Temporal organization of the brain: Neurocognitive mechanisms and clinical implications

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Abstract

The synchrony between the individual brain and its environment is maintained by a system of internal clocks that together reflect the temporal organization of the organism. Extending the theoretical work of Edelman and others, the temporal organization of the brain is posited as functioning through “re-entry” and “temporal tagging” and binds the wide range of possible times to a unified cognitive experience which is held in unison with the outside world. Dysfunction in this system is reflected in the temporal discord seen in cases of aging, sleep disorder, jet-lag, and shift-work, as well as in mental disorders and drug-induced changes in consciousness. The extent to which neuroendocrine structures contribute to the neurocognitive mechanisms which underlie consciousness has so far not been explored. Therefore, neuroendocrine mechanisms contributing to the temporal organization of the brain are reviewed. It is concluded that time—and its neuroendocrine correlate melatonin—is a binding principle for organizing conscious experience.

Keywords: Temporal organization; Edelman; Re-entry; Binding problem; Temporal disorganization; Neural correlates of consciousness; Abnormal psychology

1. Introduction

The role of time in consciousness has been studied since the ancients (see, for example, Plato, 2001). Of recent interest in this context is the suggestion that cognition is intrinsically temporal (Shanon, 2001). Consistent with this, Penrose (1994) has also proposed that “it is only the phenomenon of consciousness that requires us to think in terms of a ‘flowing’ time at all” (p. 384). Indeed, the very notion of cause-and-effect, with its assumption that causes always precede effects—which regulates human goal-directed behaviour and the achievement of a previously planned goal—is wholly dependent on the development and coding of temporal orientation (Friedman, 1989). Thus, the thesis of this paper is to review a broad base of evidence which provides a set of putative mechanisms underlying what I call temporal cognition or “temporal consciousness.” While this review is not exhaustive, it follows an integrative cognitive neuroscience approach to the study of temporal information processing (e.g., Pylyshyn, 1979; Rammsayer, 1994).

Recent research suggests that the role of time in human consciousness resides primarily in systems which maintain synchrony between the neurochemistry of the brain and the environments available to the organism. This synchrony, harmony, or “binding” of internal and external environments is maintained for the organism by a system of internal clocks. Together, these synchro-
nizing, binding systems reflect the temporal organization of the organism. These internal clocks have both neuronal and endocrine components, which will first be briefly described. This will be followed by a discussion of the implications of neuroendocrine mechanisms for the study of temporal disorganization—in other words, a loss of temporal binding—to be found in aging, in altered states of consciousness, and, more extremely, in mental illness.

2. Neuronal mechanisms of temporal organization

Virtually every physiological system is rhythmic (Glass & Mackey, 1988; Moore-Ede, Sulzman, & Fuller, 1982). For example, breathing, heart rate, blood pressure, muscle tone, activity level, and state of consciousness, are all regulated by internal biological clocks. Partly because of this diversity of needs for timing the functioning of organs throughout the body, the brain itself has been suggested to be a clock. For example, Melges (1989) proposes the dependency of time parameters on the brain, stating: “when the brain is impaired by diffuse chemical or neuronal imbalances, all components of time sense—sequence, rate, and temporal perspective—go awry” (p. 102). Likewise, Fraser (1975) suggests the whole brain is an “organ of time sense” (cited in Melges, 1989, p. 110).

However, there is evidence that different regions of the brain regulate different aspects of temporal organization. For example, the suprachiasmatic nucleus of the hypothalamus (SCN) is thought to tag 24-h cycles. That is, it seems to be an endogenous circadian clock (having an approximately 24-h period) and thereby regulates sleep and wakefulness, even in the absence of environmental fluctuations in light and dark (Moore & Card, 1985). In addition, when the timing of the light/dark cycle is phase-shifted, the sleep–wake cycle is reset or “re-entrained” and neuronal firing in the SCN is a critical participant in this adaptive shift to changed environmental conditions (Arendt et al., 1987; Armstrong, Cassone, Chesworth, Redman, & Short, 1986; Lynch et al., 1978).

While it is thought that the SCN regulates the body’s rhythms in relation to the day–night cycle, other structures seem to track a linear form of temporal information. With respect to the latter, for example, the hippocampus tags information about the past while the frontal cortex tags expectancies for the future. Melges (1989) summarizes the role of brain structures in timing cognitive functioning. Melges (1989) reviews evidence that the disruption of the left hippocampal–limbic–prefrontal network is critical in the irrelevant associations, perseveration, and loss of drive and initiative observed in schizophrenia. Moreover, Barkley (1997) has suggested the fundamental dysfunction in Attention Deficit Hyperactivity Disorder (ADHD) is a temporal processing dysfunction that is characterized by an inhibitory deficit in the prefrontal cortex. Consistent with Melges (1989), functions attributed to the frontal lobe such as delayed gratification, comparison of possibilities, and future expectations, all are disrupted in schizophrenia. Likewise, there is a growing literature suggesting these same temporal dysfunctions appear in children and youth with ADHD (Barkley, 1997; Kerns, McInerney, & Wilde, 2001; West et al., 2000). Immediate memory breaks down and filtering of irrelevant information is disrupted. Under these conditions, according to Melges, “the then would invade the now” (p. 115) and, in the language of the binding problem (see, for example, Edelman & Tononi, 2000), the world would become “temporally unbound.”

Other studies suggest that temporal organization overlaps with attentional processes regulated by transient synaptic assemblies (Crick, 1984), suppression of neural responses (Luck & Beach, 1999), long-range reciprocal connections (Damasio, 1989), and temporal correlations or temporal tagging of features (Alais, Blake, & Lee, 1998; Rickert, Duke, Putzke, Marson, & Graham, 1998), dynamic units, or elements (Mandelblit & Zachar, 1999). For example, cortical neurons have been shown to code visual stimuli in terms of the timing of their presentation (Alais et al., 1998). In addition, differences in recognition memory between early-stage Alzheimer’s patients and non-Alzheimer’s controls appeared only in remembering when not in remembering what they had seen (Rickert et al., 1998). Moreover, Henson (1998) found that detection or tagging of an immediate repetition is a necessary element in the process of recall of items presented close together but not far apart in time.

The synchronization of diverse, discontinuous, or missing elements into a unitary perceptual experience has been proposed to depend on “re-entry” mediated by reciprocal connections (Wray & Edelman, 1996). However, it may also depend on neural activity in multiple regions occurring simultaneously (Damasio, 1989). This makes sense in terms of Edelman’s simulation studies in which neurons responding to various attributes of the same object were synchronized and neurons responding to different objects were asynchronous (Edelman & Tononi, 2000). They also found synchronization at different time scales, with groups of neurons showing firing bursts on the order of tens of milliseconds and periodically “re-entering” another group of neurons with output at the scale of hundreds of milliseconds (Edelman & Tononi, 2000). Thus, Edelman suggests a “re-entrant” system is capable of tuning fine temporal differences and the strength and speed of these temporal interactions could participate in the self-perpetuating dynamic process of consciousness. Not only that, “this
coherent process is quite stable, being capable of sus-
taining itself continuously while changing its precise
composition. This stability means that although there is
always a large pool of synchronously firing neurons, the
neurons actually engaged in this pool change from
moment to moment” (Edelman & Tononi, 2000, p. 119).

3. Neuroendocrine mechanisms of temporal organization

Beyond the electrical signalling properties of neurons, the brain incorporates processes regulating both cellular events and events occurring among chemicals in the gap between cells (i.e., the synapse). As such, these can be called neurochemical—even neuroendocrine—mecha-
nisms. Indeed, the brain functions as a large endocrine gland (Reinis & Goldman, 1982) and it is difficult to elicite a clear separation of the brain’s chemical processes from its electrical ones. For example, the brain’s structure and function is neurochemical (including enzymes, membrane lipoproteins and ion channels, microtubules, and neurotransmitters). These have actions affecting thoughts, emotions, and behaviours (e.g., see Reinis & Goldman, 1982).

