

Neurobiological Basis of Personal Wisdom

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Wisdom is an ancient concept that has been cross-culturally recognized throughout history (Birren & Svensson, 2005; Jeste & Vahia, 2008). Wisdom has been subject to a number of definitions, including a system of logic for understanding the world, a notion that is the basis of modern science. Wisdom has also been considered the human embodiment of Gods. Though there are a variety of definitions of wisdom, the notion of personal wisdom is considered the oldest and most familiar and generally refers to the ability to cope with life and live it to its fullest.

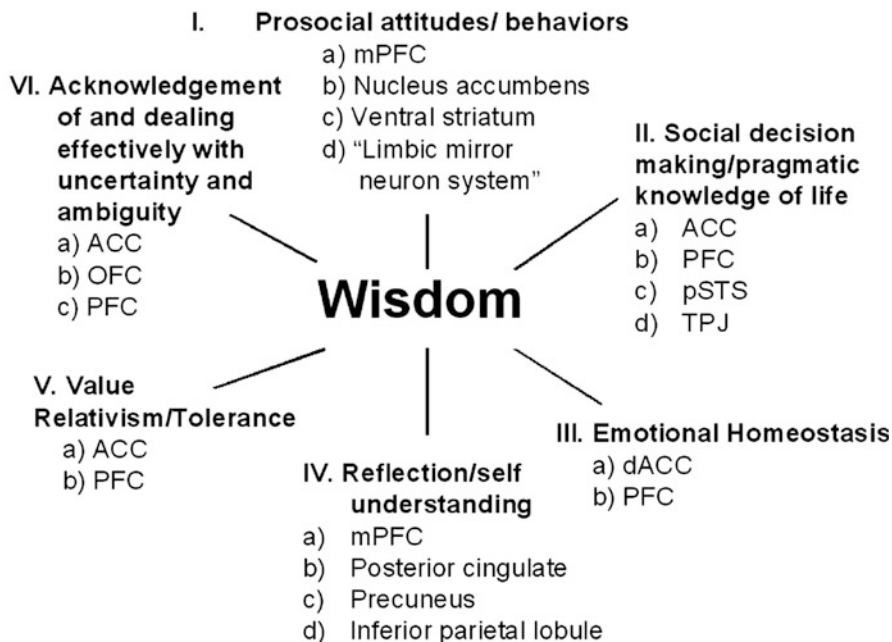
While there is not yet a universal consensus on a more specific definition for personal wisdom, we have recently attempted to define personal wisdom via an expert consensus panel using a 2-phase Delphi method (Jeste et al., 2010). This study revealed that there was considerable agreement among expert participants on personal wisdom being a distinct entity with a number of characteristic qualities that were different from those in intelligence and spirituality. Many of these qualities could be classified as belonging to a cognitive dimension (i.e., rich knowledge of life, social cognition, tolerance of ambivalence, acceptance of uncertainty), some belonged to a reflective dimension (i.e., sense of justice and fairness, self-insight, tolerance of differences among others), and others were consistent with an affective dimension (i.e., empathy and social cooperation). Additional items

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ACC = Anterior Cingulate Cortex
 dACC = Dorsal Anterior Cingulate Cortex
 mPFC = medial PreFrontal Cortex
 OFC = Orbitofrontal Cortex
 PFC = Prefrontal Cortex
 pSTS = posterior Superior Temporal Sulcus
 TPJ = Temporo-Parietal Junction

Fig. 1 Components of personal wisdom with putative neuroanatomic regions involved. *ACC* Anterior cingulate cortex, *dACC* Dorsal anterior cingulate cortex, *mPFC* Medial prefrontal cortex, *OFC* Orbitofrontal cortex, *PFC* Prefrontal Cortex, *pSTS* Posterior superior temporal sulcus, *TPJ* Temporo-parietal junction

considered to be descriptive of wisdom included emotional regulation, openness to new experiences, sense of humor, and maturity gained with experience. We have also reviewed traits associated with wisdom in published literature and have noted components from several published definitions that are consistent with the data from the above-mentioned Delphi study (Meeks & Jeste, 2009). These components include prosocial attitudes and behaviors, social decision-making, emotional homeostasis, reflection, tolerance, and dealing effectively with uncertainty and ambiguity (Fig. 1).

