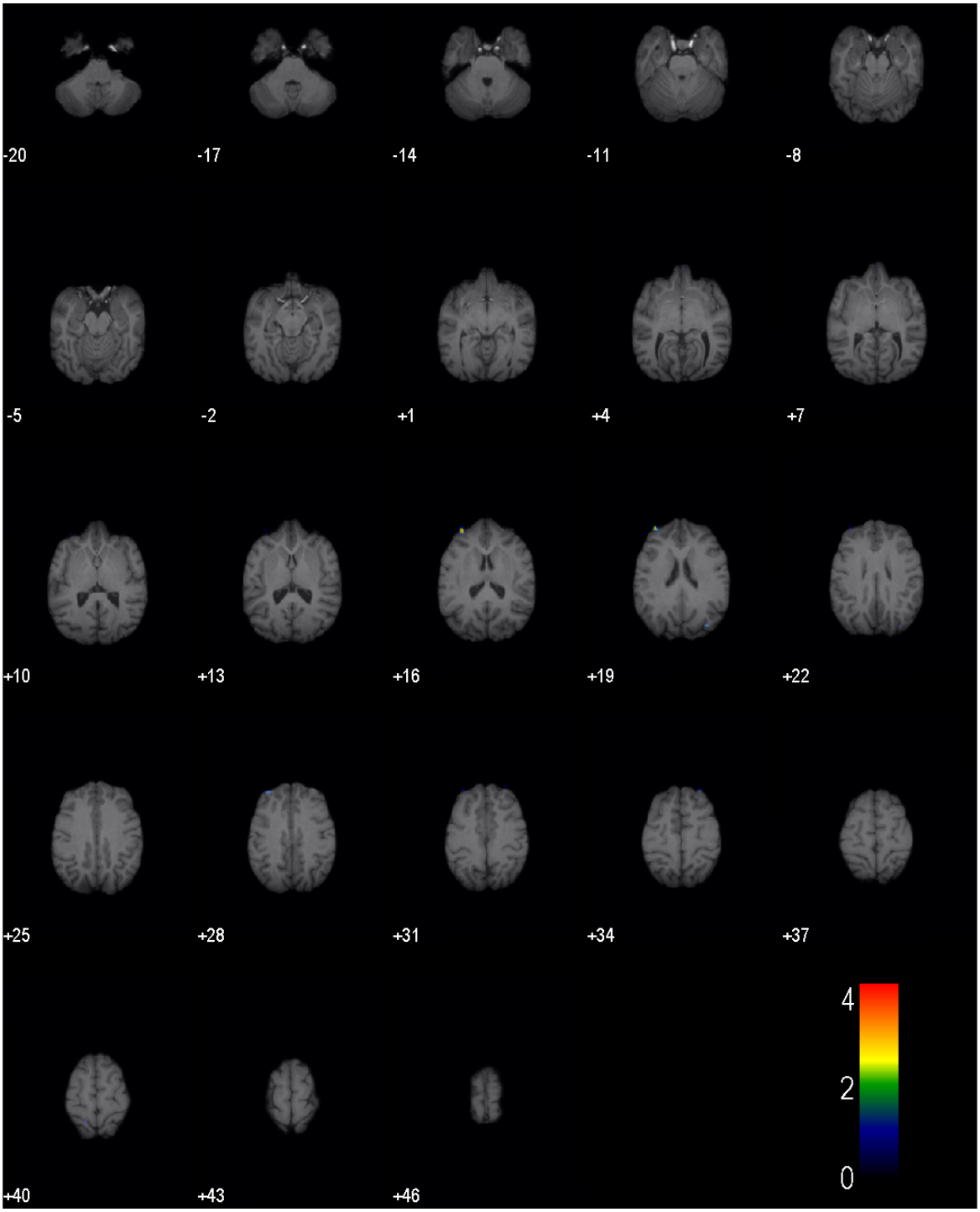


Figure A41: Low social > high social #1, resting state ROI

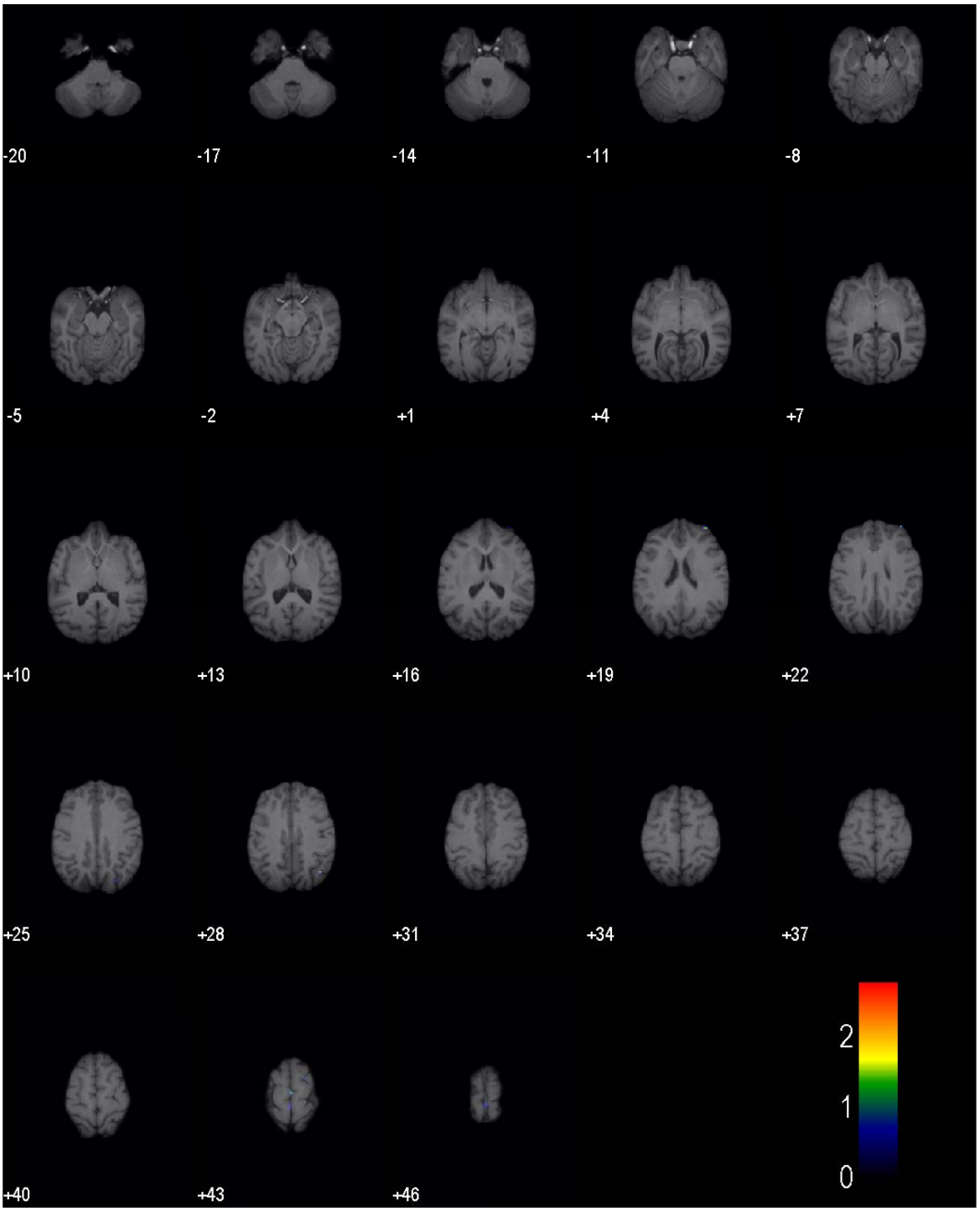


Figure A42: Low social > high social #2, resting state ROI

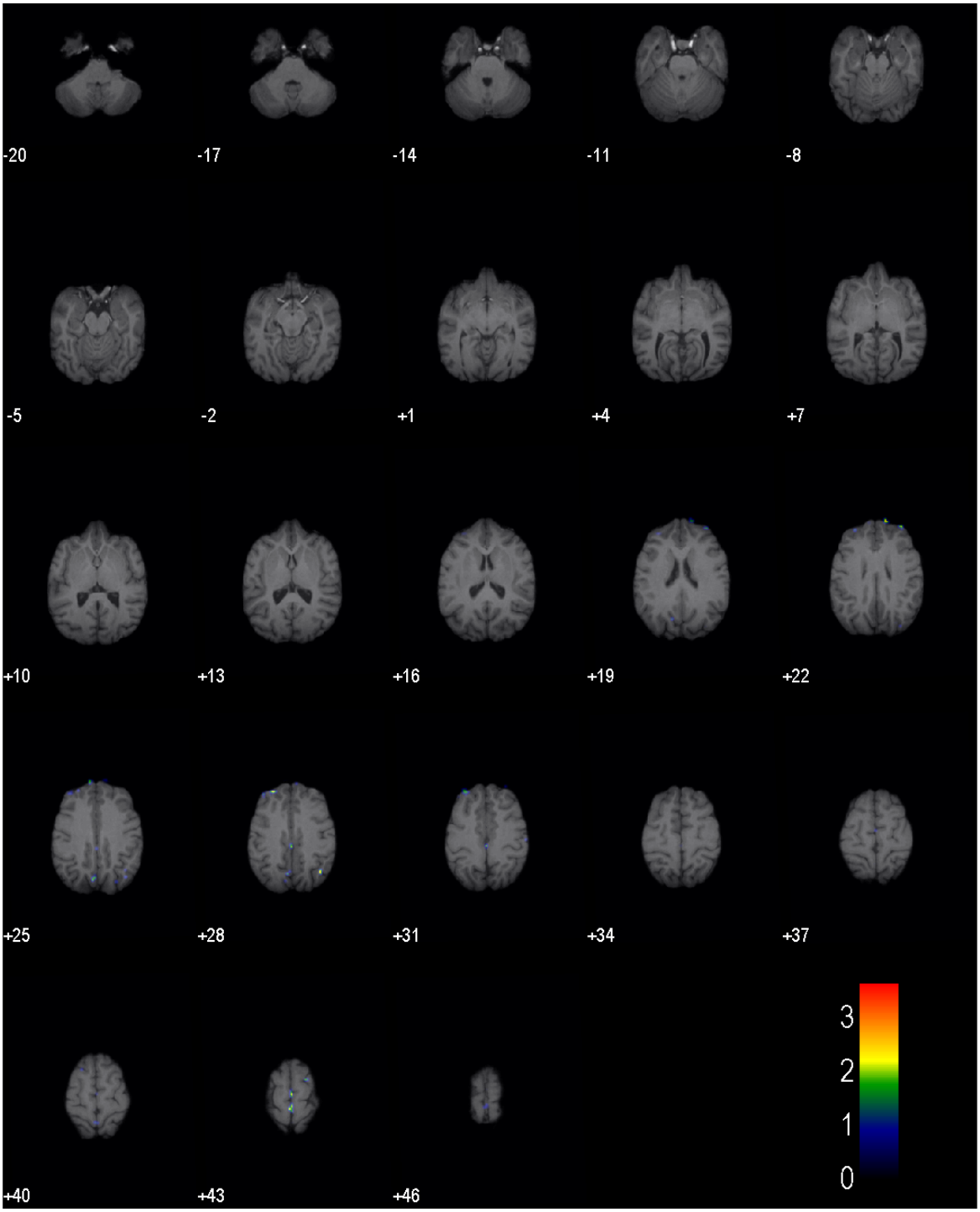


Figure A43: Low social > non-social, resting state ROI

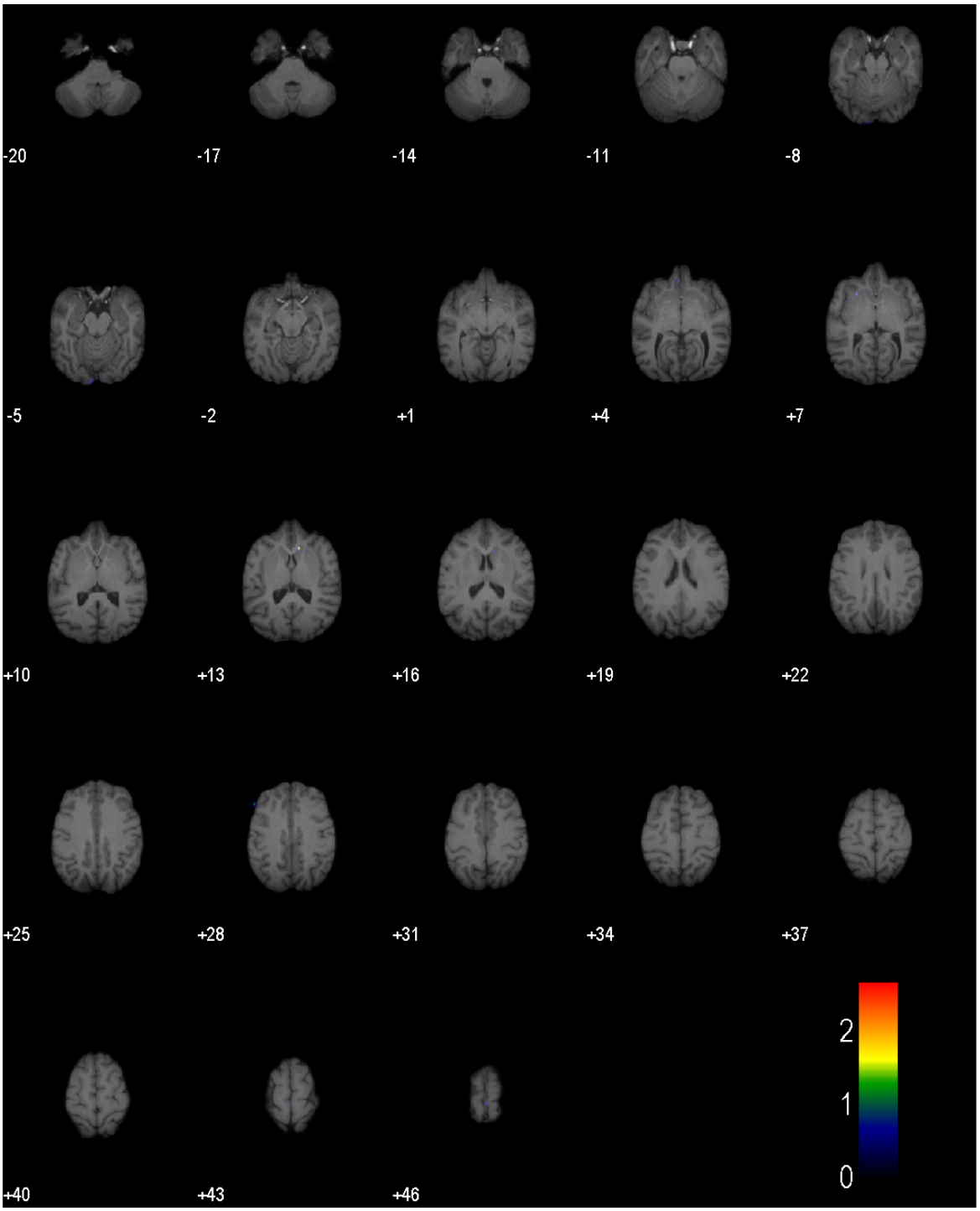