One set of recent studies describing the role of a neuroendocrine system in consciousness—and in which time plays a key role—has been conducted by Edelman’s group (Edelman & Tononi, 2000; Srinivasan, Russell, Edelman, & Tononi, 1999; Tononi & Edelman, 1998; Wray & Edelman, 1996). The research of Edelman’s group in general supports “the dynamic core hypothe-
sis.” This hypothesis suggests that conscious experience is both integrated (or unified) and at the same time differentiated (or diversified) by reciprocal neural con-
nections throughout the cerebral cortex and between the cortex and the thalamus. These neural pathways are presumed to ensure that changes in local synaptic con-
nections are held in the context of spatiotemporal cor-
relations in more distant areas of the brain. Such context-dependent changes are important in selectional learning, which Edelman and his group have examined in their simulation studies. In these studies, neuro-
transmitters and hormones play a role in modulating the process of re-entry through a set of “diffusely projecting value systems” which have evolved to carry information about the behavioural state of the organism to neurons and synapses throughout the brain. In addition, these neurochemical “value systems” signal the brain regarding salient and unexpected events like rewards, pain, and novel stimuli. For example, when something happens that might threaten survival or require adap-
tation, sudden bursts of neural firing occur and neuro-
modulators are released over most brain regions. According to this model, “value systems” limit both the events available for selection and the extent of synaptic changes that occur with experience. Edelman and Tononi (2000) give the example of orientation towards a light source being governed by neurochemical value systems; however, they state that neurochemical value systems may not be sufficient for identifying the object that is the source of reflected light.

Extending Edelman’s proposed model, additional candidates in a “re-entrant” or neural loop system are those in which “re-entrainment” commonly occurs (e.g., Quay, 1970a, 1970b, 1972). This does not differ from Edelman’s theory, as he says:

“These systems, whose importance vastly outweighs the propor-
tion of brain space they occupy, include the noradrenergic, sero-
tonergic, cholinergic, dopaminergic, and histaminergic nuclei... These neurons give rise to a vast network of axons that blanket the cortex, hippocampus, basal ganglia, cerebellum, and spinal cord, potentially influencing transmission at billions of synapses across all levels of the central nervous system... Neurons within some of the nuclei of value systems fire in a continuous or tonic manner when an animal is awake and stop firing when the animal falls asleep” (Edelman & Tononi, 2000, p. 89).

Such pathways are neuroendocrine and have the capability of synchronizing, resetting, or stabilizing each other. This process, also called “entrainment,” maintains synchronization with the time at which a regularly repeating phenomenon occurs. For example, most people wake up at a certain time each morning. They go to sleep at a certain time each night. However, when these times are shifted in the case of shift-work or delayed sleep phase insomnia, for instance, the circadian clock adapts. This adaptation involves phase-shifts or “re-entrainment.” That is, the circadian clock is reset to a later point in time than the usual bedtime, which makes it more difficult to get to sleep when desired. To do this, signals concerned with lighting and the onset of sleep activate specific neural networks at a particular time-point and “re-enter” the circadian clock to set it.

An additional example of re-entry is initiated by consciously deciding when to wake up without relying on an alarm clock. There is evidence that many people experience considerable success with this cognitive manip-
ulation (Moline & Monk, 1988; Monk, 1990; Monk & Moline, 1989). From what is known about the brain, this probably involves prefrontal cortical pathways sending signals via the thalamus to the hypothalamus where the clock is reset. There is evidence for pre-programmed neurochemical changes at the time just prior to falling asleep (Golombek, Pevet, & Cardinalei, 1995; Skene, Deacon, & Arendt, 1994). Thus, an integrated system comprised of neural and hormonal elements (including prefrontal, thalamic, and hypothalamic activation) may be important in obtaining orientation, identification, and arousal features of consciousness. Indeed, an integrated neurohormonal system is exactly what has been found when systems of biological clocks have been examined.
Many neuromodulators qualify as candidates for participation in the diffuse value systems that limit events available for selection. Such neuromodulators include serotonin and norepinephrine. These are neurotransmitters involved in regulating activities related to species survival such as sleep, eating, drinking, and sexual behaviour. Neurons which synthesize serotonin and norepinephrine are located in the brainstem and in the hypothalamus and are active during wakingness and inactive during sleep.

Neutral firing in the SCN is known to inhibit secretion of the pineal gland hormone melatonin, a sedative neuromodulator thought to play a role in re-entrainment such as occurs in shift-work and jet-lag. Likewise, the SCN and melatonin act reciprocally to time behaviour. While the SCN appears to generate the circadian rhythm in melatonin secretion, the SCN itself is acted upon by melatonin. Evidence for this comes from studies of the absence of the SCN, in which melatonin had no effect on re-entrainment (Cassone, Chesworth, & Armstrong, 1986; Frazer & Brown, 1987; Murakami, Hayafuji, Sasaki, Yamazaki, & Takahashi, 1983) and from more recent studies of melatonin receptors in the SCN (e.g., Piggins, 2002; von Gall, Stehle, & Weaver, 2002).

Thus, it is proposed here that the pathways involved in temporal organization (including the SCN, the pineal, and melatonin) are important parts in the “re-entrant” process responsible for temporal consciousness. Consistent with this proposal, the important role in temporal organization played by brain structures such as the SCN and the pineal gland has been widely acknowledged for 20 years (e.g., Cassone et al., 1986; Frazer & Brown, 1987; Murakami et al., 1983). Clearly, then, there is ample empirical evidence to suggest that the SCN, the pineal gland, and melatonin play an important role in systems synchronizing the periodic re-entry of consciousness coincident with the environmental alteration of day and night. However, the extent to which these neuroendocrine structures contribute to the complex combinations of available neurotransmitter systems which underlie consciousness itself has so far not been explored. Even so, like the question of time, the role of the pineal gland in consciousness and selective attention has been the subject of speculation since the time of the ancients. A discussion of this illustrates further a putative role of neuroendocrine processes underlying temporal consciousness.

4. The pineal and consciousness

Over 2000 years ago, the Egyptian anatomist Herophilus (325–280 B.C.) discovered the pineal organ and believed that it functions as a tap regulating the stream of “pneuma” from the third to the fourth ventricle. He considered this process, influenced by sensory input, to be the direct cause of the development of knowledge. Some time between 130 and 300 A.D., Galen named the pineal organ “soma konoeides” because of its resemblance of the pine cone but did not agree with the “tap” function of the gland proposed by Herophilus (Kappers, 1979). In the 17th century, Rene Descartes, the French philosopher-mathematician, became famous for his views on the mind-body problem. Pavlov (1927) rightly dubbed Descartes the father of biopsychology: “Our starting point has been Descartes’ idea of the nervous reflex. This is a genuine scientific conception, since it implies necessity... Thus a stimulus appears to be connected with effect with a definite response, as cause with effect... If the animal were not in exact correspondence with its environment it would, sooner or later, cease to exist” (Pavlov, 1927, pp. 7–8). The pineal gland, according to Descartes, provides the executive medium for all correspondences between stimulus and response by virtue of it being “the seat of the soul” (e.g., Carter, 1983).

As William James made clear just before the turn of the 20th century, attention oscillates not only between stimuli in the spatial environment but also in time. “When two different stimuli—e.g., a sight and a sound—are given at once or nearly at once, we have difficulty attending to both, and may wrongly judge their interval, or even invert their order. Now, as a result of his experiments on such stimuli, Wundt lays down this law—of discontinuous succession in time, of percepts which we cannot easily attend at once. Each percept then requires a separate brain-process; and when one brain-process is at its maximum, the other would appear perforce to be in either a waning or a waxing phase” (James, 1891, p. 417). Descartes referred directly to the temporal and lateralized aspects of pineal executive function in his Passions of the Soul: “When one wants to arrest his attention to consider that object for a period of time, this will retains the gland, during this time, sloping towards the same side...” (quoted in Carter, 1983, p. 129).

From the time of the ancients, the pineal gland has figured prominently in speculations about the regulation of the critical process of conscious attention. We see in the next section that these philosophical suppositions have a basis in fact.