Collectively, these qualities associated with wisdom are similar to those emphasized in previous definitions as well as in ancient religious/philosophical literature such as the Bhagavad Gita (Jeste & Vahia, 2008). Such findings

underscore the antiquity of the concept of wisdom and highlight its cross-cultural veneration. We have proposed that the similarities between descriptions of personal wisdom across times and cultures suggest it might arise from of a uniquely interacting assembly of neural systems. A review of studies in humans has further revealed putative neuroanatomical and neurochemical substrates that may subserve these component traits (Meeks & Jeste, 2009).

Advances in neurobiology, especially in functional neuroimaging, have improved our ability to study brain regions important for this trait. In addition, animal studies of homologous behavioral components and brain regions may begin to allow for a further dissection of underlying neurocircuitry. The literature suggests that not only is wisdom an ancient concept in human societies but that it is also an emergent property of advanced brain systems whose roots may be studied in more simplified brain networks. Wisdom may have evolutionary significance in facilitating human longevity despite declining physical health associated with aging (Jeste & Harris, 2010).

Applying these approaches to the study of personal wisdom comes at an opportune time, particularly since the study of wisdom has progressively intensified in recent years. Indeed, publications in peer-reviewed journals on wisdom have increased nearly 15-fold over the past 40 years (Meeks & Jeste, 2009). This chapter will examine data on the neurobiology of the six components of wisdom and briefly review studies that point to the basic neurocircuitry in other species too. Whereas wisdom is likely to be a uniquely human trait, its individual components (at least in attenuated form) may be seen in some lower animals.

As a brief introduction we will describe the neuroanatomical terms and organization of brain areas that we will discuss. First, it is important to be oriented to general terms for designating the position of brain structures according to anatomical axes. The anterior end refers to the front of the brain, while the posterior end is the back of the brain. The dorsal aspect refers to the top of the brain, while the bottom of the brain is considered ventral. Finally, laterally positioned structures are toward the side of the brain, while medial structures are positioned toward the midline.

These terms are important for understanding the location of many brain areas that will be discussed in this chapter. While the human brain is an enormously complicated structure, our discussion will focus largely upon the cortex, amygdala, thalamus, striatum, and hippocampus. The cortex forms the convoluted outer mantle of the brain and is further divided into frontal, parietal, occipital, and temporal lobes. Our discussion will focus on the frontal cortex and will extensively rely upon the positional terms we have introduced. For instance, a cortical region of special emphasis will include the frontal cortex, which is situated in the anterior pole of the brain. Just anterior to the frontal cortex is the prefrontal cortex (PFC), which consists of a heterogeneous system of subdivisions. These subdivisions are organized according to lateral regions, positioned on the outer sides of the PFC, and medial regions, positioned on the inner aspect of the PFC. The lateral PFC is further subdivided in to the ventrolateral region (VLPFC), dorsolateral region (DLPFC), and rostral region (RPFPC). The medial PFC (mPFC) is situated near the midline of

the PFC and harbors the anterior cingulate cortex (ACC), which has important connections with the other prefrontal regions. Residing beneath the cortex are the subcortical structures we will discuss which include the amygdala, thalamus, striatum, and hippocampus.

Prosocial Attitudes and Behaviors

Perhaps the most commonly included traits in definitions of personal wisdom are prosocial attitudes and behaviors. Sternberg proposed a theory that emphasized wisdom as an application of tacit knowledge that is directed by values toward a common good (Sternberg, 1990). This application of knowledge is proposed to incorporate a balance among intrapersonal and extrapersonal interests. Ardeli has emphasized the ability of knowing the positive and negative aspects of human nature. An essential aspect of wisdom is integrating this with affective capacities of positive emotion and behaviors toward others (Ardeli, 2004).