Figure A44: Low social > rest, resting state ROI

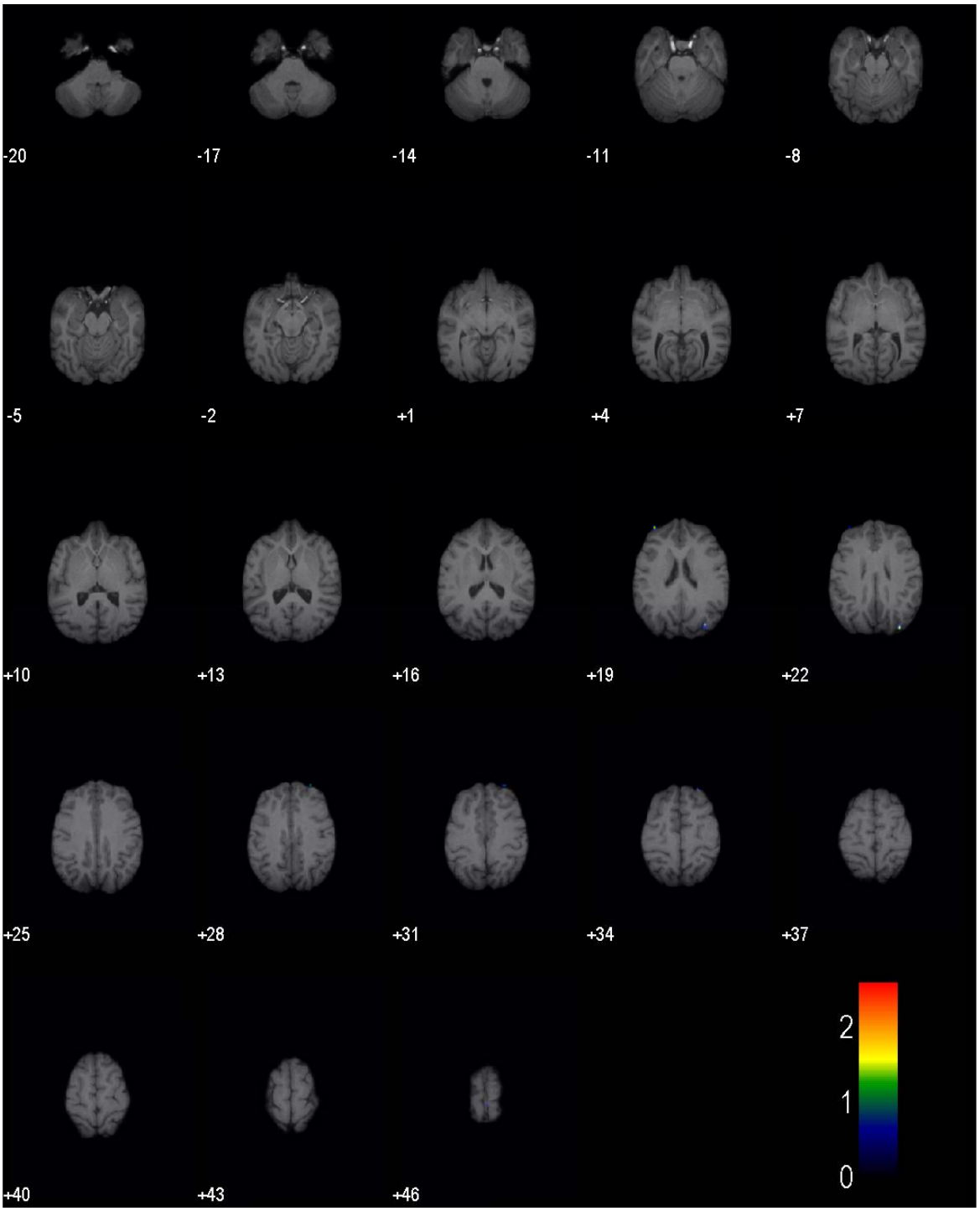


Figure A45: Non-social > high social #1, resting state ROI

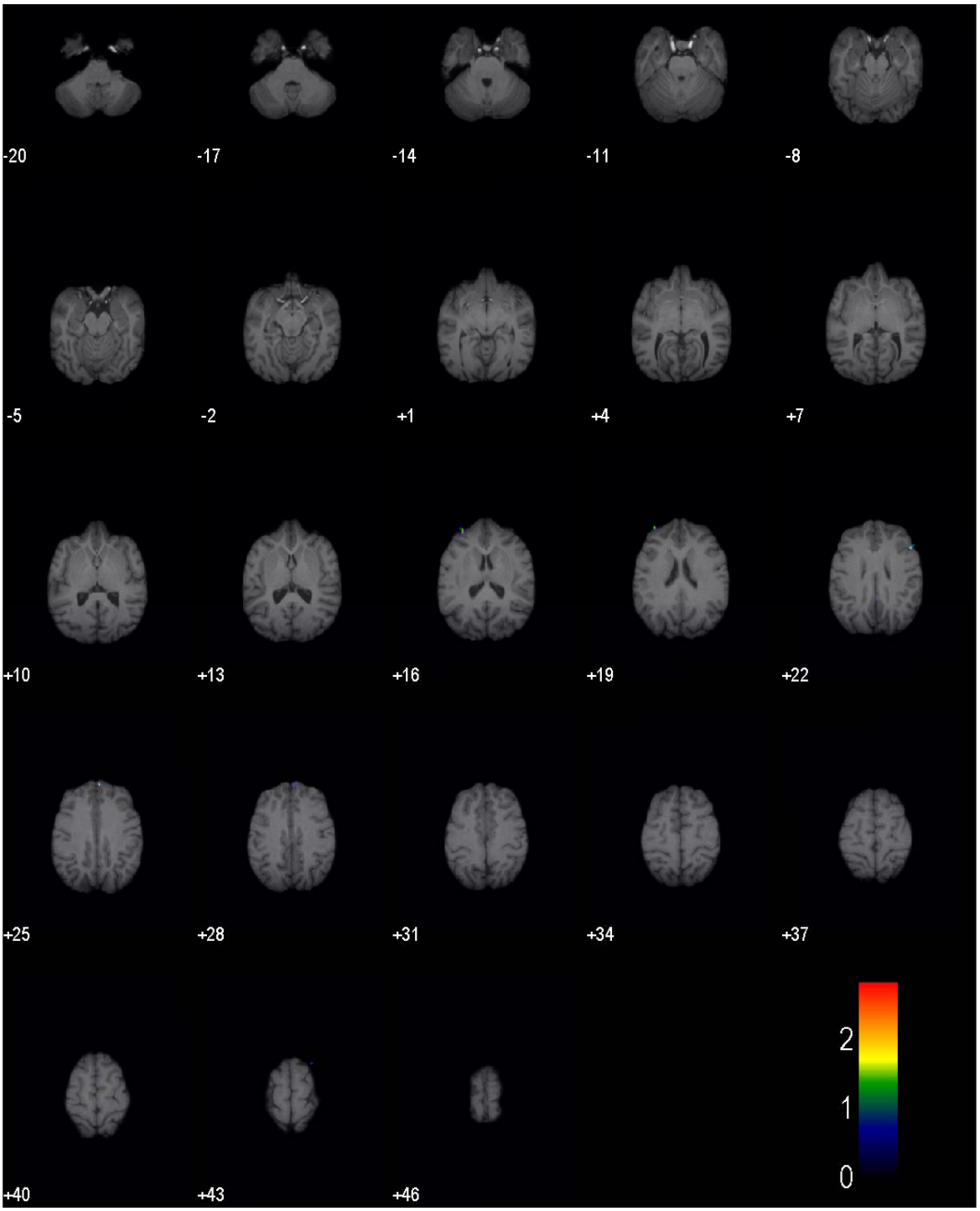


Figure A46: Non-social > high social #2, resting state ROI

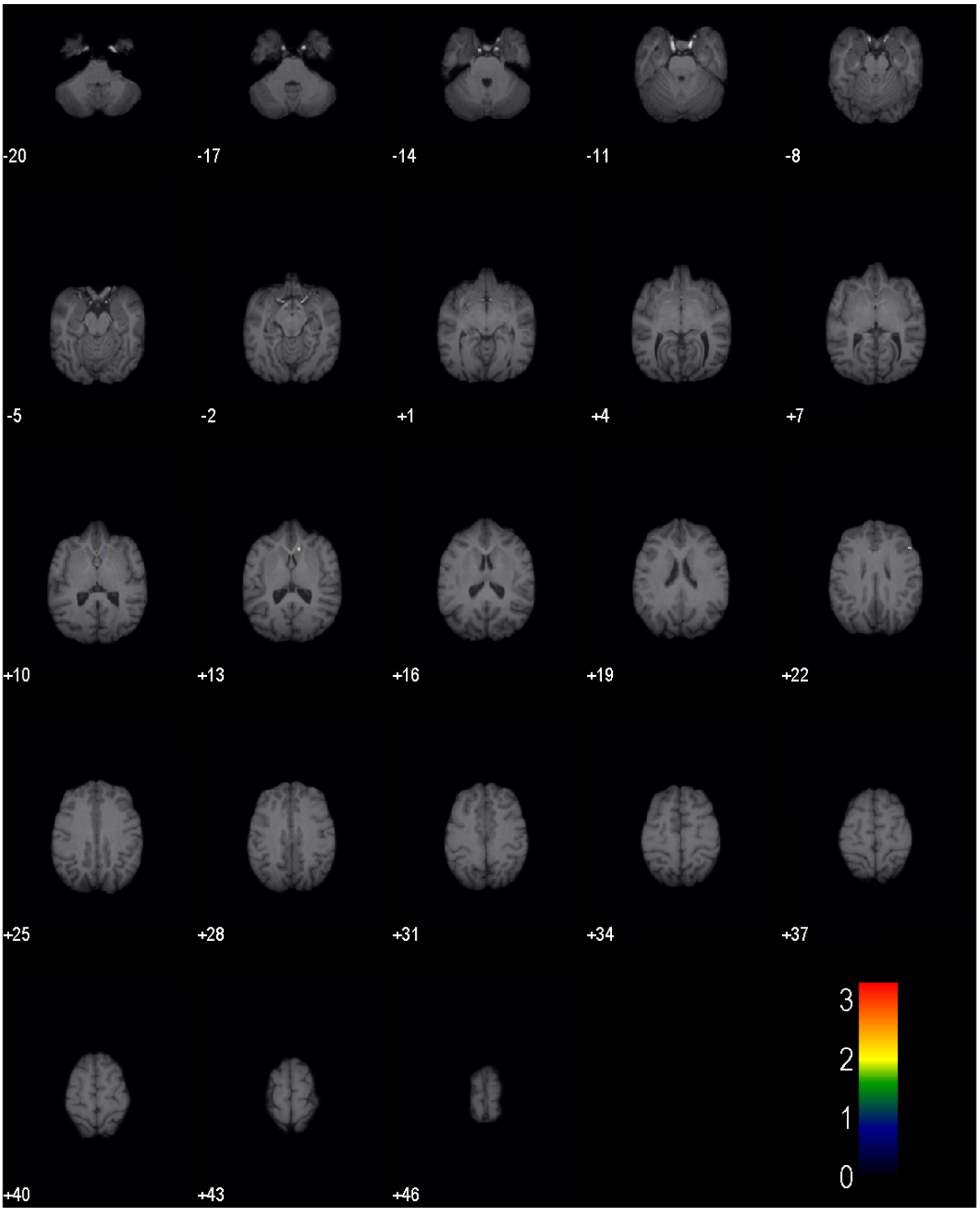


Figure A47: Non-social > low-social, resting state ROI