5. Role of the pineal in sensory attention

Following James’ (1891) commentary in relation to Wundt’s law of discontinuous succession, attentional processes have been studied as perhaps the principle executive function of consciousness—likely contributing significantly to the assumption that human consciousness can attend to only one thought at a time. In ar-
The primary line of evidence for epithalamic (pineal) anatomical systems throughout the organism (Cardinali, 1981; Reiter, 1981). Despite this per-vasive influence, much like assumptions of “time” have been ignored (Slife, 1995), the role of the pineal gland in attentional mechanisms has previously been neglected by some investigators (Brain, 1958; Kinsbourne, 1974; Penfield, 1975) and actively rejected by others (Dennett & Kinsbourne, 1992; Edelman & Tononi, 2000; Mesulam, 1981). However, a putative role in sensory attention has been appreciated in modern times for a full two decades (Dawson, Crowne, & Richardson, 1986; Geschwind & Galaburda, 1985; Reins & Goldman, 1983; Wetterberg, 1983).

The role of the neuroendocrine mechanisms in attentional processes has been well studied (e.g., Aeschbach et al., 2003; Carrier & Monk, 2000; Clynes, 1961; Halberg et al., 1961; Miller, Kastin, Sandman, Fink, & van Veen, 1974). However, a specific perceptual role for the pineal gland remains an enigma. Pineal functions have a considerable impact on chemical, electrical, and anatomical systems throughout the organism (Cardinali, 1983; Goldman, 1983; Reiter, 1981). Despite this pervasive influence, much like assumptions of “time” have been ignored (Slife, 1995), the role of the pineal gland in attentional mechanisms has previously been neglected by some investigators (Brain, 1958; Kinsbourne, 1974; Penfield, 1975) and actively rejected by others (Dennett & Kinsbourne, 1992; Edelman & Tononi, 2000; Mesulam, 1981). However, a putative role in sensory attention has been appreciated in modern times for a full two decades (Dawson, Crowne, & Richardson, 1986; Geschwind & Galaburda, 1985; Reins & Goldman, 1983; Wetterberg, 1983).

The primary line of evidence for epithalamic (pineal) control of sensory awareness and behavioural responsiveness is evolutionary. The mammalian pinealocyte is appropriately included in Collin’s sensory receptor cell line since it evolved from a photoreceptor element arising from a neuroepithelial evagination in the diencephalic roof of the third ventricle (Collin, 1979). The parietal eye contained in the pineal complex of lizards (Marczynski, Yamaguchi, Ling, & Grodzinska, 1964), often called the “third eye” in Eastern religious traditions, is a highly developed photoreceptor with a lens and a retina (Ralph, Firth, Gerr, & Owens, 1979).

For all species studied so far, the concentration of the pineal hormone melatonin increases during the dark phase of the environmental photocycle. Despite distinct ancestry, the recurrent orbital path of the earth around the sun has rendered the identical environmental pressures of alternating light and dark on all species. The common adaptation of melatonin increase during dark time by species of distinct ancestry is evolutionary convergence (Gern & Karn, 1983). The recurrent phenomenon of the photocycle is well-represented internally by melatonin rhythms (Cardinali, 1981; Reiter, 1981). Melatonin is concentrated throughout many brain regions (Anton-Tay, Diaz, & Fernandez-Guardiola, 1971; Pang & Brown, 1983) and, since it is released into the cerebrospinal fluid and into the blood (Cardinali, 1981), it can be said that each part of the organism contains a representation of the pineal gland by a specific pattern of melatonin concentration that depends on the prevailing environmental conditions. This idea resembles Edelman and Tononi’s (2000) suggestion that neuro-modulators function according to a combinatorial matrix depending on their secretion and concentrations across brain regions.

Taking this evidence together, the role of the pineal gland seems to be an integrative transduction system, responsible for transducing neuroelectrical information about light into hormonal signals (Cassone & Natesan, 1997). It seems to do this by synchronizing neuro-chemical (Cardinali, 1981; Quay, 1965), endocrine (Cardinali & Ritta, 1983; Reiter, 1983), motor (Dawson, 1990; Kovacs, Gajari, Telegdy, & Lissak, 1974; Quay, 1970a; Sampson & Bigelow, 1971), emotional (Datta & King, 1977), and intentional (Viader, Cambier, Masson, & Decroix, 1985) oscillations with respect to the photic environment—what the pineal hormone melatonin providing a measure of the duration of darkness to the organism (Binkley, 1982; Goldman, 1983; Reiter, 1981; Pang, Yu, & Tang, 1982).

The pineal gland regulates a variety of behavioural responses. This includes behaviours that vary with seasonal changes in photoperiod, such as migration and mating (Goldman, 1983; Menaker, Takahashi, & Eskin, 1978; Reiter, 1981), and with the time of day, such as sleeping (Anton-Tay et al., 1971; Mouret, 1982). In rats, pinealectomy can induce hypertension (Zanoboni & Zanoboni-Muciacca, 1967) and alters the paradoxical sleep circadian rhythm by blocking its usual anticipatory increase in the hour preceding illumination onset, while not substantially affecting slow-wave sleep (Mouret, 1982). Administration of melatonin induces sleep in cats (Marczynski, Yamaguchi, Ling, & Grodzinska, 1964), produces extinction of passive avoidance and diminishes emotionality in rats (Datta & King, 1977), and reduces taste aversion in neophobic animals (Golus, McGee, & King, 1979).

As a model of Descartes’ early suggestions that the pineal has a role in intentionally focusing attention (see Carter, 1983 quoted earlier), Dawson et al. (1986) studied visual, auditory, and tactile attention in the rat. While the studies already reviewed point to a visuomo-
tor orienting function for the pineal in rats, Dawson’s studies suggest both an attentional and an emotional or conative role for the gland (e.g., Dawson et al., 1986). Additional studies (Dawson, 1986, unpublished Masters thesis) showed that pineal lesion suppressed visual orienting and spontaneous turning behaviour towards either side of the body. In addition, there was right sided neglect in response to bilateral visual stimulation. While this study was a replication of pilot research conducted earlier (Dawson et al., 1986), pineal lesion was found to reduce the attention level in comparison with sham but not in comparison with unoperated controls. Thus, it appears that pineal lesion reduced the hypervigilance often seen in response to trauma—in this case, in response to surgical stress.

In any case, the interpretation of pineal visual function is supported by demonstrations of pineal visual evoked potentials (Dafny, 1977; Reuss & Kiefer, 1989) and pineal modulation of neuroendocrine responses to visual stress (Klein, Siegel, Conforti, Feldman, & Chowers, 1979). Moreover, there is accumulating evidence that the pineal gland may also play a role in the momentary aspects of visual attention in humans (Braunard, Rollag, & Hanifin, 1997; Goldstein et al., 1989; Sandyk & Iacono, 1993). However, studies also indicate that in addition to the gland’s role in visual function (Dawson et al., 1986), the pineal can modulate auditory (Dafny, 1977; Klein et al., 1979), and olfactory (Dafny, 1977) senses and these findings extend the purported behavioural function of the mammalian pineal gland to a polysensory modulation of attention.

The anatomical literature on the pineal reinforces its presumed sensory function in mammals (see Korf & Moller, 1984 for review). A neuronal pathway projects from the retina to the suprachiasmatic nucleus, through the lateral hypothalamus, descends through the reticular formation and ascends to synapse in the superior cervical ganglia in the spinal cord. From there, bilateral projections from the superior cervical ganglia (SCG) convey visual input to the pineal from the retina (Moore, 1980). There is strong evidence implicating modulation of pineal function by norepinephrine from SCG axon terminals—also suggesting a role for norepinephrine uptake in producing pineal dysfunction (Axelrod, 1974; Zigmund, Baldwin, & Bowers, 1985). This pathway, which ends in the transduction of photic signals into hormonal information, is characterized by central processing alternating with autonomic processing. Projections to the pineal from medial habenula (Dafny, 1983), habenular and posterior commissures (Buijs & Pevet, 1980; Dafny, 1980), and from the superior colliculi (Guillerot, Pflister, Muller, & DaLage, 1982) all taken together suggest a role for the pineal gland in integrating a diversity of sensory signals into a coherent perception experienced as consciousness.

It is interesting that with the introduction of melatonin on a nightly basis, consciousness is lost to sleep, sensory responsiveness is lost, and bodily functions are entrusted to autonomic processes. With the decreasing secretion of melatonin as light intrudes, consciousness is regained and autonomic processes are once again rendered subject to voluntary monitoring and controls.