Neuroimaging studies point to the PFC as an important brain region subserving human social function. A meta-analysis of 80 studies identified the mPFC as playing a major role in human empathy (Seitz, Nickel, & Azari, 2006). Data show that observing another person's emotional states activate neural networks in the mPFC (de Vignemont & Singer, 2006; Sommerville & Decety, 2006). Further data supporting a role for the mPFC in empathy includes studies that have shown this brain region is important in the perception of shared emotional experience (Seitz et al., 2008).

At an even greater level of resolution, a brain system that may be important to human empathy is the "mirror neuron system" within the PFC. Evidence points to a "limbic mirror neuron system," which activates when a person is experiencing an emotion and when she/he is watching another individual experience that particular emotion (Cattaneo & Rizzolatti, 2009). A separate role has been identified for parieto-frontal mirror neurons, which activate when a person is performing an action and when she/he is watching another person perform that action. The coordinated activities of mirror neuron systems are proposed to form an important basis for empathy (Rizzolatti, Fadiga, Gallese, & Fogassi, 1996). These data suggest that empathy is founded upon neural systems that actually recreate a neural representation of other's experiences within us.

Other neuroimaging investigations have examined social cooperation. Studies with fMRI have shown that social cooperation involves the mPFC and the nucleus accumbens/ventral striatum (Jean Decety & Jackson, 2004; Rilling et al., 2002; Singer, Kiebel, Winston, Dolan, & Frith, 2004). Altruism also has been shown to activate similar brain regions as social cooperation in neuroimaging studies, using paradigms such as money donation (vs. taxation), where the primary brain regions activated were striatum and nucleus accumbens (Harbaugh, Mayr, & Burghart, 2007; Moll et al., 2006).

More recent data suggest that the possible neurobiological roots of empathic behavior can be studied even in mice (Jeon et al., 2010). Prefrontal regions in mice

are associated with “observational fear learning,” which is considered a primitive form of empathy. For example, mice that observe other mice being shocked will freeze when placed back in the observation chamber the next day. This demonstrates that mice are capable of responding emotionally to cues that signal the previous distress of another mouse. The brain regions involved in this phenomenon have been shown to include the lateral amygdala and medial pain system, comprised of the ACC and mediodorsal and parafascicular nuclei of the thalamus.

Other experiments in voles have shown that two neuropeptides, oxytocin and vasopressin, are important to social behaviors (Insel, Young, & Wang, 1997). The distribution of these receptors in reward circuitry mirrors the involvement of this reward circuitry in human social cooperation (Shapiro & Insel, 1992). These experiments may allow us to better understand the neurochemical underpinnings of prosocial behaviors in wisdom.

Social Decision-Making/Pragmatic Knowledge of Life

Social Valuation

Negotiating the complexities of social networks has been recognized as an important aspect of personal wisdom. Previous descriptions of wisdom have emphasized that it requires one to be “interpersonally skilled and have judgment and communication skills that are exercised in a framework which includes substantial knowledge of human social concerns” (Holliday & Chandler, 1986).

Findings that have the most relevance to “pragmatic life knowledge and skills,” have been uncovered in neuroimaging studies of social cognition. Studies of “moral decision-making” are of considerable relevance to wisdom. Investigators have examined neural correlates for personal versus impersonal moral decisions. An example of an impersonal moral decision dilemma is one where a trolley is headed for five people. The observer can redirect the trolley from these five people toward a different set of tracks where it will kill one person instead. A personal moral decision is one where the observer may save the five people by pushing a separate person in front of the trolley. One study found that such personal moral decisions preferentially activated the ACC and the DLPFC (Greene, Nystrom, Engell, Darley, & Cohen, 2004). These regions have been implicated in cognitive conflict detection, which may be important in regulating more automatic emotional responses. These data suggest that social decision-making capacities associated with wisdom may rely upon circuitry in the ACC and DLPFC.