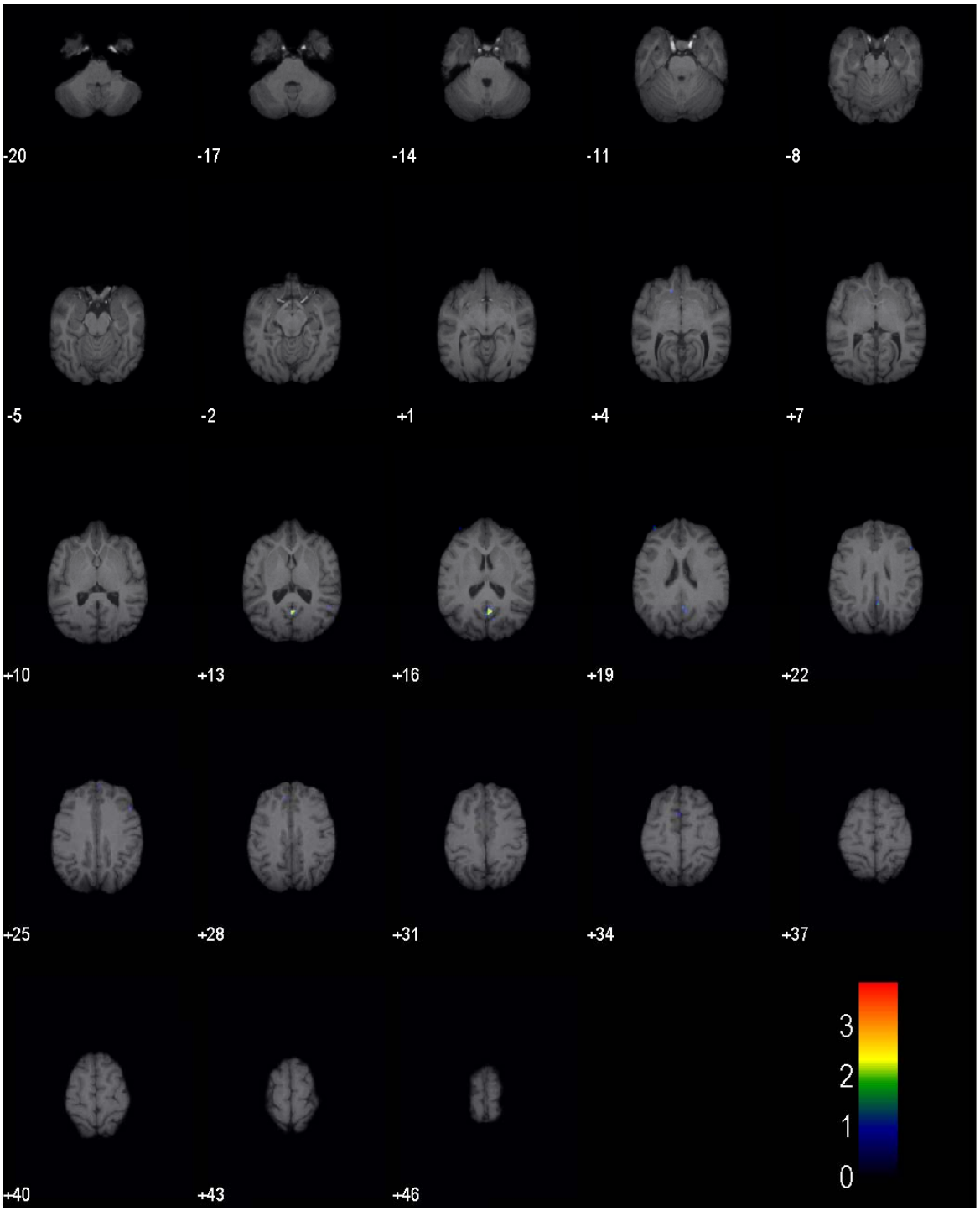


Figure A48: Non-social > rest, resting state ROI

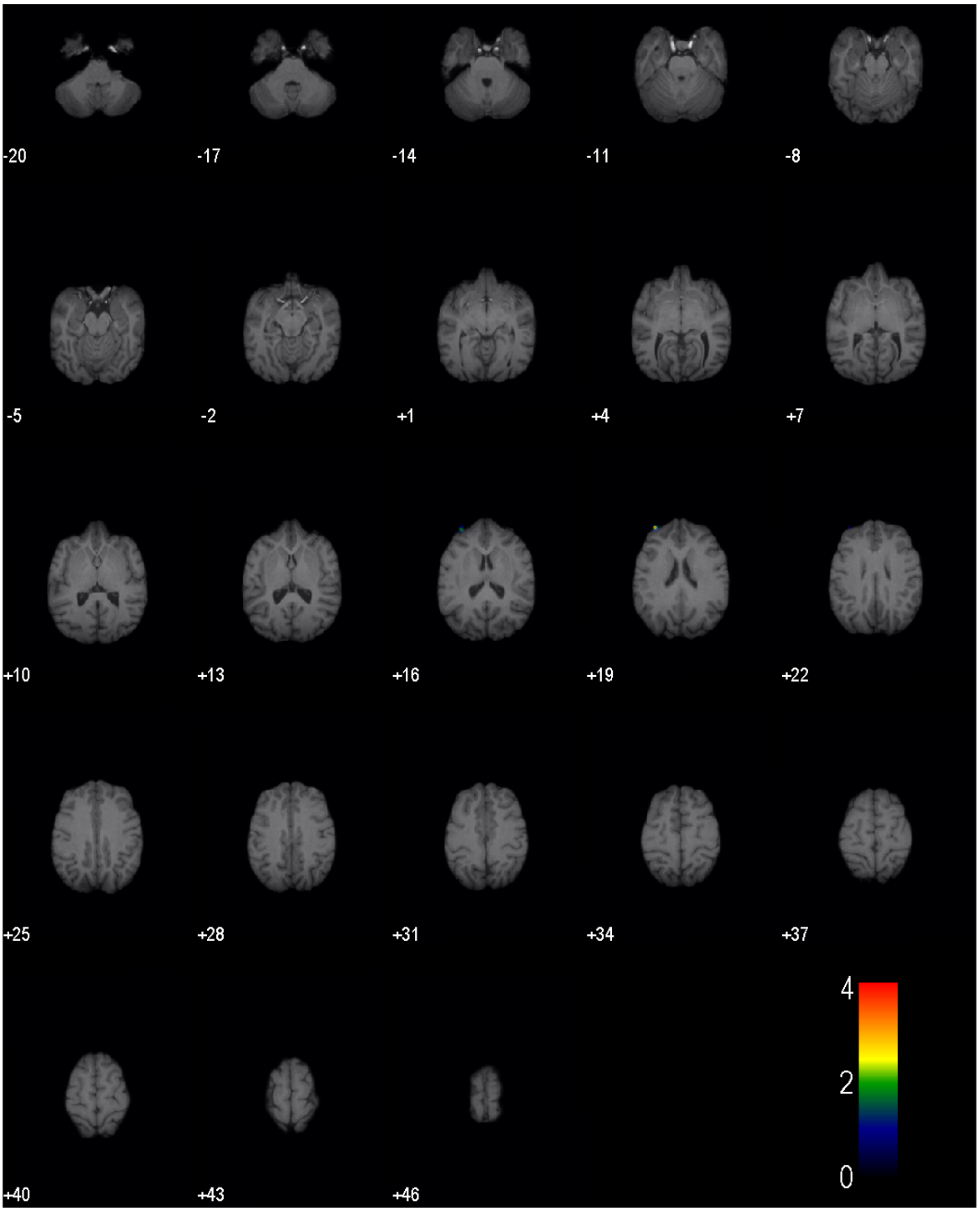


Figure A49: Rest > high social #1, resting state ROI

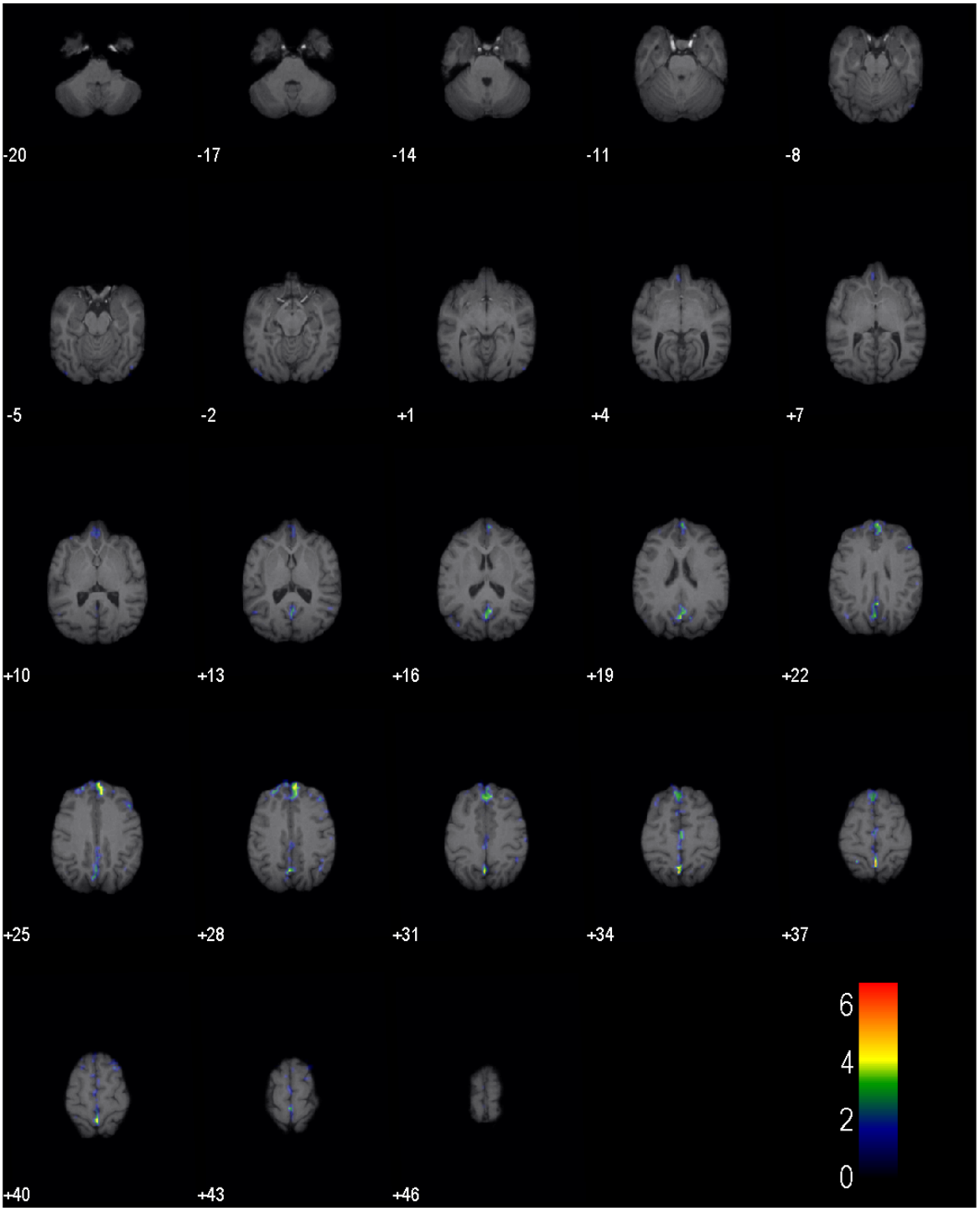


Figure A50: Rest > high social #2, resting state ROI

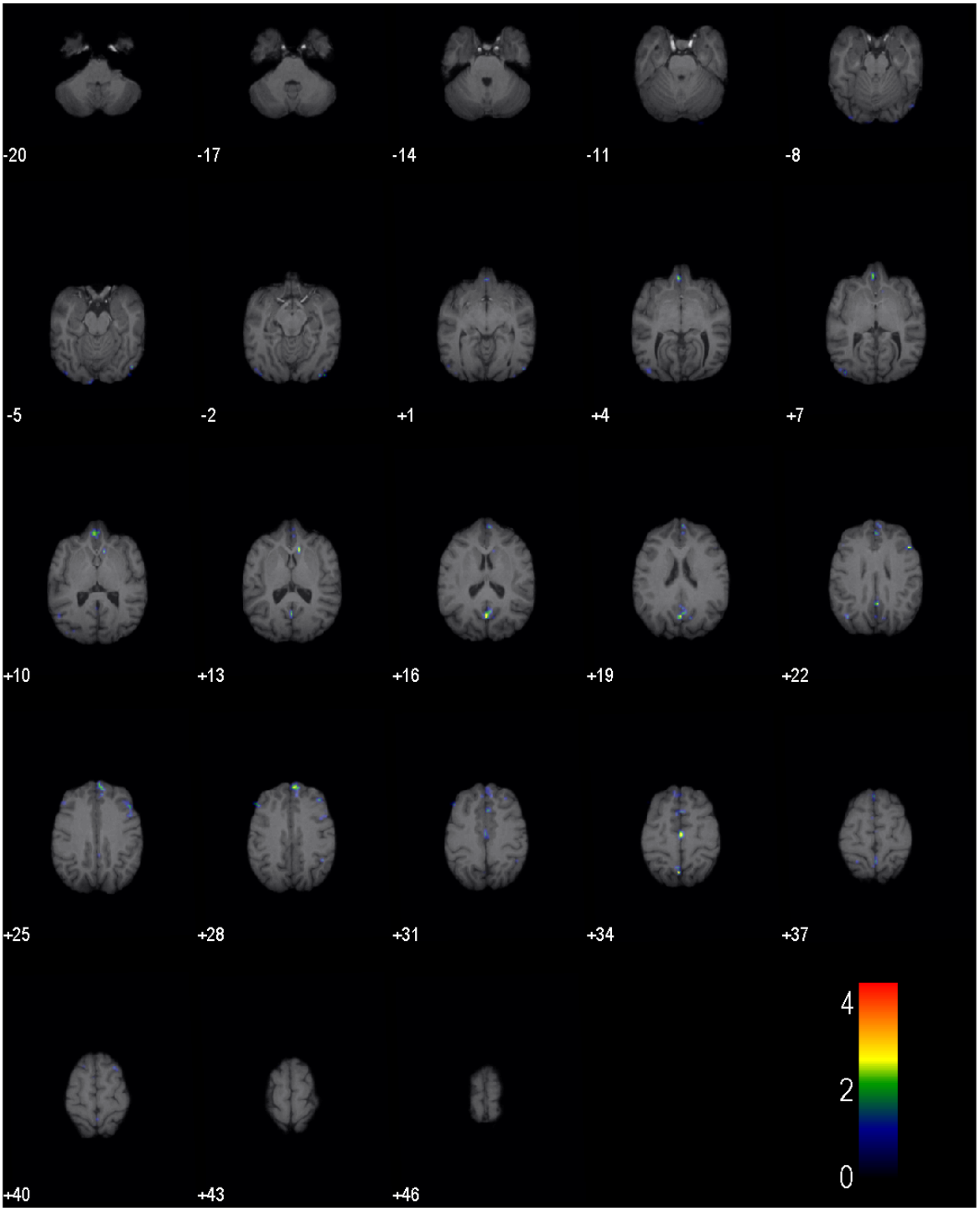


Figure A51: Rest > low social, resting state ROI