6. Melatonin and consciousness

Studies of the pineal suggest a role for melatonin in dark adaptation and object detection. There may also be a role in learning and memory, as melatonin has been found to hinder the formation of a conditioned reflex (Arushanyan & Vodolazhskaya, 1999). Consistent with this research, the alerting response to light has been shown to vary in a dose–response fashion with the degree of melatonin suppression by light (Cajochen, Zetzer, Czeisler, & Dijk, 2000). Melatonin has also been suggested to play a role in degenerative states of the retina such as retinal dystrophy (Djamgoz, Hankins, Hirano, & Archer, 1997).

In addition, there is evidence for an important role of the pineal hormone melatonin in cognitive functioning more generally. The feeling of tiredness experienced as one approaches sleep is regulated by the hypothalamus in synchrony with the pineal gland’s nightly secretion of the hormone melatonin. The inhibition of melatonin secretion with the onset of light each morning is thought to time the onset of activity after wakening (Cassone & Natesan, 1997). Melatonin is known to have sedative–hypnotic effects and can resynchronize the sleep–wake cycle under conditions known to produce insomnia (Dawson, 1990; Skene et al., 1996). As such, melatonin has been termed a “dark hormone,” being released in synchrony with the onset of darkness and decreasing coincident with the onset of light. Thus, melatonin appears to regulate the synchronization of internal and external environments. This is albeit on a longer-term scale than momentary visual experiences, but is nevertheless a critical synchronizing signal to neurochemical mechanisms underlying wakefulness with a message to shut down.

Recently, Golombek et al. (1996) reviewed melatonin’s inhibitory effects on consciousness such as sedation, hypnotic activity, pain threshold elevation, anti-convulsive activity, and anti-anxiety effects. They also review its direct effects on circadian rhythmicity through entrainment, resynchronization, alleviation of jet-lag symptoms, and phase-shifting. There is a clear time-dependency of some of these effects, a proposed interaction with the GABAergic system, and suggestions of the usefulness of pineal hormones as therapy for human disorders (Golombek et al., 1996). For example, melatonin treatment significantly decreased the desyn-
Another area of recent research on melatonin is as a sleep-inducer in children. Because of the paucity of side-effects following melatonin administration, it is seen as a good alternative to pharmacological sedation and as a complementary method to sleep deprivation (Wassmer, Quinn, Whitehouse, & Seri, 2001). It has also been tested in a recent clinical trial at BC Children’s Hospital in Vancouver and was shown to successfully reduce the chronic sleep disorders in children and adolescents with neurodevelopmental difficulties (Jan, Freeman, & Fast, 1999b; Jan et al., 2000). These difficulties, including blindness, mental retardation, autism, and so on, decrease the ability of the person to sense and interpret environmental cues which synchronize their sleep.

Moreover, melatonin has been used to facilitate measurement of the circadian sleep–wake cycle with EEG after neuroleptic treatment in one case (Wirz-Justice, Cajochein, & Nussbaum, 1997) as well as in young adults (Nir et al., 1995) and in children with seizures (Jan, Connolly, Hamilton, Freeman, & Laudon, 1999a). While melatonin has not been shown to be essential for circadian organization, it consistently reinforces functions associated with darkness and maintenance of synchrony with the solar day. Notably, melatonin responds to level of illumination (Dollins, Lynch, Wurtman, Deng, & Lieberman, 1993) and influences the timing of alertness, sleep, and waking (Arendt, Middleton, Stone, & Skene, 1999). But does this role generalize to the stabilization of temporal organization with development? Although it is not yet possible to answer this question with certainty, melatonin appears to have a role in a wide range of physiological systems (Golombek et al., 1996). As well, melatonin has been implicated in the timing of developmental milestones prenatally and in timing the onset of puberty and annual reproductive cycles in non-human animals (for review, see Arendt, 1997). These functional roles suggest safety concerns in the administration of melatonin to children and adolescents.

Its contribution to genetic transcription of neural proteins also suggests a key developmental role in timing changes in receptor binding sensitivity in the brain (von Gall et al., 2002). Recent attention has focussed on melatonin’s utility in the pediatric population. Here, melatonin has been proposed as a marker of psychiatric conditions (Cavallo, 1993; Garcia-Patterson, Puig-Domingo, & Webb, 1996; Golombek et al., 1996; Skene et al., 1996), as a method to re-establish circadian rhythms after long exposure to artificial lighting (such as on intensive care units), and as a treatment for sleep disorders associated with developmental delay or blindness (Cavallo, 1993; Jan et al., 1999b). This collection of findings argues against Arendt’s (1997) conservative stance that there are insufficient data on the use of melatonin in organic or psychiatric disease for any evaluations to be made. However, further research is certainly recommended to clarify the roles of melatonin in the treatment of sleep disorders which are frequently seen concomitantly with psychiatric disturbances.

In summary, in addition to the dynamic loops between cortex and thalamus which may integrate the diversity of conscious experience (Edelman & Tononi, 2000), what appears to integrate the diversity of temporal systems is the system of internal biological clocks, with evidence suggesting the SCN and pineal play major roles. However, it is important to acknowledge other candidates for re-entraining or re-entrant loops. These include: neural autoreceptors, slow and fast-firing neurons, differing conduction delays, cyclic gene transcription, synaptic re-uptake, and the environmental influences of synchrony in the linguistic and social domains. The role of each of these in the temporal structure underlying the representation and integration of temporal experience is another interesting topic for further research but is beyond the scope of this paper.

7. Temporal organization

It should be noted that time can be viewed either as a sensory modality or an organizing principle. As a sensory modality, time can be treated as just another sense, like vision, audition, touch, taste, and smell. In the context of the binding problem, in contrast, time is much more useful as an organizing principle. The classical frame of the binding problem is: How can neural processes explain the perception of the unity of each experience when, at any given moment, there is a near-infinite number of possible objects of consciousness? Adding time as an organizing parameter to the binding problem yields a more intriguing question: How does time underlie the cause-effect relationships inherent in the integrated binding of diverse sensory elements of human experience? Therefore, we are left with the question of what causes these intricate neural processes to have the effect of an integrated sense of being aware of something. Without falling into infinite regress, the only rational remaining “cause” is ultimate. It is Time itself.

Time is ubiquitous. Reflections of time such as cause-and-effect, aging, the life cycle, and circadian rhythms such as the sleep–wake cycle are reasonably familiar phenomena to most people. For the scientist, on the other hand, most research examines time from a linear or Newtonian standpoint, both measuring and interpreting time as a one-directional linear flow from past through present to future, moving with a uniform rate.
that is applicable to everyone. Accordingly, in recent
computational models of cognition, semantic representa-
tions are without reference to time, essentially static,
 inert, and without history. It is widely acknowledged in
physics, for example, that there is nothing that makes
any particular direction of time more valid than any
other. However, this standpoint ignores entropy, the
arrow of biological time which leads dynamical systems
inexorably toward equilibrium (e.g., Covenny &
Highfield, 1990), and is fraught with other assumptions
as well (Shanon, 1998).

For example, the Newtonian assumption of the lin-
earity of time is contradicted by a preponderance of
evidence supporting cyclicity as a more accurate tem-
poral model of living systems (see Slife, 1995). However,
the possibility exists that there may be two internal
clocks governing time-sense, one reflecting linear time,
the other cyclic time. This notion is supported by evi-
dence that human beings gauge the passage of short and
long durations using two different clocks, one corre-
sponding to wake-time, the other to body temperature
(Aschoff, 1998; Campbell, Murphy, & Boothroyd,
2001). Moreover, following Crick and Koch (1998)'s
review of experiments on “bistable percepts” and their
importance in understanding the neural correlates of
consciousness, it is important to note the bilaterality of
past and future time about the figurative fulcrum of a
fleeting “specious present” (James, 1891). Likewise,
linear and cyclic time can be viewed as two prominent
and stable perceptions of time which compete for at-
tention. Indeed, the conventional notion of time as a
one-directional flow is debated by studies suggesting the
existence of bidirectional time (e.g., Dawson, 1992a,
1992b). Much like biological time which repeatedly
flows “up” and “down” (i.e., in two directions), psy-
chological time appears to have two prominent phases
or “sides”: one is accounted for by memory, which
“looks” backward into the past; the other is explained
by expectation, which “looks” into the future and sets
goals (Cottle, 1968). Although recalled events are typi-
cally reported to be more significant than anticipated
events (Dawson, 1992a; Fidler, Dawson, & Gallant,
1992), there is no reason to think that the processes of
memory and anticipation are not carried on simulta-
neously, with one generally more available to awareness
than the other. Not merely a philosophical point, this
idea makes sense in terms of Edelman’s re-entrant sys-
tem model (Edelman & Tononi, 2000) and is supported
by evidence from fMRI studies showing that moral
emotions activate subcortical areas at the same time as
prefrontal cortex (Moll et al., 2002).