“Theory of mind” research may be of further applicability to the social aspects of wisdom. This area of research focuses on how humans understand the mental states of others (Perner & Lang, 1999). Neuroimaging studies have implicated the mPFC and posterior superior temporal sulcus (pSTS) and temporo-parietal junction (TPJ) in subserving “theory of mind” functions. Each of these brain regions plays a

distinct role in this capacity, with the mPFC primarily involved in “mentalizing” or conceiving of the inner world of others, while the pSTS responds to visual stimuli related to social cues and internal mental states (e.g., body gestures or facial expressions). The TPJ plays a role in self-other distinction (Brunet, Sarfati, Hardy-Baylé, & Decety, 2000; Fletcher et al., 1995; Gallagher et al., 2000; Goel, Grafman, Sadato, & Hallett, 1995).

While social decision-making has not been extensively addressed in other animals, studies in monkeys have examined the neurobiology for the motivation to engage in social interactions and to value certain social cues. These nonhuman primate behaviors are important for successful social integration and most likely form an important foundation for more sophisticated social skills in humans. Inquiries into brain regions mediating social valuation in primates have uncovered an important role for the cingulate cortex. In macaques, cingulate lesions result in decreased social interaction, less time spent in the proximity of other monkeys, and decreased vocalizations (Hadland, Rushworth, Gaffan, & Passingham, 2003). Social decision-making also has been a recent area of inquiry in macaques. Experiments have examined the effects of lesioning the anterior cingulate gyrus (ACC_g) on recognizing social cues. Macaques with selective lesions of the ACC_g show impairments in normal patterns of social interest for other individual male or female macaques (Rudebeck, Buckley, Walton, & Rushworth, 2006).

Emotional Homeostasis

Emotional homeostasis is widely regarded as an important dimension of personal wisdom. Theories have postulated wisdom as coordinated regulation of affect and cognition with affect regulation being an important aspect (Kramer, 1990). Prior work has described wise individuals as in possession of excellent senses of humor in the face of adversity and as peaceful (Kramer). Others have emphasized emotional management and emotional stability in the face of life’s uncertainty as an important aspect of wisdom (Brugman, 2005). Important to the attainment of this affect regulation would be a control of impulsivity and negative emotions such as anxiety and depression.

Impulse control is an important aspect of emotional regulation in wisdom (Meeks & Jeste, 2009). Impulsivity has been regarded as a disturbed inhibition of behavior, lack of reflection regarding the consequences of one’s behavior, and inability to postpone reward. Areas of the frontal cortex have been widely implicated in emotional regulation and impulse control in particular. The dorsal ACC (dACC) and lateral PFC/inferior frontal gyrus have been shown to be important for modulating impulsivity (Congdon & Canli, 2005). It has been proposed that the dACC senses conflict between instinctual emotional responses and more socially acceptable responses, whereas the lateral PFC incorporates more socially advantageous responses in working memory. It is then a coordinated action between the dACC and lateral PFC that orchestrates socially appropriate action

while inhibiting inappropriate responses. One behavioral task that is used to measure impulsivity is “go/no-go” task. This task has shown that the inferior frontal gyrus is consistently activated when behavioral inhibition is required (Horn, Dolan, Elliott, Deakin, & Woodruff, 2003).

Of further relevance to the study of emotional regulation is the capacity for cognitive reevaluation of emotions. The importance of this ability is illustrated by the therapeutic effects of reframing negative emotional experiences through cognitive behavioral therapy (CBT). Data suggest that this form of therapy allows the PFC to decrease excess activity in limbic areas such as the amygdala (Cooney, Joormann, Atlas, Eugène, & Gotlib, 2007; Goldin, McRae, Ramel, & Gross, 2008; Ochsner, Bunge, Gross, & Gabrieli, 2002; Phan et al., 2005). Indeed, the simple act of being able to label one’s emotions with words has been shown to increase VLPFC activity and decrease amygdala activity (Hariri, Bookheimer, & Mazziotta, 2000; Lieberman et al., 2007). Collectively, these findings point to an important role for prefrontal inhibition of limbic reactivity in the attainment of emotional homeostasis. These data further suggest that psychotherapy may facilitate emotional regulation circuitry that may be important for the emotional homeostasis subcomponent of wisdom.