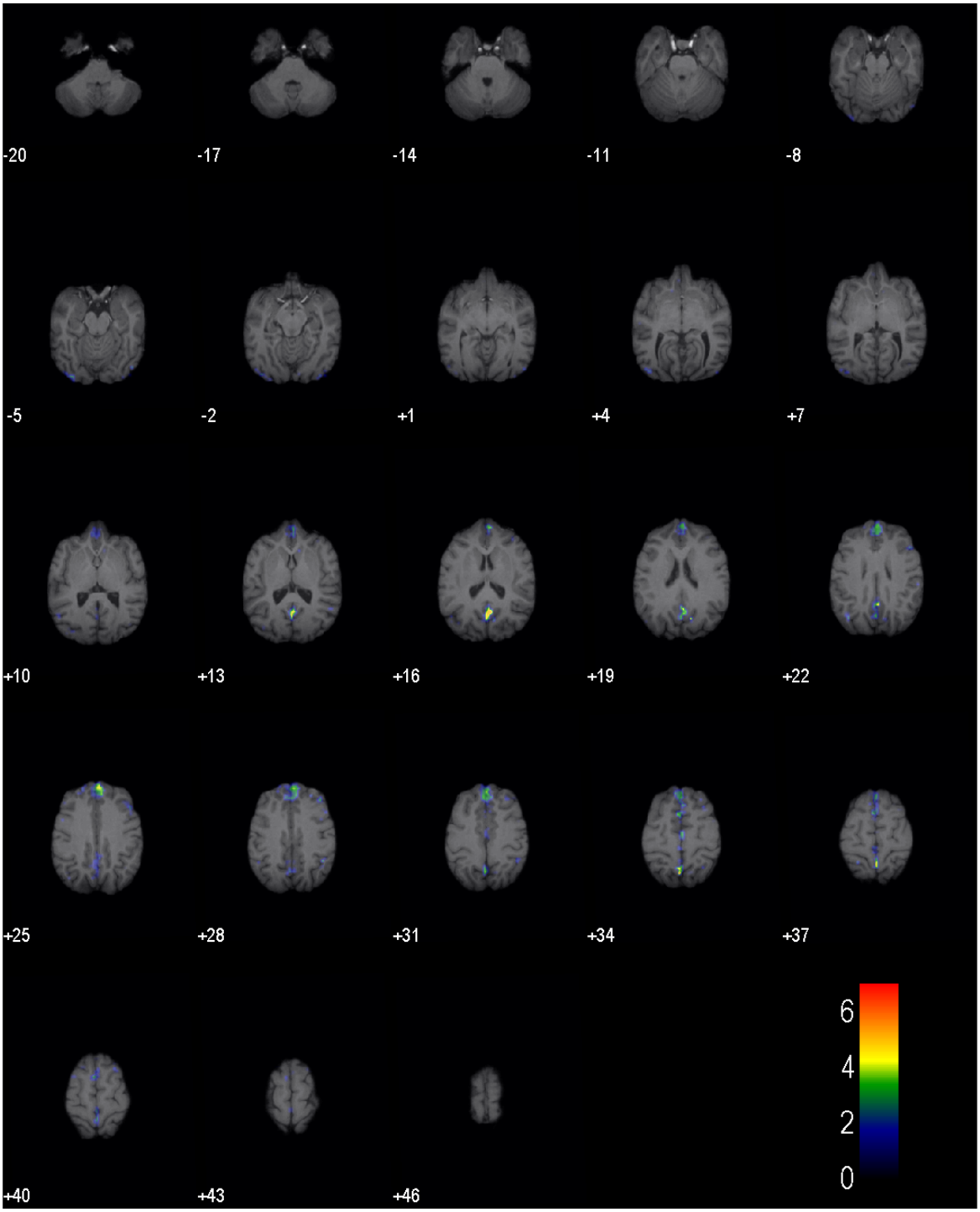


Figure A52: Rest > non-social, resting state ROI

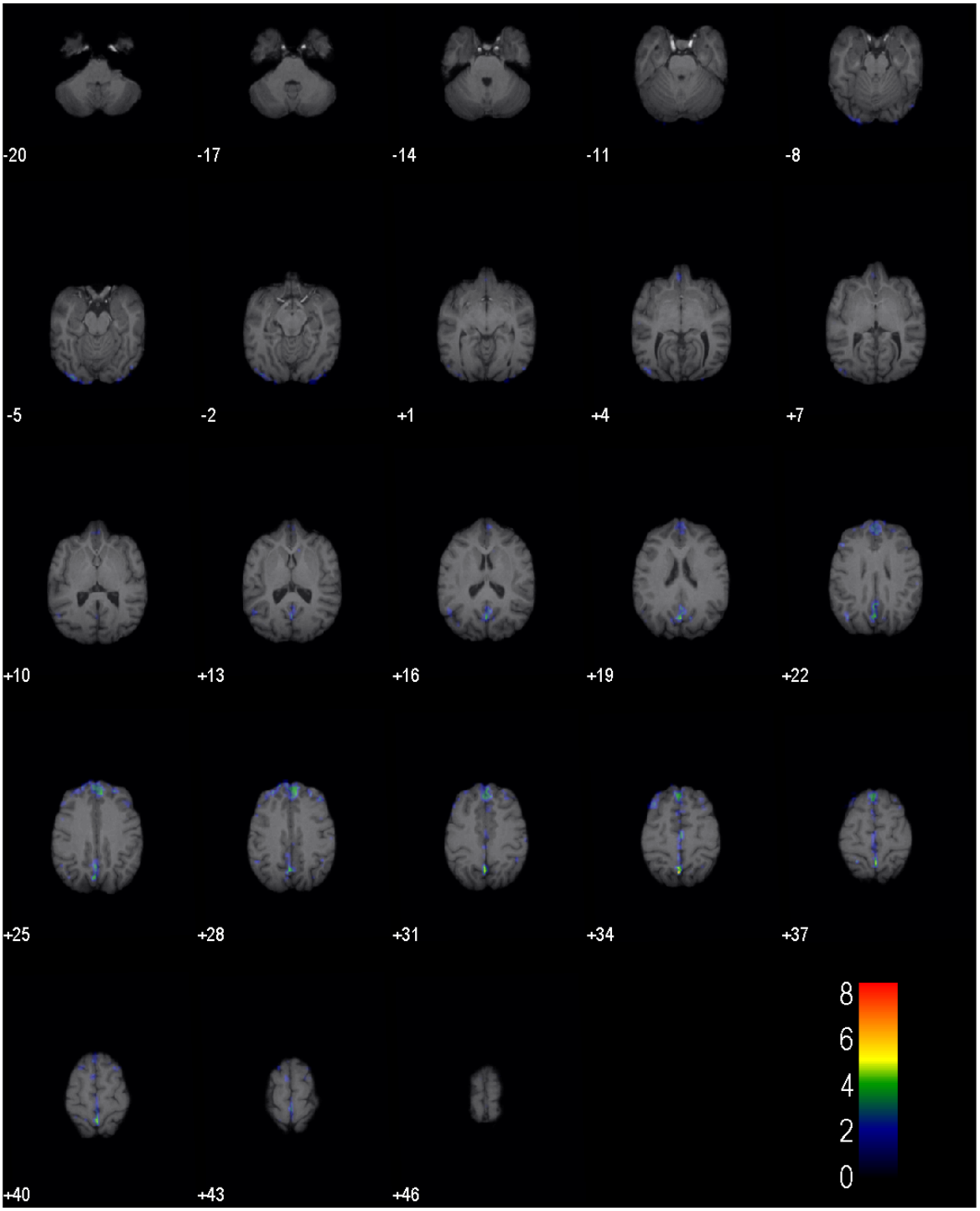


Figure A53: Both high social > low social, resting state ROI

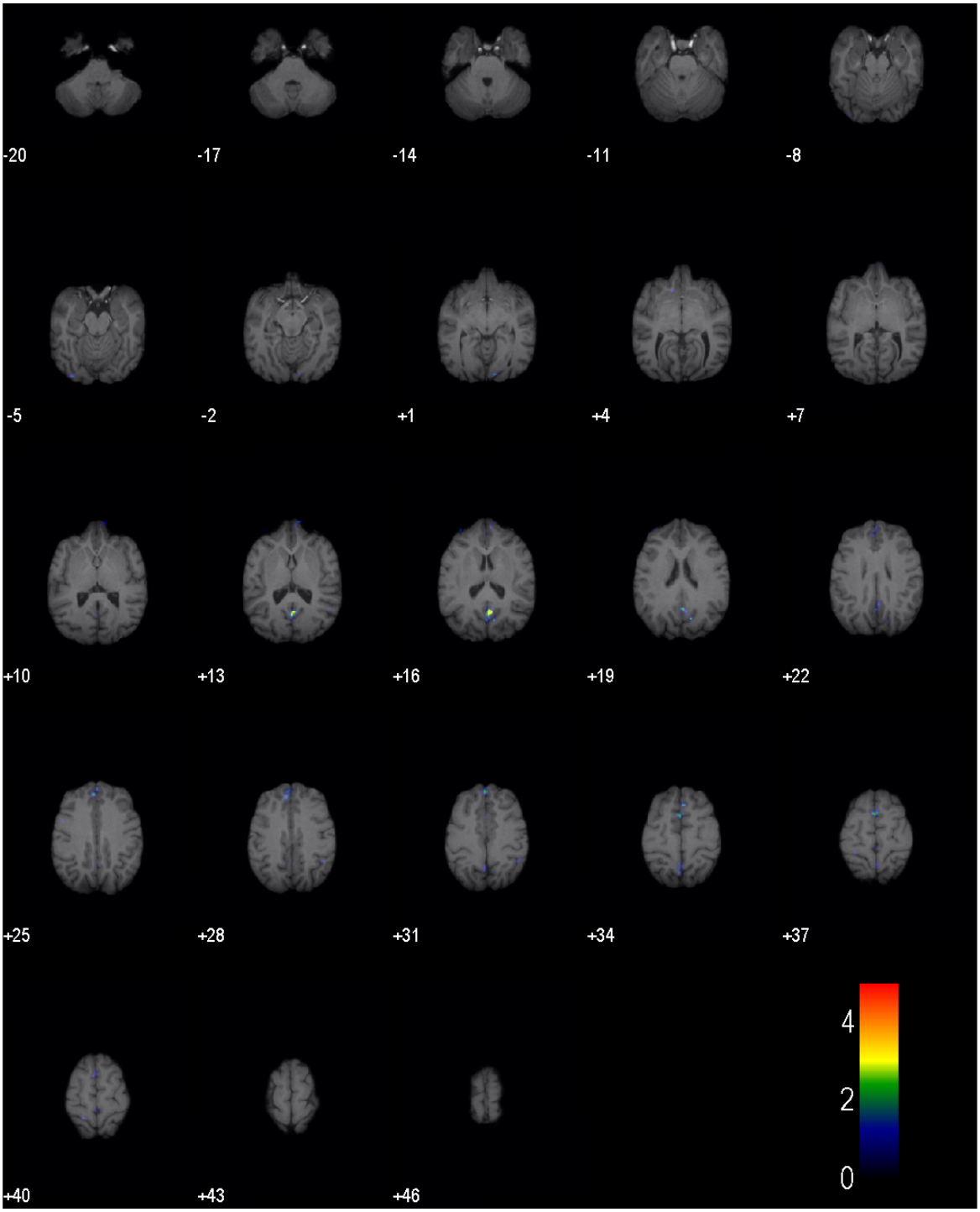


Figure A54: Low social > both high social, resting state ROI

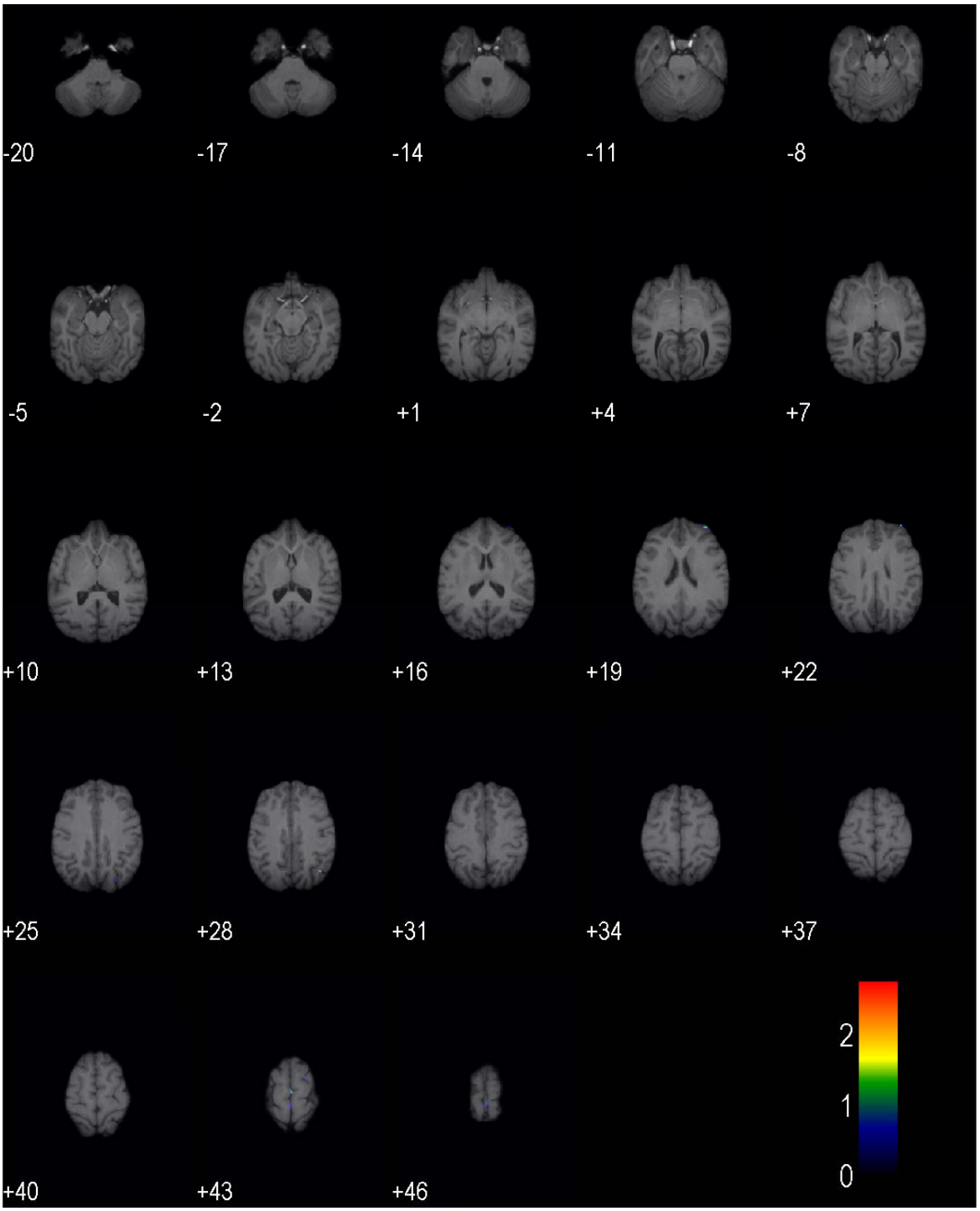