Due to this simultaneity, then, under certain condi-
tions, cognitive functions such as memory and expec-
tation can become confused—even non-existent—for
example, during trauma, after consumption of a psy-
choactive drug, or during sleep, when the processes re-
sponsible for dissociating the perceptions of past and
future are held at bay. Without a well-ordered percep-
tion of time which distinguishes memory from expecta-
tion—past experience from future plans—the differences
among childhood experiences, recent events, and future
goals might fade. The perceived context for action could
even disappear, and events ordinarily perceived to take
days, hours, or months could seem to occur within
seconds—or vice versa, events that ordinarily take sec-
conds could seem lengthened to years. It follows that
experiences associated with a disruption or distortion of
the perception of time could have a powerful impact on
the individual, as well as an interest for researchers and
clinicians.

However, it is important to say that none of this is
certain. These statements are based only on presumed
language with a social history that may not apply across
all cultures. Indeed, there is a literature describing so-
cial-cognitive (Dawson, 2000; Summers & Dawson,
2000) and ethnic differences (Hall, 1984) in the percep-
tion of time. Thus, in an effort to develop a theory of
brain-based temporal consciousness that applies to hu-
man beings across cultures, it is important to return to
the evolution of the concept of time and its importance
in promoting the biological ability of the species to
survive and adapt to environmental demands.

The narrative construct of “time” emerged over the
course of thousands of years during which human be-
ings evolved and adapted to the fluctuations in daylight
with the orbit of the Earth on its axis and the orbit of the
earth about the sun. Indeed, at least since antiquity, “the
Sun, the Moon, the…stars, which bear the appellation of
‘planets,’ came into existence for the determining and
preserving of the numbers of Time” (Plato, 2001). For
thousands of years, then, and in particular since the
invention of the escapement mechanism in the 13th
century, the wrist-watch and calendar have generally
been taken to be reasonable approximations of astro-
nomical events (e.g., Covenny & Highfield, 1990). If the
motions of planets and the sun are modelled by such
time-tools, and since planetary and stellar motions are
cyclical, then linear time is almost certainly a mistaken
assumption. Thus, these tools are used to provide an
oversimplified and imperfect social agreement about the
definition and determination of time. They model the
correspondence or degree of synchrony of the internal
cognitive map with a cyclical, non-linear external envi-
ronment, but do so in an incomplete fashion—missing,
for example, the transient fluctuations between light and
dark at dawn and dusk and the predictable seasonal
transitions in light and temperature that can only be
experienced in a recurring organic present. These phe-
nomena arguably occur throughout the human species,
regardless of cultural or linguistic influences, even
though ways of describing them might differ by region
and experience.
A great deal of research on biological rhythms indicates convincingly that a set of internal clocks evolved in response to these recurrent environmental cycles. These internal clocks generate overt cycles in physiological and behavioural events and time the frequencies of these events quite precisely (e.g., Moore, 1982; Pittendrigh & Daan, 1974). This precision arises primarily under the regulation of environmental time cues or "Zeitgebers" such as daylight alternating systematically with the darkness of night. In the absence of a light/dark cycle, though, the overt rhythm is thought to reflect directly the generator function of an internal circadian clock in a "free-running" rhythm (Aschoff & Wever, 1976). Another reflection of an internal clock appears, for example, when a photocycle reversal occurs (such as during night-shift or long jet-flights). When this occurs, the coincidence of external time cues and behaviour is transiently lost and remains inexact until resynchronization or "re-entrainment" to the new time cues is achieved. Thus, the internal clock can function independently of environmental stimuli and this function is modulated by an endogenous neuroendocrine timing system that has adapted to synchronize sensory awareness and behaviour with external time cues. As such, the temporal organization of the brain serves to integrate diverse elements across developmental time and places the person in a particular subjective time-frame. This begins to describe the role of internal clock system as an extension of Edelman's dynamic core.

So far, then, I have reviewed evidence suggesting that to coherently bind or unify the diversity of phenomenological experience, some form of temporal tagging or sensitivity to repetition across time is required (Alais et al., 1998; Edelman & Tononi, 2000; Henson, 1998; Rickert et al., 1998). If tagging is absent, or progressively degenerating, the person (such as in Alzheimer's disease) would not know when the experience occurred and would be insensitive to recognition or recall of past events, and would not distinguish these from anticipations or expectations of similar events in the future. They would have difficulty placing themselves in time. Indeed, Damasio (2002) reports an amnesia patient who lives in a "permanent present." The hippocampus, basal forebrain, and temporal lobes (which are damaged in this patient) have been identified in neuro-imaging studies as important for tagging when cognitive events occur in time. It has been known for some time that when the hippocampus is impaired, patients have difficulty retaining new memories for longer than about a minute. This is called anterograde amnesia. When parts of the temporal cortex are damaged, on the other hand, patients seem unable to recover long-term memories—this condition being known as retrograde amnesia. Thus, the temporal lobe and its subcortical partner (the hippocampus) seem to be responsible for tagging events with specific references to the relative timing of phenomenological experience.

According to Damasio (2002), these structures participate in "mind time" which represents the phenomenological content of everyday questions like "When did I get married? When were my children born? and How old am I?" The patient discussed above could not answer these questions. However, his biological cycles were well-organized (Damasio, 2002). While it might be tempting to separate the circadian "body time" from a "mind time," this would be a mistake paralleling "Descartes' Error" which inaccurately separated the mind from the body (Damasio, 1994). While presuming the separation of "mind" from "body" based on a single case, separating body-time from mind-time would also ignore the possible existence of neural networks and neurochemical interrelationships among these networks in the organization of temporal consciousness. Furthermore, evidence for consciousness as a hierarchical and reciprocally interactive whole would be neglected (see, for example, Edelman & Tononi, 2000).

The large literature supporting the roles of the hippocampus, basal forebrain, and temporal cortex in the temporal organization of cognition has only been briefly summarized here. Further explanation is beyond the scope of this paper which rests primarily on a description of neuroendocrine mechanisms underlying the experience of time—and on the cognitive implications of this temporal organization of the brain. Thus, research reviewed here suggests the neuroendocrine pathways involving the SCN, pineal gland, and melatonin should be appended to our understanding of the temporal organization of the brain and consciousness more generally. It is an interesting hypothesis that these structures might interact in a core temporal structure which maintains temporal coherence in a personally experienced "present" despite the enormous potential number of times in which we might find ourselves, even within a single day.

Two additional points emerge with respect to the neurophysiological organization of time. First, brain regions other than those located in Edelman's proposed corticothalamic dynamic core have been found to be critical in marking the timing of events. For events to have a coherent "flow" that is ordinarily ascribed to consciousness, there must be brain structures which generate an internal model of the external world in terms of time. Indeed, such structures are the hippocampus, amygdala, hypothalamus, reticular activating system, and the epithalamus (commonly called the "pineal gland"). These regions presumably provide a kind of background for predicting events and preparing consciousness to interpret incoming sensory-perceptual experience.