Investigations of impulsivity in rodents have been pursued and include the go/no-go and stop-signal reaction time tasks, five-choice serial reaction time task (5CSRT), and delay-discounting paradigms. These models have been previously reviewed in depth (Winstanley, Eagle, & Robbins, 2006). Using these models, neuroanatomical foundations of impulsivity have been investigated. Though there are conflicting studies in rodents, some have shown that regions of the ACC and orbitofrontal cortex (OFC) are important to impulse control (Muir, Everitt, & Robbins, 1996; Winstanley, Theobald, Cardinal, & Robbins, 2004). Furthermore, a recent study has revealed close parallels between human and rodent ACC in depression. Mice subject to social-defeat stress showed similar reduction in ACC immediate early genes (IEGs) as did postmortem samples from clinically depressed human beings (Covington et al., 2010).¹

Value Relativism/Tolerance

Value relativism and tolerance of other people’s value systems is often considered an important component of personal wisdom. For instance, past descriptions of personal wisdom have described it as a trait in which one recognizes the relativity of various formal systems through life experiences and is able to manage contradictory points of view.

¹ IEGs are molecules important to the plasticity of the cell. They have been shown to play critical roles in learning and memory.

Studies examining tolerance have focused on the study of societal prejudices toward race and ethnicity. Neuroimaging data have revealed that a regulation of prejudicial responses involves dorsal ACC detection of prejudice and subsequent inhibition by the lateral PFC with presumed downstream deactivation of the amygdala (Amodio et al., 2004; Cunningham et al., 2004). Studies on “theory of mind,” have proposed that the lateral PFC inhibits one’s own perspective, enabling one to consider someone else’s state of mind or view. This proposal is supported by research on persons with lesions in the lateral PFC. These subjects are markedly self-focused and have difficulties accurately interpreting social cues from others (Samson, Apperly, & Humphreys, 2007; Samson, Apperly, Kathirgamanathan, & Humphreys, 2005).

While value relativism and tolerance are components of wisdom that are difficult to investigate in other species, studies in bonobos and chimpanzees have examined social tolerance and cooperation (Hare, Melis, Woods, Hastings, & Wrangham, 2007). According to the “emotional-reactivity hypothesis,” one route by which social problem solving can evolve is through the selection of emotional systems controlling fear and aggression (Hare & Tomasello, 2005). According to this hypothesis, it is predicted that bonobos will socially cooperate more effectively than chimpanzees because their tolerance levels are higher. When presented with a food reward that is highly monopolizable, bonobos are indeed more successful at cooperating to retrieve it which is in parallel to their higher tolerance while co-feeding as compared to chimpanzees (Hare et al., 2007).

Acknowledgment of and Dealing Effectively with Uncertainty and Ambiguity

Personal wisdom is often associated with an ability to accept and cope with life’s uncertainty and the ambiguity inherent in decision-making. Both Aristotle and Plato emphasized an awareness of the limits of personal knowledge as a characteristic of the wise (Rouse, 1956; Ross, 2011). A core aspect of wisdom has been defined as “a willingness and exceptional ability to formulate sound, executable judgments in the face of this uncertainty” (Kekes, 1983). Other investigators have argued that wisdom involves recognizing the dialectical nature of knowing while having the discipline and humility to ponder and choose the best solution possible (Sternberg, 1990).

In humans, cognitive flexibility and dealing effectively with uncertainty have been examined by having subjects confront uncertain and ambiguous decisions. A prior study reviewed experiments in which persons were confronted with decision-making where outcomes have known probabilities and the individuals must decide between “safe” and “risky” decisions. This was contrasted with ambiguous decisions where the probability of specific outcomes was unknown. It was found that making decisions in the face of ambiguity most consistently activated the

DLPFC, dorsal ACC, and insula. Risky decisions activated the OFC, mPFC, caudate, and ventral ACC (Krain, Wilson, Arbuckle, Castellanos, & Milham, 2006). A separate investigation found that persons who preferred ambiguous over risky decisions had higher activity in the lateral PFC, whereas ambiguous versus unambiguous decisions activated the dorsal ACC and DLPFC (Huettel, Stowe, Gordon, Warner, & Platt, 2006).