Figure A55: Both high social > non-social, resting state ROI

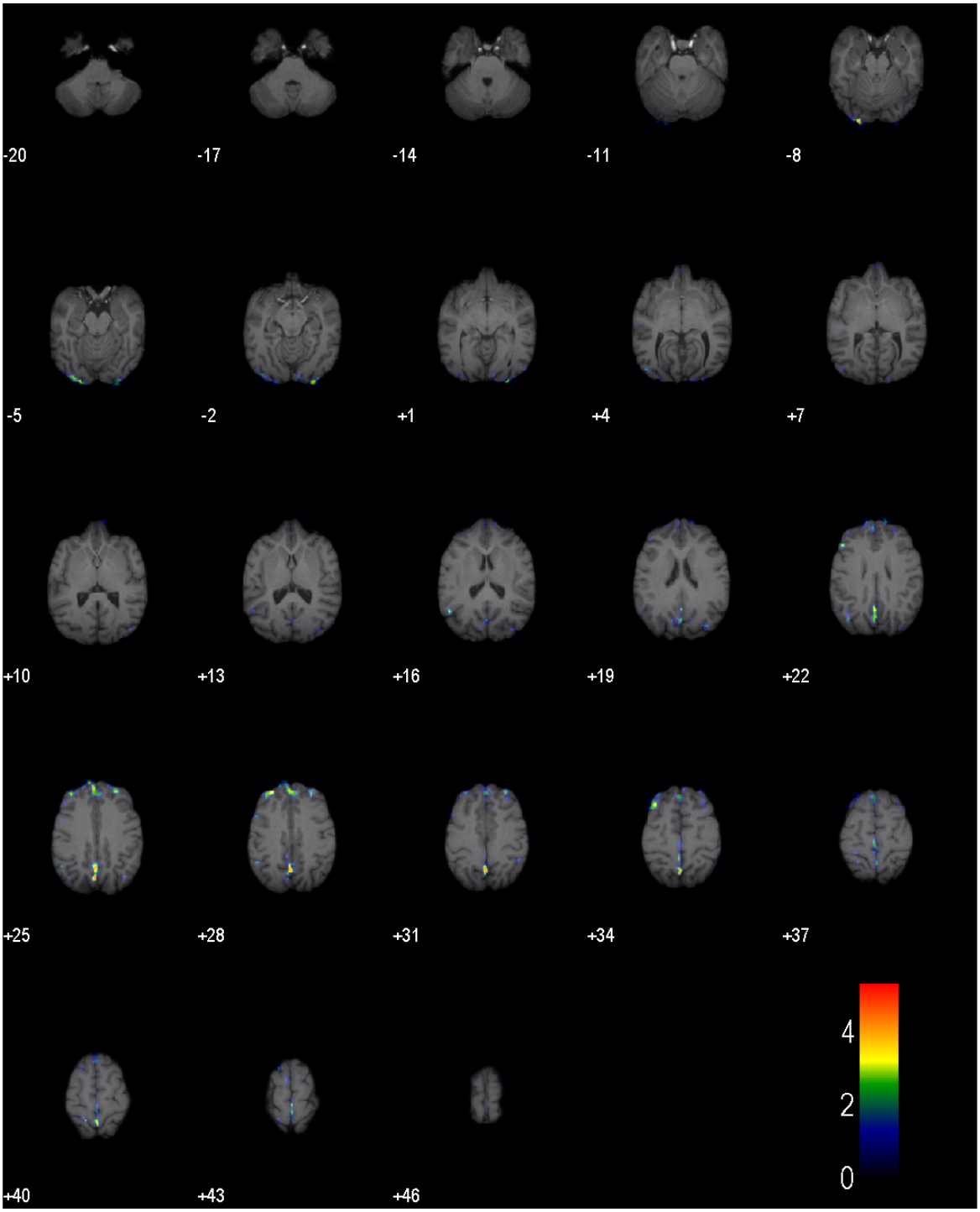


Figure A56: Non-social > both high social, resting state ROI

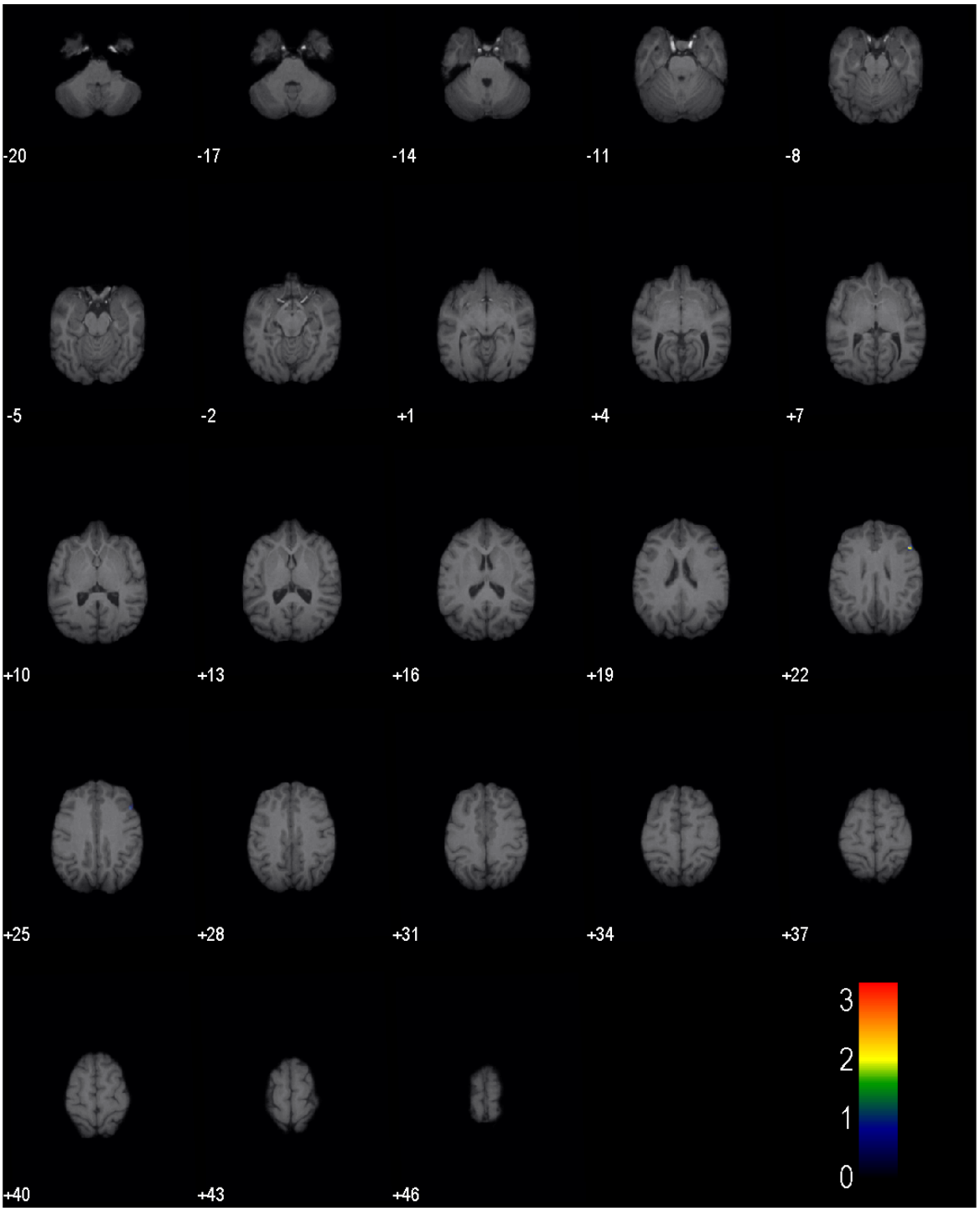


Figure A57: Both high social > rest, resting state ROI

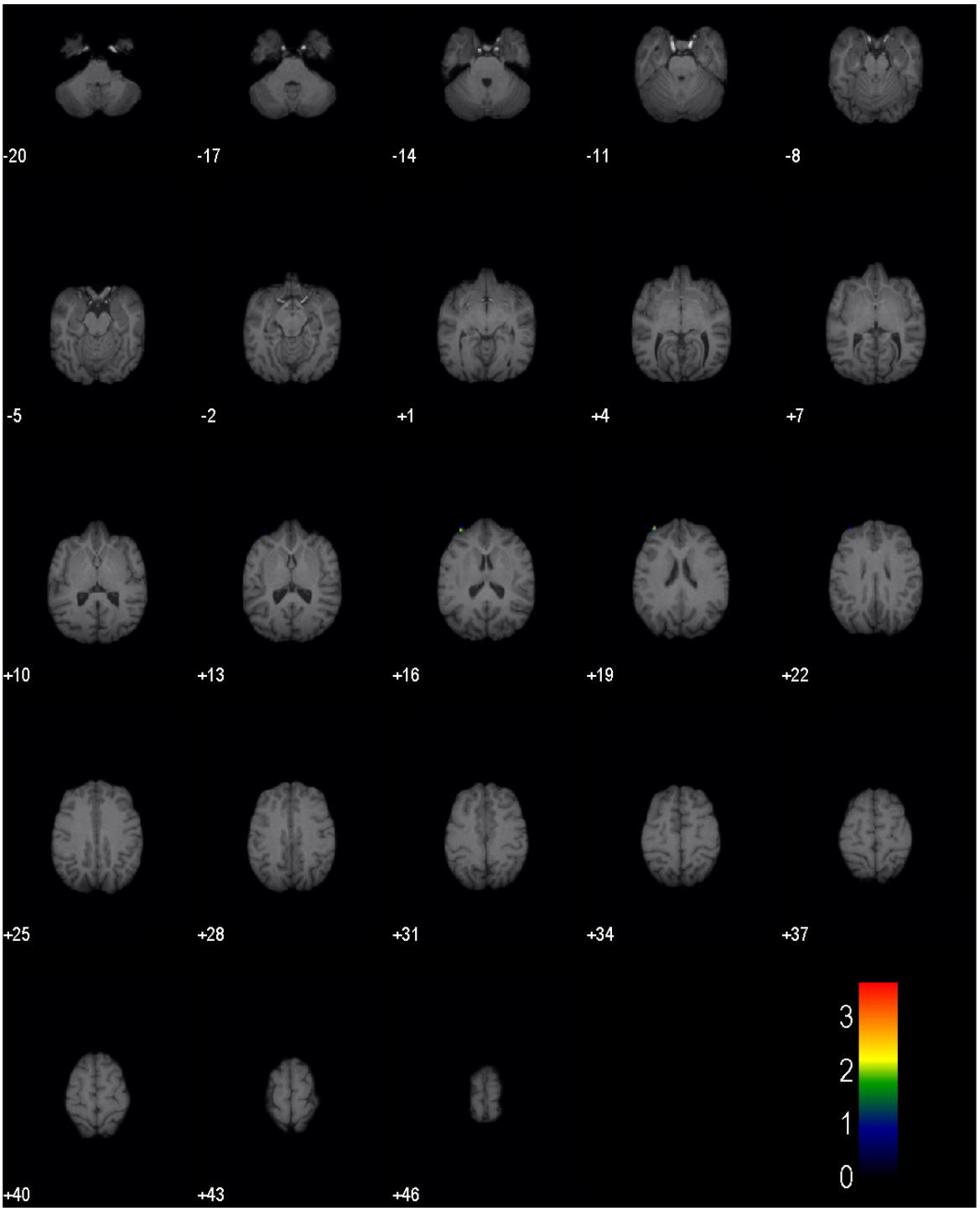


Figure A58: Rest > both high social, resting state ROI