In terms of motor processing, the central role of the cerebellum in time estimation—as a primary source of
934 temporal codes—has been reinforced by recent research
935 (Lalonde & Hannequin, 1999; Tracy, Faro, Mohamed, Pinsk, & Pinus, 2000). Likewise, studies of the timing of
936 movements in dyslexia, Parkinson's disease, and develop-
938 mental coordination disorders have implicated both
939 the cerebellum (Nicolson, Fawcett, & Dean, 1995; Vol-
940 man & Geuze, 1998) and the basal ganglia (Lalonde &
941 Hannequin, 1999; Wing, Keele, & Margolin, 1984).
942 Along with these brain regions, the prefrontal, sensori-
943 motor, and temporal cortices have been shown to be
944 involved in self-paced and primary time estimation
945 (Ortuno et al., 2002; Rivkin et al., 2003; Tracy et al.,
946 2000). Thus, the areas of the brain concerned with
947 temporal tagging and sensorimotor synchronization
948 may be the part of the dynamic core that underlies the
949 critical and predictable return of consciousness to spe-
950 cific stimuli on a minute-by-minute, hourly, or daily
951 basis. In this way, a well-integrated experience of a flow
952 of consciousness through time is formed.
953 So far, we can take from these studies the suggestion
954 that temporal tagging could be an important component
955 process in binding or integrating diverse elements of
956 perceptual experience across development. In addition,
957 there appear to be numerous brain structures responsi-
958 ble for binding experience in memory and sleep, with
959 experience that runs on a moment-by-moment basis
960 while keeping these various levels of experience in syn-
961 chrony with the rhythms of nature and movement. In-
962 deed, as Melges and Fraser have suggested, the entire
963 brain may be involved. An understanding of what the
964 brain is doing to accomplish this feat is only beginning.

8. Temporal disorganization

When the integrative relationships between the vari-
966 ous representations of time are disrupted, temporal
disorganization is the result. Aging, drug-induced al-
terred states of consciousness, and mental illness are all
discussed as examples of symptoms of disorganized
temporality. For the following sections, it may be
972 helpful for the reader to remember an over-simplified,
but guiding concept: When mechanisms underlying lin-
974 ear cause-and-effect are turned off, mechanisms under-
975 lying cyclicity are turned on—and vice versa. The
976 situation is admittedly more complicated, however, as
977 this dichotomous heuristic does not account for spo-
978 radic, chaotic, or random behaviour seen in disrupted
979 sleep cycles in the elderly or for “time-transcendence”
980 (Kastenbaum, 1989) seen in dementias or psychoses.
981 Even so, in general, the heuristic should help the reader
982 to remember that temporal organization has various
983 sources, and disruption of any particular source might
984 have reciprocal or otherwise differing effects. Evidence
985 for the disruptions listed will not include an analysis of
986 the relative contribution of the various components of
987 the dynamical mechanisms underlying temporal con-
988 sciousness.

9. Temporal disorganization in aging

Temporal disorganization becomes most apparent
990 when one examines the literature on aging. It is sup-
992 posed by experts in the field of biological rhythms that the
circadian (about 24 h) cycle can furnish information
994 that can be used to control or even alleviate behavioural
deficiencies that arise as the life cycle nears its end (e.g.,
995 Samis, 1978). Temporal disorganization during old age
996 include: a non-linear age-related increase in the sub-
998 jective rate of time passage (Fraisse, 1963; Gallant, Fi-
999 der, & Dawson, 1991; Janet, 1877), a decline in future
1000 perspective (Dawson, 1992b; Fidler et al., 1992; Frank,
1001 1939; Janet, 1877), and a decay of the sleep–wake cycle
1002 (Dawson & Crowne, 1988; Dawson, Crowne, Richard-
1003 son, & Anderson, 1987; Jones, Kimeldorf, Rubadeau, &
1004 Castanera, 1953; Peng & Kang, 1984; Richter, 1927;
1005 Samis, 1978; Slonaker, 1912; Wax & Goodrick, 1978;
1006 Welsh, Richardson, & Dement, 1985). Taken along with
1007 recent findings of clock genes (Piggins, 2002; von Gall
1008 et al., 2002), these penultimate changes support Samis’
1009 (1969) claim that temporal disorganization is a hallmark
1010 of the aging process.

Where consciousness undergoes most change is over
1012 the course of development, both through childhood as
1014 linear cause–effect relations are learned and encoded in
1015 the brain, and later during old age—when fluid intelli-
1017 gence, cause–effect relations, and circadian organization
tend to break down. Based on the evidence for physio-
1018 logical underpinnings of temporal organization in brain
1019 structures and processes already described, it is logical
to suppose that these symptoms of temporal disorgani-
1020 zation have their source in dysfunction residing in these
1022 same structures and processes. For example, like so
1024 many other areas of the brain, the pineal gland has de-
1026 velopmental significance as its concentrations of in-
1027 doleamines, catecholamines, and melatonin decline over
1028 the life span (Tang, Hadjiconstantinou, & Pang, 1985).
1026 Based on the pineal’s hypothesized connection to at-
1027 tentional processes discussed earlier, this may relate to
decrements in attention known to occur with increasing
1028 age (James, 1891; LeVere, 1983). There is evidence that
1029 the pineal and melatonin may play a role in stabilizing
1030 behavioural cycles that decline as a function of age
1031 (Armstrong & Redman, 1991; Dawson, 1990; Quay,
1032 1972; Ruzsas & Mess, 2000), and this may relate to early
1033 waking and sleep disorders in the elderly. In addition,
deterioration of the SCN may be associated with spo-
1034 radic sleep over the 24-h period (Bliwise, Rye, Dihenia,
1036 & Gurecki, 2002; Mishima, Okawa, Hisumi, & Hishik-
1037 awa, 2000), whereas an age-related decline in the ability
to phase-shift to a change in the photoperiod seems to

1043 10. Temporal disorganization in drug-induced altered 1044 states of consciousness

1045 Although sedative and hypnotic drugs are well-known 1046 to alter the perception of time (e.g., Rammsayer, 1999), 1047 aside from its effects on the timing of sleep, the effects of 1048 melatonin on temporal organization of consciousness 1049 have not been studied. However, a chemically related 1050 class of substances are the indoleamine psychedelics. The 1051 psychedelics (including LSD and psilocybin) are perhaps 1052 best known for inducing potent changes in the cognitive 1053 organization of time that are memorable for many years 1054 after intoxication. Some recent case studies support this 1055 well-documented effect on cognitive time distortion in 1056 LSD intoxication (Dawson, 2001; Hayes, 2000). Likewise, 1057 Strassman (2000) posits pineal dimethyltryptamine 1058 (DMT) as a so-called “spirit molecule” responsible for 1059 experiences of a timeless and “eternal presence.” Baruss 1060 and Vletas (2003) also examine temporal disorganiza- 1061 tion during altered consciousness that results from in- 1062 gestion of psychedelic drugs.

1063 An important caution to be taken from this research 1064 is that the scientist-practitioner must separate the tem- 1065 poral effects of drug use from temporal disorganization 1066 in the absence of drugs. Even so, research studies of 1067 psychedelics carry important clinical and pharmaceuti- 1068 cal implications for assessing and treating those indi- 1069 viduals who report using psychedelics, including 1070 marijuana (Melges, Tinklenberg, Hollister, & Gillespie, 1071 1970).

1072 11. Temporal disorganization in mental illness

1073 Various disruptions in the brain’s organization of 1074 time have already been mentioned. These have impor- 1075 tant clinical implications, particularly in facilitating our 1076 understanding of the desynchronization or “unbinding” 1077 of consciousness seen in certain mental illnesses. Such 1078 mental illnesses include insomnia, amnesia, pain sensi- 1079 tivity, inattention, and degenerative disease. Acknowl- 1080 edging overlapping dynamics among different clinical 1081 conditions, from this point onwards, I will focus strictly 1082 on temporal disruptions which occur during psycho- 1083 logical disorders. The implications of these will hope- 1084 fully shed light on the temporal organization of 1085 cognitive status.

1086 Before beginning this section of the review, however, 1087 it is important to point out a rather basic assumption. 1088 That is, the term “disorder” (APA, 2000)—as widely 1089 used in the Diagnostic and Statistical Manual (DSM-IV-TR)—strongly implies a temporal problem. A sense that 1090 things are “disordered” can convey a sense of things being “out of order,” “in the wrong order,” or not occur- 1091 ring in the expected sequence, at the expected time, and the like. Thus, considered broadly, the global use of the term “disorder” in reference to psychiatric or psy- 1092 chological dysfunction can already be viewed as point- 1093 ing to temporal disorganization as a strong association 1094 (even if it is not causative) of psychological problems.