The emphasis on being able to make decisions in the face of uncertainty suggests an important component of behavioral and cognitive flexibility in the wise individuals, whereby they may entertain a possible problem solution but also be able to consider other modes of more adaptive thought or action according to changing information. Cognitive flexibility has been addressed in animals through behavioral tasks of reversal learning, attentional set-shifting, and task switching (Takei et al., 1992). The PFC and striatum have been largely implicated in these cognitive capacities. Other regions implicated in such tasks include the OFC, mediodorsal thalamic nucleus, nucleus accumbens, and mPFC (Birrell & Brown, 2000; Block, Dhanji, Thompson-Tardif, & Floresco, 2007; McAlonan & Brown, 2003; McEnaney & Butter, 1969).

Discussion

Personal wisdom is a long-known and cross-culturally valued attribute whose empirical biological study is currently in its infancy. Indeed, research efforts are still in the process of establishing a consensual definition for wisdom. Although defining a consensus description of wisdom is an important first step in investigating its neurobiology, it should be noted that many psychological constructs that we seek a neurobiological understanding of also possess controversial definitions. For instance, DSM-IV criteria for psychopathology continue to undergo numerous revisions, yet these conditions are an area of prolific neuroscientific research (Coghill & Seth, 2011; Gurley, 2009). Furthermore, intelligence is a commonly disputed construct and yet is one of the most intensely studied psychological traits (Colom, Karama, Jung, & Haier, 2010; Langer et al., 2011; van den Heuvel, Stam, Kahn, & Hulshoff Pol, 2009). Similarly, happiness, consciousness, love, and creativity all have evasive definitions but have become subjects of neurobiological investigation (Ascoli & Samsonovich, 2008; Burgdorf & Panksepp, 2006; Carlsson, Wendt, & Risberg, 2000; Heilman, Nadeau, & Beversdorf, 2003; Lewis & Macgregor, 2010). Indeed, animal models have been proposed for studying positive psychological traits such as creativity, in addition to many psychiatric conditions (Bailey, McDaniel, & Thomas, 2007; Nestler & Hyman, 2010; Neumann et al., 2010).

In conclusion, personal wisdom is a revered and age-old concept in the history of humanity. While empirical research on wisdom is in its early stages, recent studies suggest that the individual components of personal wisdom may be related to the functioning of specific areas of the brain. The PFC appears to play an especially

important role since it is implicated in virtually every subcomponent of wisdom. Accordingly, we have previously proposed a working model in which the PFC and ACC work in a coordinated manner to modulate brain regions associated with emotionality and immediate reward. In so doing, this inhibition may promote social decision-making, emotional homeostasis, tolerance, and capacities for dealing effectively with uncertainty and ambiguity. The mPFC may be especially important in mediating self-reflection and introspection (Meeks & Jeste, 2009). An orchestrated balance between these areas may underlie personal wisdom.

In this chapter, we have reviewed studies that support this model and have also begun to explore how investigations in other species may begin to further inform our understanding of neurobiology of the proposed components of personal wisdom. Clearly, these theories are very speculative at this point. However, the aim of our discussion is primarily to promote discussion on the topic of the neurobiology of wisdom and to develop a heuristic framework for approaching its study. These data add to a growing interest in the neuroscience of wisdom (Hall, 2010). Collectively, these pursuits should provide a template on which further experiments specifically focused on uncovering neurobiological foundations of personal wisdom may be initiated.

Acknowledgement This work was supported, in part, by the Stein Institute for Research on Aging, and by the National Institute of Mental Health grants (T32MH019934, and P30MH080002).

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