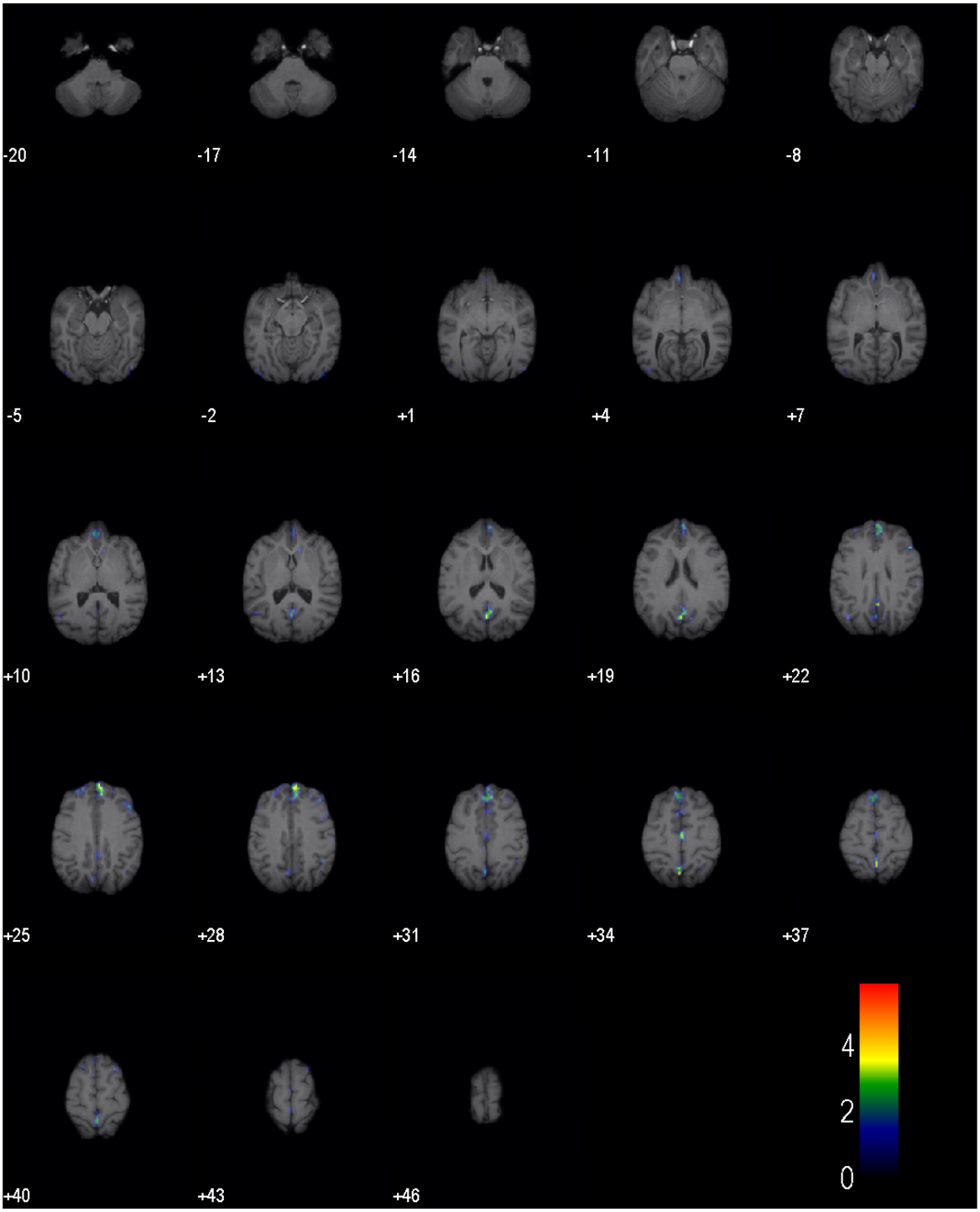


Figure A59: All social > non-social, resting state ROI

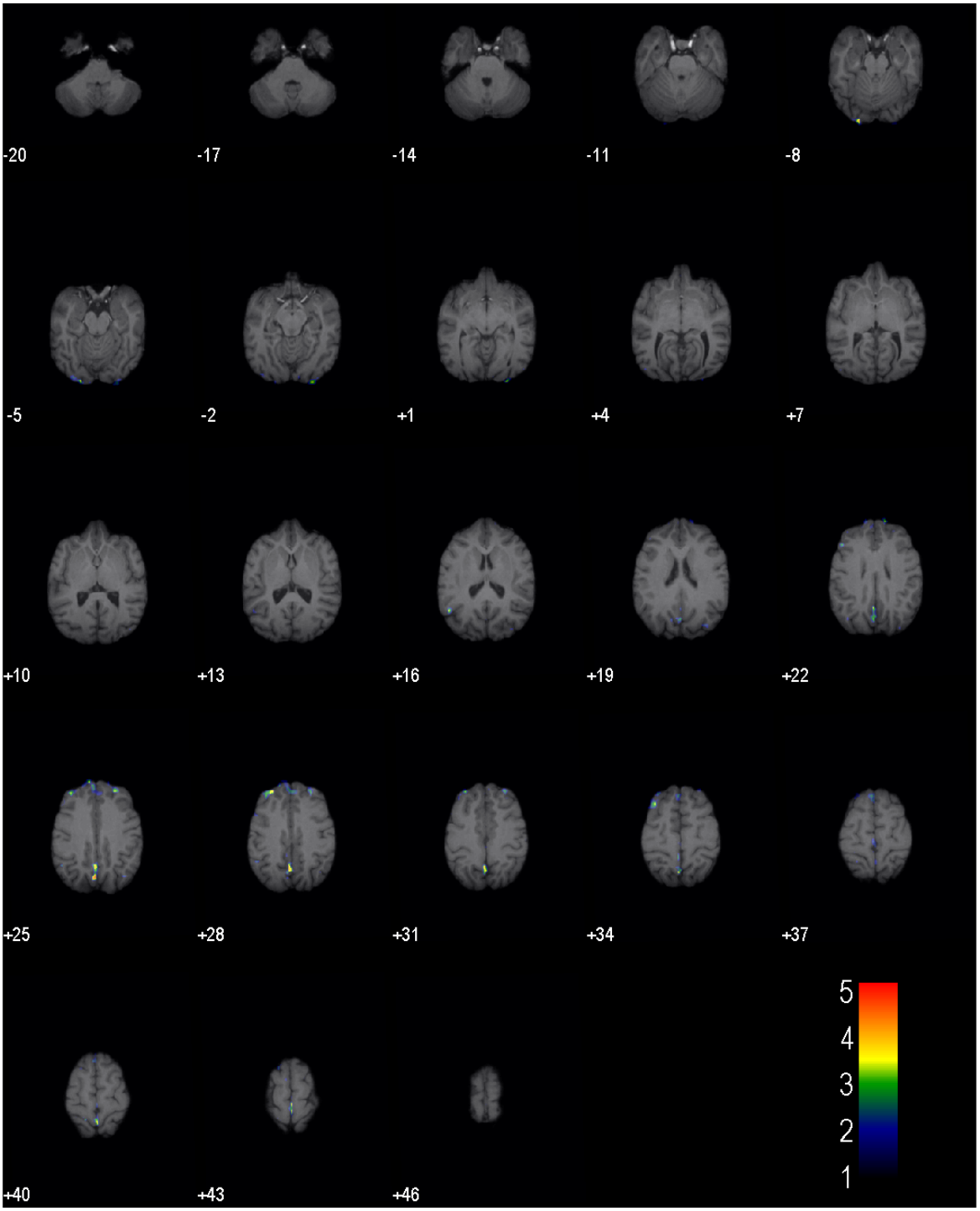


Figure A60: Non-social > all social, resting state ROI

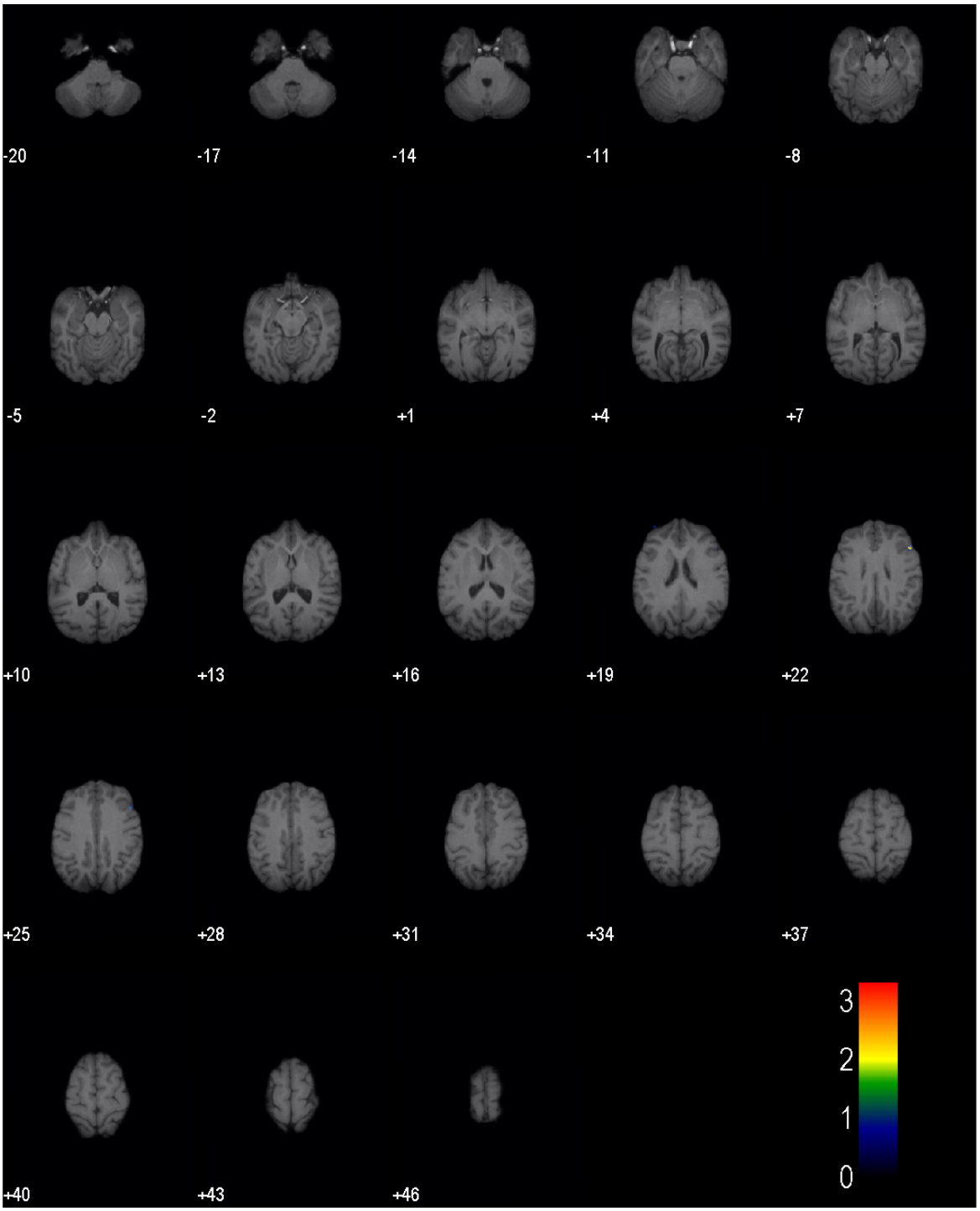


Figure A61: All social > rest, resting state ROI

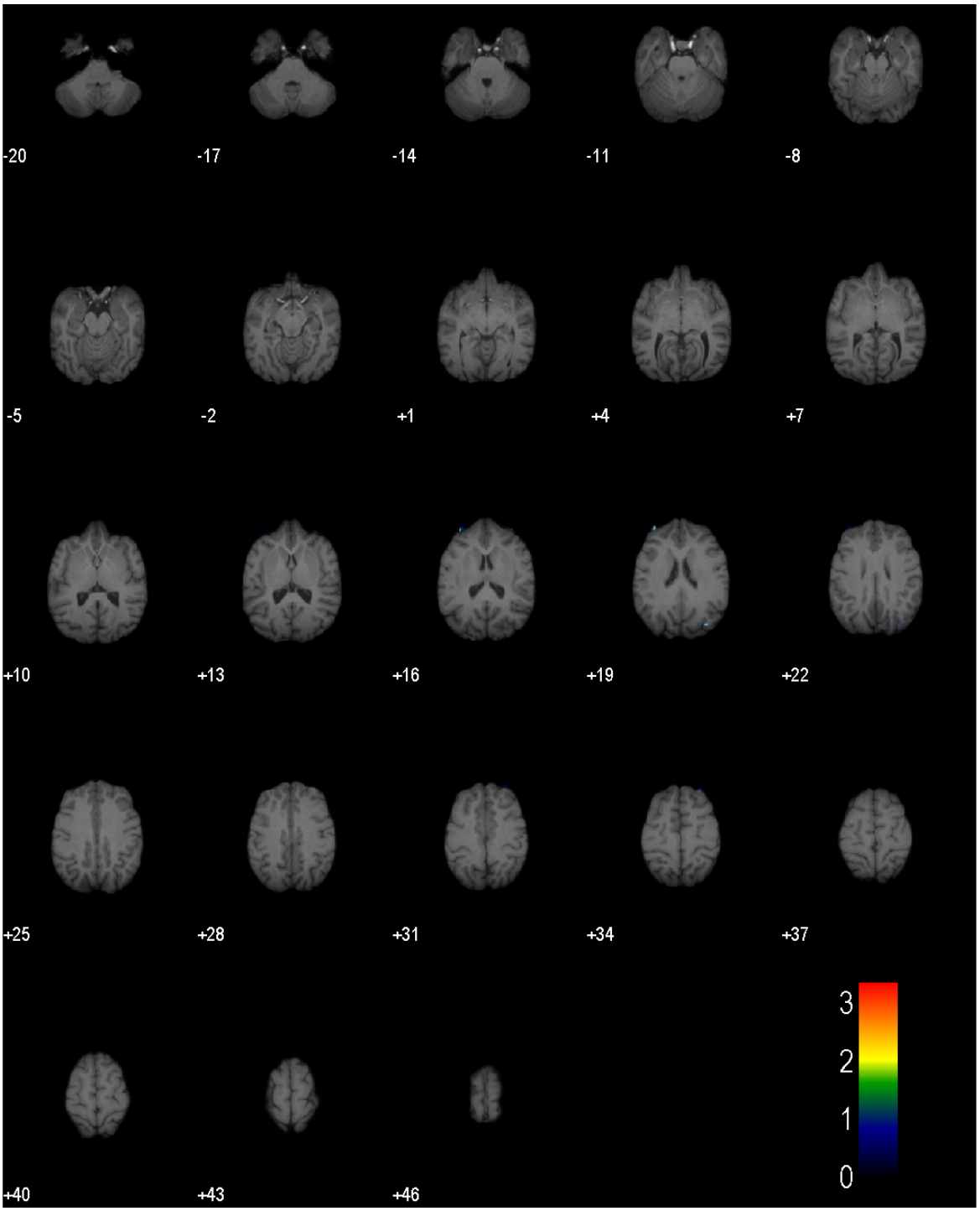