1096 However, while not relying on this general observa- 1097 tion as a proof—but as an assumption—of this principle, 1098 it remains important to present a wide array of psy- 1099 chological disorders which can be identified as associ- 1090 ated with difficulties in temporal binding or in temporal 1092 organization. Assuming also that psychological disor- 1094 ders are symptomatic of altered consciousness, identi- 1095 fying the array of disorders associated with temporal 1096 changes in consciousness would strongly suggest that 1097 the temporal organization of consciousness is an im- 1098 portant phenomenon in clinical assessment and treat- 1099 ment planning.

1101 Following these assumptions then, the examples of 1102 psychological disorders provided below are those in 1103 which literature could be found which described evi- 1104 dence of changes in temporal organization of brain, 1105 behaviour, and cognition. Exclusions include, for ex- 1106 ample, attachment disorder and personality disorder. 1107 Even though there are changes in temporal organization 1108 in attachment disorders and personality disorders 1109 (Dapkus, 1985), these are not included here due to a lack 1110 of documented temporal changes in the brain in these 1111 disorders. Another exclusion from this section is sleep disorders—except as they appear below in a theory of anxiety—as they have been referred to already.

1112 This is not an exhaustive list. Because my own re- 1113 search program on time extends back some 20 years, the 1114 search strategies used to yield these references took place 1115 correspondingly over a period of many years using such 1116 indexes as PubMed, PsycInfo, as well as manual sear- 1117 ches through Index Medicus and Social Sciences Cita- 1118 tion Index. Key terms searched included “temporal 1119 organization,” “temporal disorganization,” “time and 1120 psychological disorders,” and “time and x” (where x is 1121 the disorder of interest).

1123 11.1. Attention deficit hyperactivity disorder

1124 One condition eliciting substantial clinical concern in 1125 recent years is Attention deficit hyperactivity disorder 1126 (ADHD). ADHD is characterized by a behavioural in- 1127 hibition syndrome which prevents a child from inhib- 1128 iting spontaneous behavioural responding. The child with 1129 ADHD is extremely distractible, unable to focus, and 1130 unable to sit still. Difficulty organizing, scheduling, or 1131 planning for the future is often seen in ADHD, sug- 1132 gesting a failure of temporal organization or “time
1199 2001). Other indications of temporal disorganization in schizophrenia include decreases in circulating melatonin levels, combined with difficulties falling asleep (Vigano et al., 2001). In a randomized, double-blind, cross-over clinical trial on 19 patients diagnosed with schizophrenia, melatonin significantly improved sleep (Shamir, Rotenberg, Laudon, Zisapel, & Elizur, 2000). Abnormally high prolactin levels in schizophrenia also suggest marked neuroendocrine disturbances (Vigano et al., 2001).

Another study looked at the disability in social skills in schizophrenia patients. This disability is widely treated by helping patients to structure or organize their activities throughout the day. One study used actigraphy to study temporal organization of activity and rest and showed that a patient with chronic schizophrenia had a highly irregular temporal structure, as well as delayed sleep-phase insomnia (Haug, Wirz-Justice, & Rossler, 2000).

Persons with schizophrenia are known for their disorientation in time. The passage of time can vary significantly, with days seeming like months, weeks, or even seconds. As well, the ability to order and predict events in time is compromised (Dapkus, 1985), but the literature is conflicting on the association of temporal disorientation and intellectual abilities. In one study, temporal disorientation about age was not found to be associated with pre-morbid intellectual impairment or past medical treatment (Buhrich, Crow, Johnstone, & Owens, 1988). In other studies, temporal disorientation was found to be associated with global intellectual impairment (Liddle & Crow, 1984) but not with the content of spiritual or religious delusions (Applebaum, Robbins, & Roth, 1999).

Prior time information (related to a duration yet to be experienced) and posterior time information (related to a duration being currently experienced) appear to be reversed in schizophrenics. For example, brain laterality associated with time information has been found to be a mirror image of non-schizophrenics (Mo, 1990). Other studies propose psychotic thought as a mode in which continuity, successivity, and simultaneity are not recognized (Morin, 1995). The non-unitary nature of delusions is emphasized (Brockington, 1991), thus implying that psychotic thought is disintegrated and lacks “temporal binding.”

11.4. Anxiety disorders

Based on their review of the animal literature, Golombek et al. (1996) have suggested melatonin has anti-anxiety effects. But regarding anxiety disorders such as obsessive-compulsive and panic disorders, evidence for the involvement of melatonin appears to be largely negative (Hajak et al., 1997; Millet et al., 1998). Even so, this does not discount some form of temporal disorganization that does not involve melatonin. For example, Dapkus (1985) has proposed that obsessive-compulsive disorder is characterized by a fixation to time. Likewise, there is a temporal relationship between panic onset and the avoidance of inescapable situations observed in agoraphobia (Thyer & Himele, 1985).

Posttraumatic stress disorder (PTSD) is another anxiety disorder for which there is no evidence of association with changes in melatonin. However, PTSD...
is—by its very name—characterized by temporal disorganization. According to the DSM-IV-TR, PTSD occurs in a situation that provokes an intense fear for one’s own life or the life of another. Helplessness and horror are associated emotions, and in children, agitation or disorganized behaviour can reflect a posttraumatic response. This includes symptoms of loosening of cause–effect relations as characterized by disrupted “temporal binding” as described earlier. Such temporally disorganized symptoms include recurrent memories and dreams or flashbacks, associational cueing through resemblance, and disorganized behaviour. Likewise, PTSD is characterized by recurrent and intrusive memories of the event, including repetitive play in which the trauma is reenacted over and over again. Recurrence is often internalized in the dreams of the individual, at times without a report of a coherent context or meaning of the dreams.

A sense of reliving the trauma, including “illusions, hallucinations, and dissociative flashback episodes” can also occur (APA, 2000). On exposure to cues that resemble or symbolize the traumatic event, severe psychological distress or reactivity can appear. In contrast, and at the same time, the individual engages in denial or avoidance of stimuli associated with the trauma by removing themselves from the person or thing that reminded them of the event, avoids or denies any memory of the event, and experiences a sense of foreshortened future (APA, 2000). In PTSD, difficulties associated with changes in consciousness include difficulties getting to or staying asleep.

Frequently, yet unfortunately, PTSD is the reason for removal of children from their parents’ care and, as a result, attachment disorders can overlap with PTSD. Effects of trauma on the subcortical regions of the brain are beginning to be mapped, though little is known about the precise changes in the structure of the brain as yet. In recent studies, life-threatening stress has been shown to reconfigure the molecular organization of these regions (see Teicher, 2002 for review). Teicher (2002) has suggested that experience is changed in a manner that prepares the individual to adapt in a dangerous world. This change is thought to be mediated by long-term increases in secretion of cortisol, a hormone which may be toxic to the brain (Carrión et al., 2002).

As a result, brain damage can occur and, in some cases, the cost is a tendency towards violence that may not be reversible (Teicher, 2002).

Anxiety disorders have been related to circadian disorganization. However, consistent with well-validated cognitive models of anxiety disorders, recent research suggests that the role of cognitive attributions about sleep might play a larger role than the disorganization of underlying temporal mechanisms in the etiology of anxiety disorders. For example, Harvey (2002) suggests a reciprocal and inverse relationship between insomnia and anxiety level which is governed by cognitive attributions and emotional arousal. This reciprocal relationship is mediated by excessively negative cognitive activity which triggers autonomic arousal and emotional distress (Harvey, 2002). Selective attention to sleep-related threat cues may lead to an overestimate of the perceived effect of lack of sleep on daytime performance. Escalating arousal and distress may spiral into a very real deficit in sleep and daytime functioning.