Figure A62: Rest > all social, resting state ROI

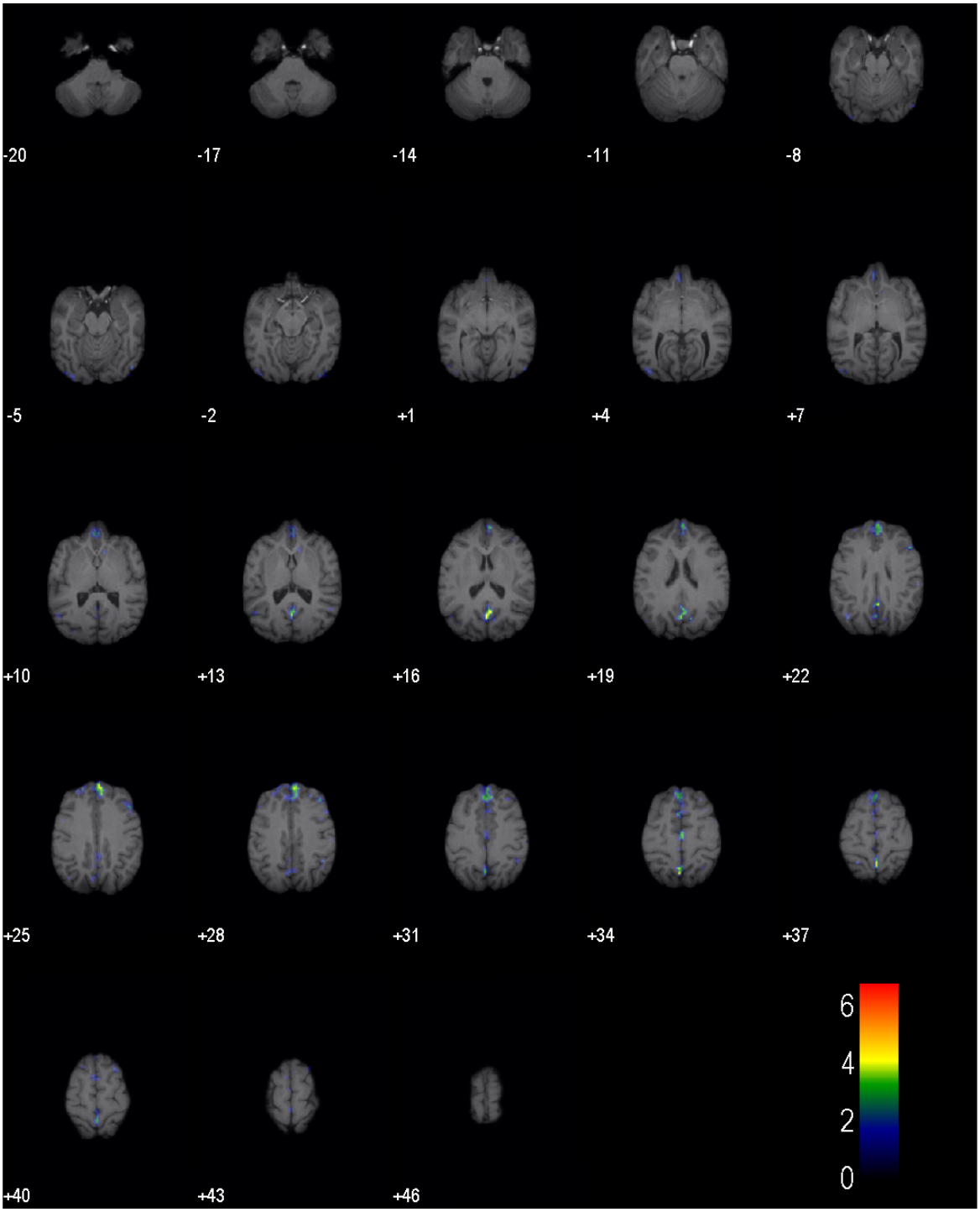


Figure A63: Rest > all tasks, resting state ROI

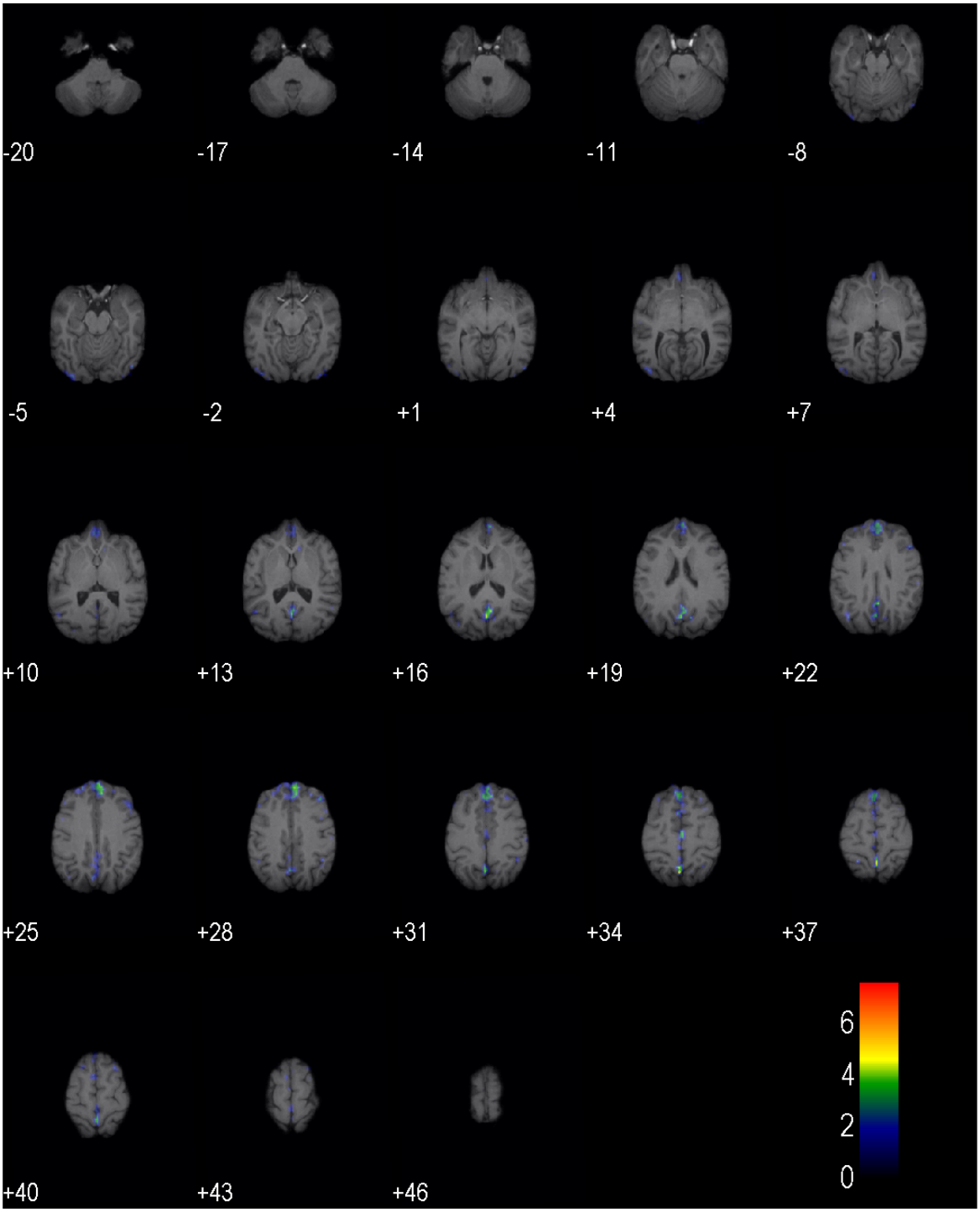
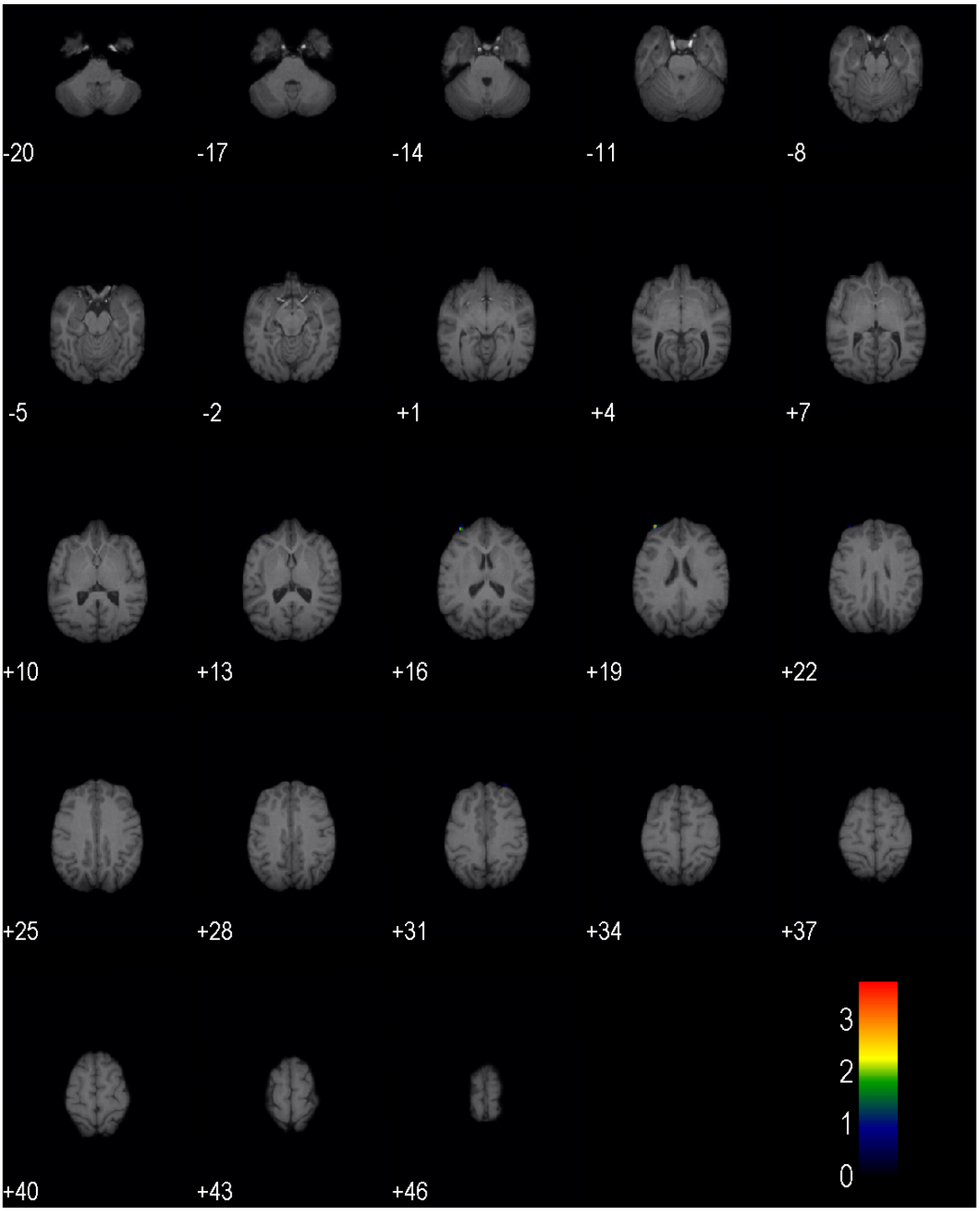


Figure A64: All tasks > rest, resting state ROI



Condition averages in whole brain. Color bar indicates intensity value. Anterior commissure at Z = 6.

Figure A65: Non-social average, whole brain

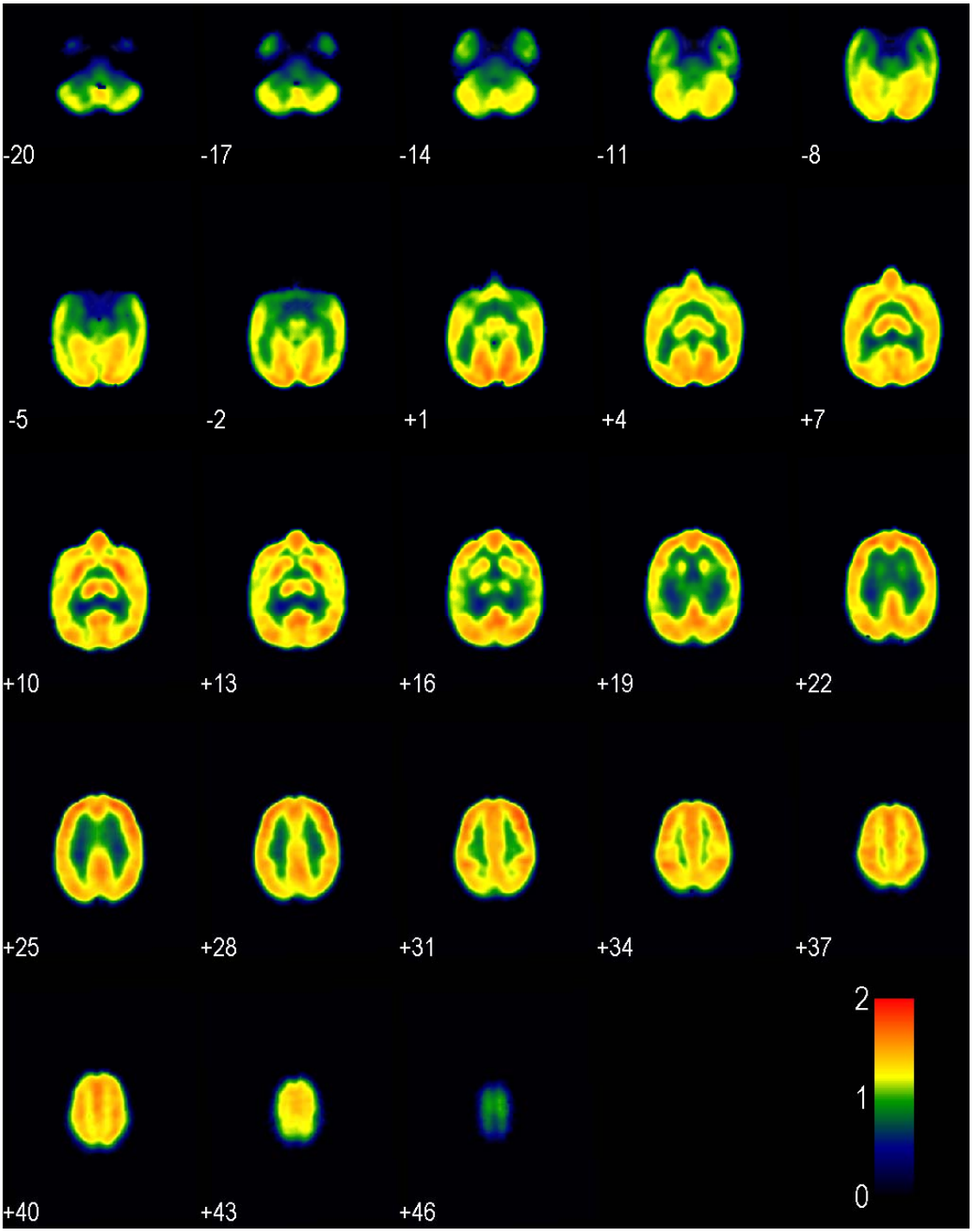


Figure A66: All social average, whole brain

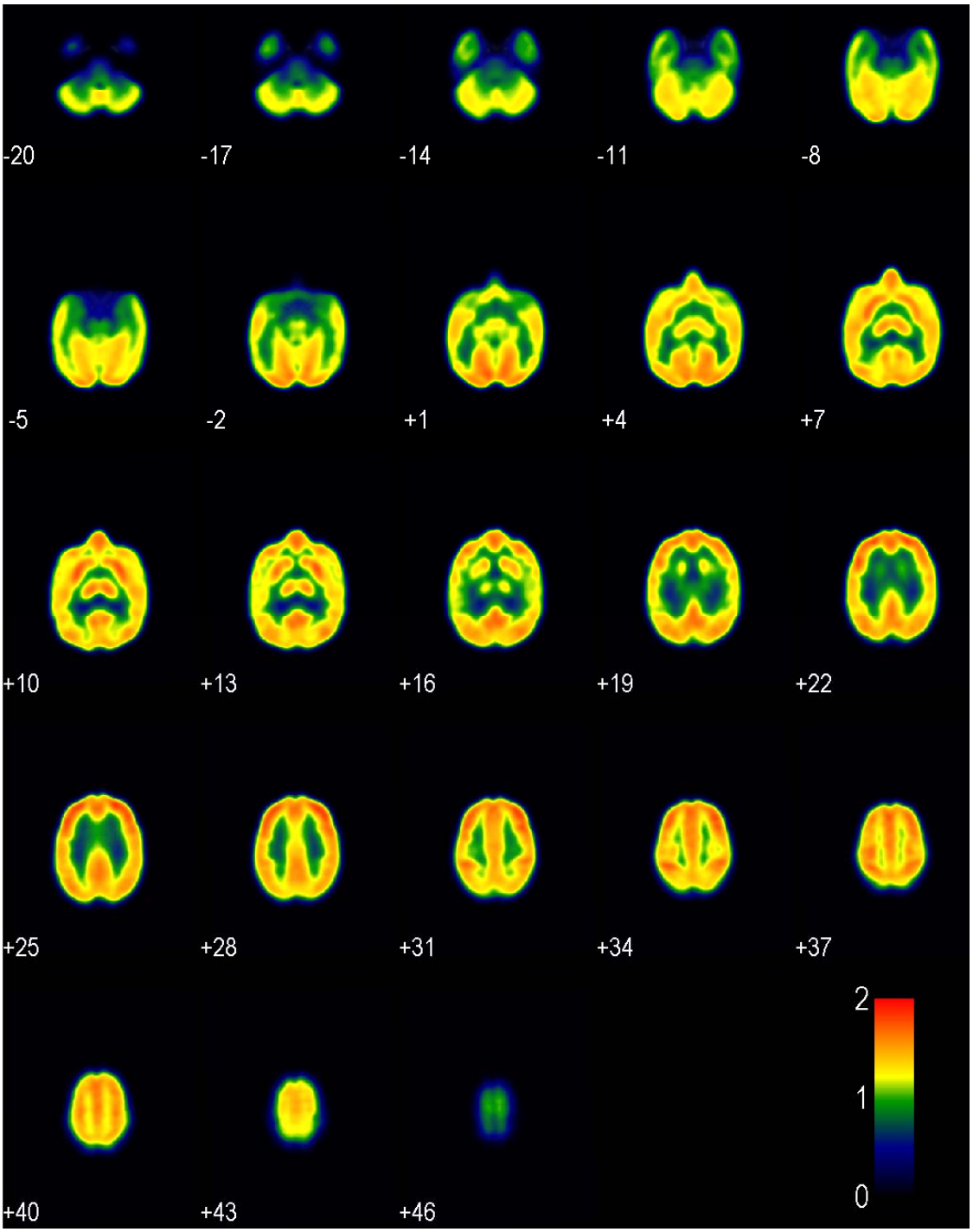
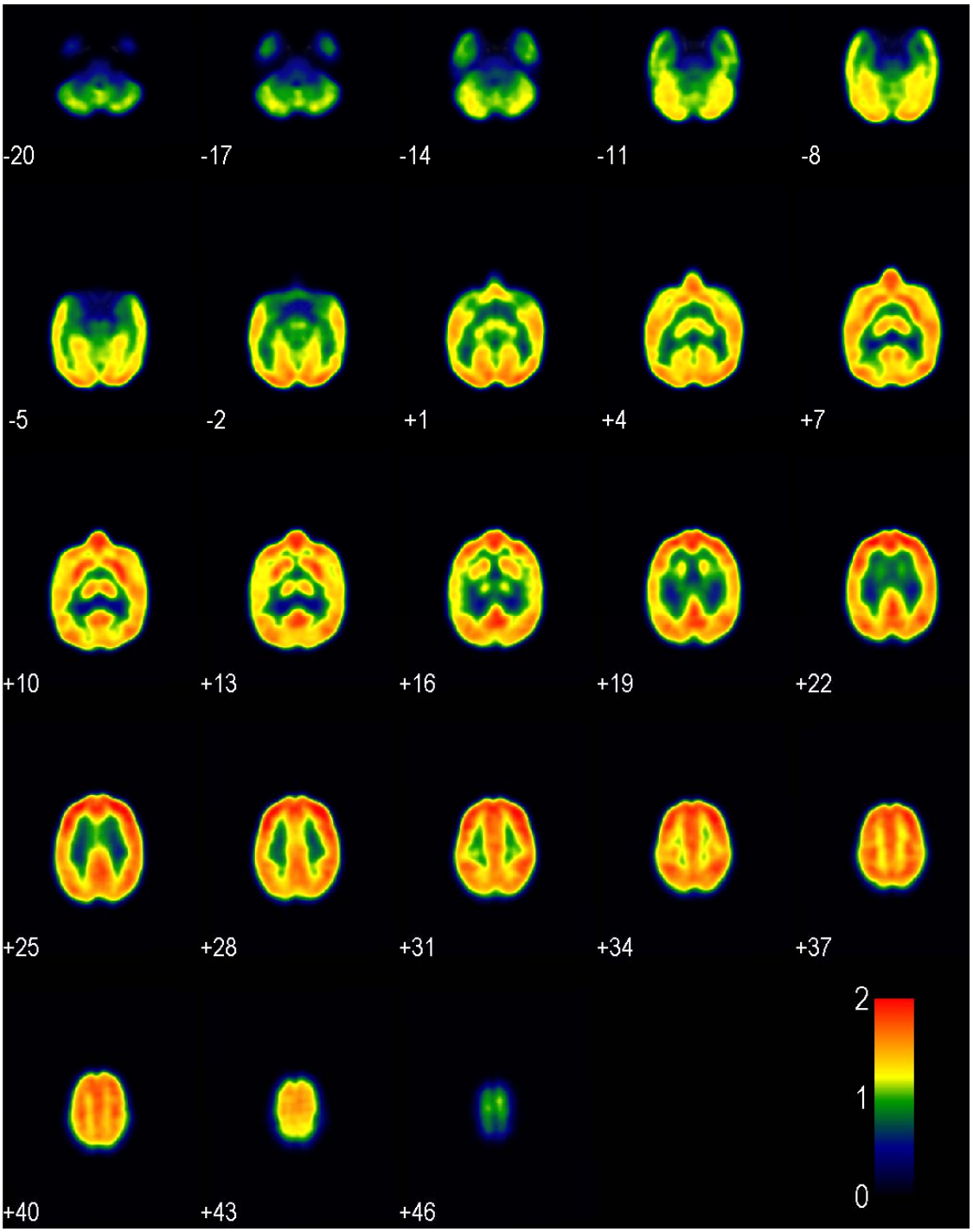


Figure A67: Rest average, whole brain



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