### 11.5. Affective disorders

Temporal disorganization at the seasonal scale is well-known in seasonal affective disorder (e.g., Lam & Levitt, 1999; Terman & Terman, 1999). Temporally disorganized circadian rhythms have been widely acknowledged in affective illness and phototherapy can be either a trigger or treatment for depressive episodes (Wehr, Rosenthal, & Sack, 1988). Hypotheses of affective illness based on the temporal structure of circadian rhythms include the abnormal free-run, phase advance, phase instability, and reduced amplitude hypotheses (Yamada & Takahashi, 1994). Furthermore, the human clock gene has been proposed to underlie changes in circadian rhythms in cyclic mood disorders such as bipolar illness (e.g., Saleem et al., 2001) This may relate to children with rapid cycling mood disorder whose sleep disorders were helped by melatonin administration (Jan et al., 1994).

Frequency differences can reflect changes in temporal organization as well. For example, depression scores are associated with low estimates of frequency with which positive events happen to oneself and high estimates of the frequency with which negative events happen to oneself and others (Kaney, Bowen-Jones, Dewey, & Benton, 1997). It follows that positive events could be bound through inappropriately low frequency estimates and negative events could be bound by inappropriately high frequency estimates. In addition, future orientation tends to shorten in depression and to lengthen, on the other hand, in mania (Melges, 1989).

Temporal disorganization can include the belief that life is over. Distinct from the depression which culminates in suicidality, one case study examined three individuals with right frontotemporal structural lesions who developed the delusion of being dead known as Cotard’s syndrome (Pearn & Gardner-Thorpe, 2002). Loss of facial memory (Leafhead & Kopelman, 1997) and co-morbid depression have been found to be associated with Cotard’s nihilistic death delusion (Hansen & Bolwig, 1998). Descartes’ “cogito” (extreme doubt) provides an analogy to Cotard’s syndrome including non-existence of the world and self (Jalley, 1994).

### 11.6. Spiritual problems

Spiritual issues might also include differences in temporal organization. Whatever their convictions,
1358 experiences in which person either feels “at one with
1359 God” or “abandoned by God” can bring on over-
1360 whelming feelings, and can disintegrate or “unbind”
1361 previous belief systems about a person’s place in or-
1362 dinary time (see Wulff, 2000). The non-linear time of the
1363 right hemisphere has been suggested as an important
1364 aspect of temporal organization in people with mystical
1365 experiences (Wulff, 2000). Brain changes in such
1366 “spiritual” states are exemplified in recent brain imaging
1367 studies of yogi’s, nuns, and Monks in deep prayer or
1368 meditation (Newburg, 2002).

1369 11.7. Dissociative fugue, amnesia, and identity disorder

1370 In their study of dissociative identity disorder, Van
der Hart and Steele (1997) utilize Paul Janet’s distinc-
tion between placing some accounts of events too high
in the hierarchy of perceived reality, and placing other
explanations too low. In their study, they address ways
in which traumatic memories can interfere with the
normal sense of time. Therapeutic recommendations
include reorganizing the phase relationships between
events.

1371 In addition, Edelman and Tononi (2000) propose
dissociative states of amnesia support their model of the
dynamic core. Indeed, they propose that a major func-
tional split within the dynamic core would be expected
in the case of split brain surgery or other neurological
disconnection syndromes. Psychological trauma, disso-
ciation syndromes, and schizophrenia might also be
conditions in which a previously single, dominant dy-
namic core splits into two or more “subcores” (p. 152).

1372 A more discrete explanation comes from Forrest (2001)
who proposes that the orbitofrontal cortex has a pro-
tective inhibitory role in temporal organization. Ac-
cording to this notion, sensitivity of this area of the
brain to discontinuity in the early caregiving experience
may, in the case of dissociative identity disorder, be
responsible for the lateral inhibition between differing
self-representations which in normal individuals remains
integrated in a unified concept of self.

1373 11.8. Alzheimer’s disease

1374 Damasio (2002) describes the faulty placement in
time seen in Alzheimer’s disease and there are well-
known changes to the brain in these patients. These
changes include dendritic plaques and tangles in struc-
tures responsible for memory such as cerebral cortex
and hippocampus. Sundowning—defined as the exacer-
bation of Alzheimer’s symptoms in the afternoon or
evening—has also been tied to disorganized circadian
rhythms (Volcier, Harper, Manning, & Satlin, 2001),
decreased melatonin secretion, and indications of suc-
cessful treatment with melatonin (Cardinali, Brusco,
Liberczuk, & Furio, 2002; Mishima et al., 2000).

12. Conclusion

Consistent with recent thinking, biological clocks are
connected in a system of chaotic attractors (Glass &
Mackey, 1988). For example, one set of clocks is re-
ponsible for regulating the biological need for sleep,
food, and reproduction. Other clocks regulate neural
loops that together form memories, consciousness, and
time perception at various scales. When the organization
of these clocks moves out of alignment, both physical
and mental illness can occur. The most direct manifes-
tations of changes in the organization of these clocks is
in the relative timing of biological needs, memories of
recalled events, attention to when events are occurring,
and expectations of when events are most likely to oc-
cur. Of most interest to psychology and psychiatry,
these manifestations of temporal organization have de-
velopmental significance and are often disrupted in both
ordinary changes in consciousness and in mental illness.

A broad range of psychiatric disorders have been
reviewed, all of which have documented physiological
evidence of temporal disorganization. Is it possible that
the temporal mechanisms of the brain could be a com-
mon factor underlying these ailments? Melges (1989)
points out that “time distortions may be a manifesta-
tion of, or a mechanism for, mental illness” (p. 99). In
summary and according to Melges, sequencing prob-
lems are common in organic brain disease and psycho-
problems with rate are often seen in bipolar
 disorders, and difficulties with temporal perspective
have been associated with borderline personality disor-
ders. These are in addition to the manifestations of
temporal disorientation in mental illnesses already dis-
cussed. Thus, it is an important question to explore
whether treatment interventions could benefit by taking
this into account.

The wide range of mental illnesses associated with
temporal breakdown strengthens the likelihood that
time is an important etiological factor underlying mental
illness (e.g., Armstrong & Redman, 1991; Cavallo, 1993;
Garcia-Patterson et al., 1996; Golombek et al., 1996;
Pacchierotti, Iapichino, Bossini, Pieraccini, & Castro-
giovanni, 2001; Skene et al., 1996). In addition, recent
genetic studies suggest mutations in the human clock
gene are at least partially responsible for changes in
temporal organization seen in autism, schizophrenia,
and bipolar illness (Saleem et al., 2001; Wimpory et al.,
2002). Thus, the primary purpose of the present paper
has been to show that time is—through its physiological
manifestations—a unifying and binding element for the
diversity of conscious experience. For example, when
the unison of genetic, neurochemical, or hormonal time
is disorganized, cognitions are also very likely to be
experienced as disorganized or chaotic (Shanon, 1998;
Shanon, 2001). Therefore, the relative contributions of
genetics and environment to the organization of the
The practical importance of this research stream includes the widening clinical application of melatonin to its immunosuppressive and hypnotic properties (Bergstrom & Hakanson, 1998; Pierpaoli, Regelson, & Fabris, 1993; Reiter, 2003). As these new applications emerge and undergo scientific investigation, clinicians will increase their awareness about the effects of pharmacological and cognitive-behavioural interventions on the temporal organization of consciousness. The relevance of pineal function, melatonin, and temporal cognition to basic questions about consciousness and to clinical applications in medical and mental health contexts increases the importance of research on these matters.

In conclusion, then, this paper has hopefully shown that time is a binding principle for organizing conscious experience. It has physiological markers which function by attempting to synchronize the genetic, hormonal, neurochemical, neuroelectrical, behavioural, and environmental dimensions impinging on the identified person. As these dimensions interact, their reciprocal influences tag each other and the matrix of these tags correspond to a spatiotemporal code (i.e., in the language of physics, this is the “world-line” of the individual). A vast diversity of temporal meanings is derived from this code as the brain processes and translates it into useful information through “re-entrant pathways.” These meanings are then integrated to provide each individual with a coherent temporal signature which—in narrative terms—tells the person “that was in the past,” “the time is right,” “it is not time yet,” and so on. This ultimately brings uniqueness, harmony, and unison to the specific interactions identified with an individual’s life. When neuroendocrine pathways which are responsible for synchronizing consciousness with its various available environments are disrupted, changes in consciousness and mental illness are more likely to be observed.

References


secretion in man to a 12-hour phase shift in the light/dark cycle.


